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Ammonia Exposure Based on the Length of Work to Lung **Function Abnormalities Among Traditional Scavengers**

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Lung function abnormalities can be caused by smoking habits or air pollution. Sanitary landfills can produce ammonia, which can cause lung function abnormalities. This study aimed to determine a relationship between ammonia exposure based on the length of work and lung function abnormalities among traditional scavengers at the Sumur Batu Landfill, Bekasi City, West Java Province, Indonesia. This analytical observational study applied quantitative methods and cross-sectional design. A total of 85 scavengers were selected using purposive sampling from March to May 2023. Data was obtained using a respondent characteristics questionnaire, spirometry, and spectrophotometer and analyzed using the Cox Regression Model. Most respondents (54.12%) had lung function abnormalities, and 79.17% had worked ≥8.5 years. The adjPR of ammonia exposure based on the length of work to lung function abnormalities was 3.413 (95% CI 1.51—7.71). There were confounding variables between ammonia exposure based on the length of work and lung function abnormalities: smoking status and lung disease record. In conclusion, ammonia exposure based on the length of work strongly correlates with lung function abnormalities in scavengers after adjusting for the lung disease record and smoking behavior.

Keywords: ammonia, length of work, lung function abnormalities, scavengers

Introduction

Lung function abnormalities are a combination of diseases and disorders that can affect lung function. This can be caused by smoking habits, exposure to radon, asbestos, air pollution, exposure to chemicals and dust in the workplace, as well as bacteria, viruses, and fungi. Some mild symptoms of lung disorders often overlooked are persistent coughing, wheezing, and difficulty breathing.² Lung function abnormalities have several risk factors: smoking habits, including passive smoke, allergens, and occupational risks, including air pollution. Air pollution is a high-risk factor for respiratory diseases, including lung disorders such as asthma and chronic obstructive pulmonary disease (COPD). Air pollution can increase the COPD risk by 36.6% and asthma by 27.95%.3

Several lung disorders, such as COPD, asthma, and pulmonary fibrosis, are quite common cases in the world. In 2019, 3.23 million people in the world died from COPD.4 Pulmonary fibrosis is estimated to have a prevalence of 13 to 20 per 100,000 people worldwide. In 2019, 262 million people worldwide suffered from asthma, which caused the deaths of 455,000 people. While, in Indonesia, according to the 2013 Indonesian Basic Health Research, 9.2 million people (3.7%) experienced COPD.6 In 2018, the prevalence of asthma reached around 1.2 million people or around 2.4%.7 The COPD and asthma are also included in the 10 diseases with the most cases per 100,000 population.3

Based on the National Waste Management Information System data, the highest waste composition in Indonesia is food waste (41.55%).8 Food waste belongs to organic waste, which is easily decomposed. This process will produce gases that can pollute the air. Some of them are irritants, especially ammonia (NH₃). Landfill gas contains between 1,000,000 and 10,000,000 ppb ammonia, or 0.1% to 1% ammonia by volume. Low ammonia levels in ambient air (50 ppm) can lead to eye and respiratory tract irritation, throat inflammation obstructing the airway, cough, and pulmonary edema. 10

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The Sumur Batu Landfill is located in Bekasi City, West Java Province, Indonesia. The landfill still implements an open dumping method and has been piled up for dozens of years without management. The landfill has also exceeded capacity (overloaded), affecting the roads at the landfill being filled with rubbish and leachate. Waste accumulation at the landfill can be the source of air pollution. This can occur due to various dangerous gases, including ammonia, which comes from the decomposition of accumulated organic waste. 11

Ammonia, an air pollutant, can affect public health. Scavengers at the Sumur Batu Landfill have a rest area located on site. This situation allows them to breathe air pollutants continuously while working or resting. To date, no previous study has examined ammonia exposure based on the length of work and its impact on lung function abnormalities in scavengers at this location. Therefore, this study aimed to determine a relationship between ammonia exposure based on the length of work and lung function abnormalities among traditional scavengers at the Sumur Batu Landfill, Bekasi City, West Java Province, Indonesia.

Method

A cross-sectional study was conducted on traditional scavengers as they are informal workers with less information on the risks of occupational diseases due to suboptimal use of personal protective equipment (PPE). This study took place at the Sumur Batu Landfill site in March-May 2023. The population of this study was all the scavengers working at the location. The samples were determined using a purposive sampling technique. This technique was employed because the data was population-based, and in this study, the total population was unknown for certain. Scavengers working at the location and agreeing to participate were included in this study. However, those refusing to be interviewed, using spirometry, and providing incomplete data were excluded. The sample size was calculated using the Lemeshow two-proportion formula, based on an odds ratio (OR) of 2.48 from Amerta and Wirawan¹² and a P2 of 0.4 from Dwicahyo.¹³ The number of scavengers who participated as samples in this study was 85 people.

The dependent variable examined in this study was lung function abnormalities in the Sumur Batu Landfill scavengers, while the independent variables were ammonia exposure based on the length of work. The length of work variable was included as an independent variable because this variable could influence the exposure to ammonia among the landfill scavengers. Confounding variables included age, sex, education level, body mass index (BMI), lung disease record, smoking status, and habit of using masks.

The primary data used were ammonia levels in the air, temperature, humidity, and wind speed at the Sumur Batu Landfill as measured using a spectrophotometer; the lung function was measured using spirometry; and characteristics of respondents (the length of work, age, sex, education level, BMI, lung disease record, smoking status, and habit of using masks) and data related to respiratory symptoms were measured using a questionnaire. STATA statistical software (free version) was employed to analyze the frequency and proportion distribution of each variable. This study used $\alpha = 0.05$, power of 80%, prevalence ratio (PR), and confidence intervals (CI) of 95%. Data were analyzed using the Cox Regression Model.

Interviews were held in one of the rest areas at the location. Initially, the scavengers' consent was asked if they were willing to participate in the interview and the spirometry test. After they gave their consent, they were directed to go to the assigned interview place. They were asked to rest while being interviewed about their characteristics (the length of work, age, sex, education level, BMI, lung disease record, smoking status, and habit of using masks). After the interview, the scavengers were given an explanation and instructions for carrying out the spirometry test maneuver three times. The average value of the measurement was collected.

Results

Ammonia data was collected on May 10, 2023, from 11:30 a.m. to 4:00 p.m. (GMT+7/Western Indonesian Time). Based on the results in Table 1, the highest level of ammonia (NH $_3$) at the Sumur Batu Landfill is at 0.960 ppm, located in the area behind the landfill close to residential areas. The four measurement points for ammonia levels were still below the quality standard, according to the Decree of the Indonesian Minister of Environment and Forestry (KEP-50/MENLH/11/1996) concerning Odor Level Standards, at 2 ppm. 14 In Table 1, the temperature measures at four points are 34.1°C, 34.2°C, 36.6°C, and 34°C, respectively. These results showed a quite consistent temperature from the four measurement points. The highest temperature was 34°C, and only at the Sumur Batu Landfill Ticket Post reached 36.6°C. By measuring air humidity, the highest figure was obtained behind the landfill close to residential areas at 61.3%, and the lowest was at the Sumur Batu Landfill Ticket Post area (51.4%). For the wind speed, the highest figure was at the Sumur Batu Landfill Ticket Post, reaching 1.17 m/s, and the lowest was found behind the landfill close to residential areas at 0.24 m/s.

Table 1. Results of Measurement of Ammonia Concentrations at Sumur Batu Landfill

Variable	Point 1	Point 2	Point 3	Point 4	
Sampling location	Behind the landfill (close to residential areas)	Semi-permanent settlement	Sumur Batu Landfill Ticket Post Area	The landfill's main area where new waste comes in	
Ammonia concentration (ppm)	0.960	0.818	0.272	0.215	
Temperature (°C)	34.1	34.2	36.6	34.0	
Humidity (%)	60.8	58.1	51.4	61.3	
Wind speed (m/s)	0.17-0.24	0.76-1.11	0.57-1.17	0.43-1.06	

For each spirometry measurement result, forced expiratory volume in one second (FEV₁) and forced vital capacity (FVC), lower and upper limits, interquartile range, outliers, and mean or median are calculated and presented in a box diagram in Figure 1. The box shows the interquartile range (IQR, 25-75th percentile), and a horizontal line inside the box represents the median; circles indicate outlier values for FVC. FEV₁ presents a normal distribution, while FVC presents an abnormal distribution. In contrast, the data on the length of work is not normally distributed, as seen in Figure 2.

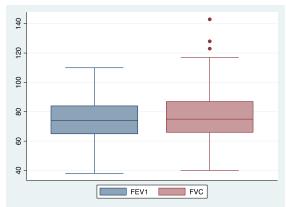


Figure 1. Boxplot of FEV1 and FVC Spirometry Results



Figure 2. Boxplot of Ammonia Exposure Based on the Length of Work

Table 2 shows that 54.12% of the 85 scavengers suffer from lung function abnormalities. The most common category of lung function abnormalities is restriction, with a total of 33 respondents (38.82%). This data shows that more than half of respondents at the Sumur Batu Landfill suffer from lung function abnormalities, possibly due to pollutants in the landfill, including ammonia. However, it does not rule out the possibility of some other influential factors. Respondents who are landfill scavengers are mostly aged under 40 years (52.94%), males (61.18%), have a low level of education or ≤junior high school education (92.94%), with a normal BMI (65.88%), have no record of lung disease (87.06%), and have non-smoking status (54.12%). In addition, they do not use masks or nose coverings while working (74.12%).

Table 2. Distribution of Variables

Variable	N	%
Lung Function Abnormalities		
Normal	39	45.88
Obstruction	8	9.41
Restriction	33	38.82
Combination	5	5.88
Ammonia Exposure Based on the Length of		
Work	37	43.53
Junior (<8.5 years)	48	46.47
Senior (≥8.5 years)		
Age		
Old (≥40.5 years)	40	47.06
Young (<40.5 years)	45	52.94
Sex		
Male	52	61.18
Female	33	38.82
Education Level		
Low education (≤junior high school)	79	92.94
Secondary education (senior high school)	6	7.06
Higher education (>senior high school)	0	0
Body Mass Index		
Very thin (<17)	4	4.71
Skinny (17-<18.5)	13	15.29
Normal (18.5-25.0)	56	65.88
Overweight (25-27)	4	4.71
Obesity (>27)	8	9.41
Lung Disease Record		
No	74	87.06
Yes	11	12.94
Smoking Status		-
Non-smoker	46	54.12
Light smoker (≤199)	20	23.53
Medium smoker (200-599)	14	16.47
Heavy smoker (≥600)	5	5.88
Habit of Using Masks	22	05.00
Yes	22	25.88
No	63	74.12
Total	85	100

Table 3 shows the distribution of lung function abnormalities based on length of work, age, sex, education level, BMI, smoking status, lung disease record, and habit of using masks. Scavengers working for ≥8.5 years have a high proportion of lung function abnormalities (79.17%). Most respondents suffering from lung function abnormalities are aged 40.5 years and older, males, overweight-obese, medium-heavy smokers, have a record of lung disease, and do not wear masks while working. These results showed a significant relationship between length of work, lung disease record, and medium-heavy smoking status with lung function abnormalities. Meanwhile, age, sex, education level, BMI, light smoking, and habit of using masks are not found to have a significant relationship with lung function abnormalities (Table 3).

The Cox Regression Model shows the risk value of ammonia exposure based on the length of work for lung function abnormalities (Table 4). Crude risk is the crude PR of length of work to lung function abnormalities without controlling for confounding factors, with a p-value of 0.001. Adjusted risk is a PR adjustment for ammonia exposure based on the length of work for lung function abnormalities after controlling for lung disease record and smoking status, with a p-value of 0.003. Both showed significant associations with strong risk. This study found that ammonia exposure based on the length of work was significantly related to impaired lung function with an adjPR of 3.413 (95%CI: 1.51-7.71) after being controlled for lung disease record and smoking status. Therefore, scavengers working for \geq 8.5 years have a 3.4 times greater risk of experiencing lung function abnormalities compared to those working for \leq 8.5 years.

Table 3. Distribution of Each Factor to Lung Function Abnormalities According to Groups of Exposure

		Lung functio					
Variable	Ab	normal	No	rmal	Total		p-value
	N	%	N	%	N	%	
Ammonia Exposure Based on							
the Length of Work	38	79.17	10	20.83	48	100	0.001
≥8.5 years	8	21.62	29	78.38	37	100	
<8.5 years							
Age							
≥40.5 years	26	65	14	35	40	100	0.201
<40.5 years	20	44.44	25	55.56	45	100	
Sex							
Male	30	57.69	22	42.31	52	100	0.574
Female	16	4848	17	51.52	33	100	
Education Level							
Low	35	3.03	31	46.97	63	100	8.0
High	11	57.89	8	42.11	19	100	
Body Mass Index							
Overweight-Obesity	7	58.33	5	41.67	12	100	0.839
Thin	9	52.94	8	47.06	17	100	0.975
Normal	30	53.57	26	46.43	56	100	
Lung Disease Record							
Yes	11	100	0	0	11	100	0.030
No	35	47.30	39	52.70	74	100	
Smoking Status							
Medium-heavy	19	100	0	0	19	100	0.025
Light	4	20	16	80	20	100	0.091
Non-smoker	23	50	23	50	46	100	
Habit of Using Masks							
No	37	58.73	26	41.27	63	100	0.331
Yes	9	40.91	13	59.09	22	100	

Table 4. Comparison of the Association between Unadjusted and Adjusted Prevalence Ratio of Ammonia Exposure Based on the Length of Work for Lung Function Abnormalities

Variable	Unadjusted Risk (95% CI)	Adjusted Risk (95% CI)
Ammonia Exposure Based on	3.661	3.413
the Length of Work	(1.71-7.85)	(1.51-7.71)

Discussion

The results of ammonia measurements at four points of location found that the ammonia levels at the Sumur Batu Landfill were below quality standards at <2 ppm. Several meteorological factors can influence ammonia concentrations. According to Ayathollah $et\ al.$ ¹⁴ these factors are temperature, humidity, and wind speed. Measurements of these four points were carried out during the day, from 11:30 a.m. to 04:00 p.m. (GMT+7/Western Indonesian Time). This causes the temperature at the Sumur Batu Landfill to be quite high, ranging from 34°C-36°C. If the air temperature is high, it can cause the air to become loose, resulting in low concentrations of pollutants in the air. 14-16

Humidity and wind speed can also affect air pollutant concentrations. The measurement results showed that the point with the highest concentration had the highest humidity and the lowest wind speed. In humid air, pollutants will be trapped in water droplets, causing a decrease in the concentration of these pollutants. Besides, the wind speed can also affect pollutant concentrations. The weaker the wind speed, the greater the pollutant concentration. This is because weak air movement will cause small shocks. Hence, the concentration of polluting gases in the area will remain large because it will not be too affected by the shocks. 15-18

This study found a strong relationship between length of work and lung function abnormalities (AdjPR=3.413) after controlling for lung disease record and smoking status. Length of work is a variable used to indirectly measure the accumulation of the exposure to ammonia in traditional scavengers. These findings suggested the possibility that long-term exposure to ammonia played an important role in causing lung function abnormalities, particularly in the traditional scavengers getting exposed to it each day. It is important to note that the participants resided in the landfill area.

These results are in line with a study conducted at Bantar Gebang Landfill, Bekasi City, Indonesia, which found a significant relationship between work experience and lung function, with a 3.5 greater risk level for scavengers with >10-year length of work. Another study conducted in Puducherry, India, also showed a relationship between length of work and obstructive lung function. Of the total minimum sample of 264 waste management workers, 94 workers had worked for >5 years, and 54.3% (51 workers) showed obstructive lung results, with a two-times higher risk than workers who had worked for ≤ 5 years. 20

Based on the results of these two previous studies, the length of work with symptoms of lung function abnormalities had a significant relationship and could be a risk factor for an individual to experience symptoms of lung disorders due to chemical hazards in the workplace. Ammonia found at the landfill is produced by bacteria decomposition of organic waste.¹³ People exposed to air pollutants from waste for a long period could cause recurring respiratory tract disorders, leading to a decline in lung function.¹⁸

A study at the Jatibarang Landfill, Semarang City, Indonesia, stated that the non-carcinogenic risk would be negligible within 20 years. In a lifetime projection (exposure duration of 30 years), non-carcinogenic risks were considered unsafe for scavengers at the Jatibarang Landfill. The scavengers received an average intake of 0.032 mg/kg/day, with an average body weight of 55 kg.²⁰ Ambient air contaminated with ammonia can have a negative impact on the respiratory system. Ammonia is colorless but has a pungent odor and is very toxic, even at low levels. This substance can only be detected by human senses at a concentration of 0.003 ppm. Chronic impacts of exposure to ammonia with a concentration of higher than 35 ppm include lung, kidney, and brain function, growth and development disorders, and decreased blood quality.²¹

Exposure to ammonia gas or ammonium hydroxide can cause corrosive injuries to the conjunctiva of the eyes, lungs, digestive system, and skin due to the alkaline and hygroscopic properties of ammonia. Low ammonia levels (50 ppm) in the air can cause acute effects on the eyes and nose, as well as throat irritation, coughing, and bronchoconstriction. More severe clinical effects, including inflammation and narrowing of the throat, can obstruct the upper respiratory tract and cause pulmonary edema. Chronic exposure to ammonia gas can irritate the respiratory tract, cause chronic cough, asthma, and pulmonary fibrosis, cause chronic irritation of the eye membranes, and cause dermatitis.

Anhydrous ammonia, whether in gas or liquid form, reacts easily with body fluids, producing ammonium ions. This process is highly exothermic and can affect surrounding tissue. The resulting base causes necrosis in body tissue through protein denaturation and lipid saponification. In addition, this process also causes the extraction of water from body tissues, thereby triggering an inflammatory response.²² The irritating impact of ammonia gas on the mucous membranes of the upper respiratory system and human eyes is usually detected at a concentration of 100 ppm with an exposure duration of 5-30 seconds.

Long-term or frequent exposure causes individuals to experience chronic sinusitis, so they are not sensitive to the smell of ammonia. 23 The longer a person works in a place contaminated with ammonia gas, the more exposure they receive, even though the daily concentration is low. This causes a decrease in respiratory function characterized by low FEV₁ and FVC values. This observed decrease is a symptom of obstructive pulmonary disease, which is often accompanied by wheezing, coughing, and phlegm production. 24

Smoking has been confirmed as a major cause of lung function abnormalities.²⁵ Lung disease records such as tuberculosis can also exacerbate lung function decline.²⁶ In this study, both variables distorted the association between ammonia exposure based on the length of work and lung function, becoming overestimated. Consistently, previous studies also suggested that smoking behavior, as well as lung disease records, could lead to lung function decline.^{13,27-29} Smoking has detrimental health effects on every aspect of lung structure and function, including impairing the lung's defenses against infection and causing ongoing lung injury, leading to lung disorders.^{15,16,28,30} Lung diseases caused by smoking include COPD, emphysema, and chronic bronchitis. If a person suffers from asthma, the tobacco smoke produced by cigarettes can trigger or worsen attacks.³¹

Another risk factor for symptoms of lung disorders is a record of lung disease. A person with a record of lung disease may experience a decrease in the muscles' ability in the respiratory system. This can disrupt the permeability of the respiratory tract and can end in a decrease in the function of the respiratory organs, leading to disorders in the respiratory tract, including the lungs.³² A person with a record of respiratory disease such as asthma is more vulnerable to exposure to ammonia gas in landfills.³³ Several diseases which can affect the vital capacity of the lungs are asthma, pneumonia, chronic pulmonary emphysema, tuberculosis, and some other respiratory diseases.¹³

There are several limitations in this study. The non-response rate of respondents was 10.5% since the study was conducted during working hours. However, this problem was addressed and resolved by recruiting other scavengers to participate. This non-response rate had no impact on the results due to the similar characteristics of the respondents. Nevertheless, information bias can be caused by non-differential classification errors, which may underestimate the findings obtained. This could happen because the variable measurement of the habit of using masks was based on the answers given by respondents and observations during interviews.

The correct way of using masks and the habit of using masks outside the measurement period were not asked. The ammonia measurement results might be below the threshold value as the measurement time was influenced by the rainy weather conditions the previous night and wind direction. Therefore, continuous ammonia measurement is required. Other air pollutants can cause decreased lung function but were not examined in this study. For these limitations, this study has good internal validity so that it can be generalized to the target population and traditional scavenger populations in other areas that have the same characteristics as this study.

Conclusion

There is a strong relationship between the length of work and lung function abnormalities in traditional scavengers after controlling for smoking status and lung disease record. Ammonia levels measured during data collection are below the threshold value due to the influence of weather conditions and wind direction. Scavengers at the Sumur Batu Landfill are at high risk of developing lung problems from the accumulation of waste in the landfill, which has lasted for years without proper management and produces air pollutants, such as ammonia, from decomposing organic waste. This air pollution can cause lung function abnormalities. The landfill scavengers should always wear masks while working, and the local government must monitor ammonia levels regularly.

Abbreviations

COPD: chronic obstructive pulmonary disease; BMI: body mass index; PR: prevalence ratio; CI: confidence interval; FEV1: forced expiratory volume in one second; FVC: forced vital capacity.

Ethics Approval and Consent to Participate

This study has complied with the code of ethics of Universitas Pembangunan Nasional "Veteran" Jakarta Health Research Ethics Commission Number 208/V/2023/KEPK, established on May 15, 2023.

Competing Interest

The author declares that no significant competing financial, professional, or personal interests might have affected the performance or presentation of the work described in this manuscript.

Availability of Data and Materials

Data are not available due to the ethical restrictions of the research. Participants of this study did not agree that their data should be shared publicly.

Authors' Contribution

MSJ, FN, NKF, and AB conceptualized and designed the study. MSJ and FN searched the literature. MSJ, FN, and NKF prepared the questionnaire and collected the data. MSJ, FN, and NKF analyzed the data and prepared the manuscript. FN, NKF, and AB reviewed the manuscript. All authors read and approved the final manuscript.

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Article 2

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The Correlation of Age with Thrombocytes and D-Dimer Values in COVID-19 Patients at Hospital X in Jakarta, Indonesia

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Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal)

The Correlation of Age with Thrombocytes and D-Dimer Values in COVID-19 Patients at Hospital X in Jakarta, Indonesia

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Abstract

Coronavirus disease (COVID-19), caused by the SARS-CoV-2 virus, spread globally, with research indicating that prognosis severity can be assessed by thrombocyte and D-dimer levels; while, patient age serves as a mortality predictor. This study aimed to analyze the relationship between age with thrombocytes and D-dimer in COVID-19 patients. This cross-sectional study used laboratory testing samples from 667 COVID-19 patients at Hospital X in Jakarta, Indonesia, collected from August 2020 until May 2021. The data was collected using cluster random sampling and analyzed using descriptive statistics and the Chi-square test (95% CI). The results showed that age and thrombocytes positively correlated with the D-dimer levels in COVID-19 patients (p-value <0.001). Age ≥48 and thrombocytes below normal (<150.000/mm³) could increase the normal D-dimer levels in COVID-19 patients. This study could enrich hospital management to prevent and reduce the severity and mortality of COVID-19 patients being treated at hospitals.

Keywords: age, COVID-19, D-dimer, thrombocyte

Introduction

Coronavirus disease 2019 (COVID-19) caused by a virus infection called Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) is a global pandemic with various risks. The virus was first reported in Wuhan, China, in December 2019 and spread rapidly to almost all countries in the world. COVID-19 has spread in 213 countries and infected millions of people worldwide. As of October 13, 2021, the number of global COVID-19 cases had reached more than 219 million cases with more than 4.5 million mortality. The first case of COVID-19 in Indonesia was reported on March 2, 2020, in Depok City, West Java Province. The number of new cases reported continued to increase until it reached 43,925 new cases per day on July 15, 2021. As of October 18, 2021, the total number of COVID-19 cases reached 4,235,384, with 142,999 mortality. The Indonesian Government carried out testing, tracing, and treatment (3T) in the context of controlling and breaking the chain of transmission of COVID-19. Of all the provinces in Indonesia, Jakarta has the highest total cases, with 860,146 cases, or around 20.3% of national cases.

People infected with SARS-CoV-2, both symptomatic and asymptomatic, can infect others via droplets.⁴ Objects and surfaces contaminated with droplets can also be a medium for transmitting COVID-19 despite small risks. After 3-14 days of being infected with the virus, a person may experience asymptomatic, mild, moderate or severe symptoms. Mild symptoms include fever, cough, sore throat, nasal congestion, headache, muscle aches, and anosmia. Moderate symptoms are accompanied by dyspnea or shortness of breath. While the symptoms are severe, acute respiratory infections begin to occur, characterized by a decrease in oxygen saturation to <90% in the room air.⁵⁻⁷ Age is related to levels of immunity and metabolism of the human body. The older a person gets, the more the body's immunity decreases. Countries with large elderly populations have been shown to have higher death rates.¹

Correspondence*: Nanik Prasetyoningsih, Department of Health Policy and Administration, Faculty of Public Health, Universitas Indonesia, Depok, Indonesia. Email: prasetyoningsihnanik@amail.com; Phone: +62 815-7872-9391 Received: April 24, 2024 Accepted: July 8, 2024 Published: July 31, 2024 Patients with moderate to severe symptoms are at risk of experiencing blood clots, cytokine storms, and even mortality; therefore, they need intensive care at the hospital. From admission to the hospital until completion of treatment, patients must be closely monitored for oxygen saturation (SpO2), anemia, leukocytosis, chest x-rays, increased NLR, thrombocytopenia, D-dimer levels, and CRP.⁷ Previous studies have shown that high levels of D-dimer can be found in COVID-19 patients with severe to critical symptoms. Examination of D-dimer levels can also be used as a parameter to determine the risk of blood clots, as well as detecting infection or inflammation in the body.⁸⁻⁹ In addition, increasing D-dimer levels can be a predictor of disease progression (prognosis) to mortality.⁸⁻¹⁰ In Sharp and Ghodke's study, there was a significant relationship between age and D-dimer r(151) = 0.244 [p=0.02(<0.05)]. The variation in D-dimer levels with age in women was 0.0869, and in men was 0.0454. The variation in D-dimer levels after menopause was 0.0659; in premenopausal women, it was -0.027. Negative values in the premenopausal age group indicate the presence of factors that are not present in the postmenopausal age group of women.¹¹

Among the laboratory parameters examined, there is the highest risk of mortality, which includes routine blood tests (lymphocytes, leukocytes, number of neutrophils and platelets, and hemoglobin), coagulation indicators (D-dimer and prothrombin time), liver function and markers of aggression (albumin, total bilirubin, aspartate, and alanine transaminase), markers of kidney function (urea nitrogen and creatinine), and inflammatory factors (CRP, IL-6, LDH, procalcitonin, ferritin, and cardiac troponin). In patients with low levels of platelet, this condition may indicate thrombocytopenia, a condition that is prone to causing bleeding. In people with thrombocytopenia, platelet levels are less than 150,000/mm3. On average, thrombocytopenia occurs in the second week, so the number needs to be monitored as it is a predictor of worsening condition and mortality of COVID-19 patients. Thrombocytopenia is a hematological disorder often encountered in older adults. The general causes are immune thrombocytopenia purpura (ITP), drug induction, bone marrow failure, or infection. Age-related changes in the organs and vascular system also increase the risk of thrombocytopenia.

Based on such situation and condition, it is necessary to carry out a more in-depth study regarding predictors of mortality due to COVID-19, one of which is to determine the relationship between age, platelets, and D-dimer in COVID-19 patients. Even though the COVID-19 pandemic has ended and continues to evolve, a study aimed at optimizing treatment measures for relevant patients is still very significant. The study is expected to provide some valuable reference materials that can inform current and future healthcare strategies, contributing to improved patient outcomes and potentially reducing the overall impact of the disease. This study is crucial for developing effective treatments, managing outbreaks, and enhancing global preparedness for similar future health crises.

Method

This study was a non-experimental study using a cross-sectional study. Data was obtained from the medical records of COVID-19 patients at Hospital X in Jakarta, Indonesia, from August 2020 to May 2021, with a total of 667 patients after selecting criteria and completeness of the data. The data was carried out using cluster random sampling, which means the cluster is a small representation of the entire population. The inclusion criteria for research subjects were patients aged >18 years, confirmed positive for COVID-19 via the RT-PCR test, and hospitalized. The confidentiality, integrity, and availability of medical records were ensured to protect the patients' privacy and comply with regulatory standards in health care. In comparison, patients aged <18 years and with incomplete medical records were excluded from this study. The medical record data collected included general characteristics of the patient (age and sex) and laboratory tests (D-dimer and thrombocyte).

General characteristics and laboratory test results were summarized and presented as categorical data, showing the frequency (n) and percentage (%) of each category. This data was then analyzed using the Chi-square test to determine any significant association between different categories. To determine the level of significance, this study used an α of 0.05 with a confidence level of 95%. The p-value was used to examine conclusions from bivariate analysis. If the resulting p-value was small, the events were concluded as unrelated, independent, or interdependent.

Results

Out of a total of 667 patients, the results of the descriptive analysis showed that the proportion of COVID-19 patients

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was dominated by the age group of 18-47 years (50.2%), while the proportion of the age group of ≥ 48 years was 49.8%. Males dominated in this study at 57.7% compared to females at 42.3%. Laboratory results of thrombocytes showed that 67.8% of COVID-19 patients had normal outcomes ($\ge 150.000/\text{mm}^3$), and 32.2% were below normal ($< 150.000/\text{mm}^3$). On D-dimer laboratory results, the proportion of patients with normal ($\le 500 \text{ ng/mL}$) results was 94.2%, and 5.2% had D-dimer laboratory results above normal (> 500 ng/mL) (Table 1).

Table 1. The Description of Patient Characteristics and Laboratory Test

Variable	Frequency (n = 667)	Percentage (%)	95% CI (Lower-Upper)
Age			
18-47 years	335	50.2%	(46.5-54)
≥48 years	332	49.8%	(46-53.5)
Sex			
Male	385	57.7%	(53.8-61.6)
Female	282	42.3%	(38.4-46.2)
Thrombocyte			
Normal (≥150.000/mm³)	452	67.8%	(64.2-71.5)
Below normal (<150.000/mm ³)	215	32.2%	(28.5-35.8)
D-dimer			
Normal (≤500 ng/mL)	628	94.2%	(92.2-96)
Above normal (>500 ng/mL)	39	5.8%	(4-7.8)

Note: CI = confidence interval

Table 2 shows the correlation between the age groups and thrombocyte levels (p-value = 0.624). The result of the odds ratio (OR) value was 1.19, meaning that patients aged ≥ 48 years had a 1.19 higher likelihood of getting thrombocyte output below normal ($\geq 150.000/\text{mm}^3$). Table 3 shows the positive correlation between the age groups and D-dimer levels (p-value <0.001). The result of the OR value was 2.85, which means that patients aged ≥ 48 years had a 2.85 higher likelihood of getting above normal D-dimer output. Table 4 shows the positive correlation between the age groups and D-dimer levels (p-value = 0.004). The result of the OR value was 2.61, which means that patients with thrombocytes below normal ($< 150.000/\text{mm}^3$) had a 2.61 higher likelihood of getting above normal D-dimer output.

Table 2. Correlation Between Age and Thrombocyte of Patients

	Thro	ombocyte		95% CI	
Variable	Normal n (%)	Below normal n (%)	p-value	(Lower-Upper)	
Age					
18–47 years ≥48 years	317 (94.6%) 311 (93.7%)	18 (5.4%) 21 (6.3%)	0.624	*1 1.19 (0.62-2.27)	

Table 3. Correlation Between Age and D-Dimer of Patients

	D	-Dimer		95% CI (Lower-Upper)	
Variable	Normal n (%)	Below normal n (%)	p-value		
ge					
18–47 years ≥48 years	264 (78.8%) 188 (67.8%)	71 (21.2%) 144 (43.4%)	<0.001	*1 2.85 (2.03 - 4.00)	

Table 4. Correlation Between Thrombocyte and D-Dimer of Patients

	D-Di	mer		95% CI (Lower-Upper)	
Variable —	Normal n (%)	Below normal n (%)	p-value		
Thrombocyte					
Normal (≥150.000/mm³)	434 (69.1%)	194 (30.9%)		*1	
Below of normal (<150.000/mm ³)	18 (46.2%)	21 (53.8%)	0.004	2.61 (1.36-5.01)	

Notes: CI = confidence interval, *Chi square, p-value < 0.05

Discussion

A low thrombocyte level may indicate a condition susceptible to thrombocytopenia, which causes bleeding. 16,17 The normal number of thrombocytes ranges from 150,000 to $400,000/\text{mm}^3$, strongly influenced by the way they are counted. 17 This study showed that age was not significantly correlated to thrombocyte levels. However, patients aged ≥ 48 years had a 1.19 higher likelihood of getting thrombocyte output below normal ($\geq 150.000/\text{mm}^3$), indicating that many below-normal thrombocytes were found in elderly patients.

D-dimers are fragments of proteins that give an idea of whether or not there is a clot in the blood. 18 This study found a correlation between a group of COVID-19 patients aged \geq 48 years with D-dimer levels above normal (>500 ng/mL). The results revealed that patients aged \geq 48 years were more likely to have higher than normal levels of D-dimer (>500 ng/ml) (p-value <0.001). Excessively high levels of D-dimer increased the risk of blood clots. Changes in the D-dimer level need to be monitored on a regular basis as an increase indicates a possible poor prognosis, even a risk of death. 19 Until now, D-dimer examination has become a parameter for symptom severity, especially in elderly patients in the early COVID-19. 20

This study's results showed that the thrombocyte levels positively correlated with the increase of D-dimer value (p-value <0.004). The abnormal thrombocyte levels can increase blood clotting in the body so that the D-dimer level increases. 21 This study agreed with a previous study that correlation analysis showed the mean thrombocyte volume had a weak positive correlation with D-dimer (r-value = 0.269, p-value = 0.013). 22 This is also in line with several previous studies which found that age, low platelet levels, and increased D-dimer levels can be an indication of the risk of death in COVID-19 patients, as well as predicting the level of severity in COVID-19 patients. 21,22

There are several research constraints which could affect the results of the study. The limitation of this study was that it was done only in one hospital; hence, the results could not be generalized to a wider population. Further clinical studies with larger sample sizes conducted at some hospitals need to be conducted to confirm this study's results.

Conclusion

In conclusion, age group, D-dimer value, and thrombocyte levels are significantly affected by COVID-19 disease. Older patients of COVID-19 are likely to have higher D-dimer values above normal. There is a positive correlation between age and elevated D-dimer levels. These findings highlight the importance of considering age when assessing COVID-19 patients. This study is expected to help doctors and policymakers adapt managerial strategies for relevant patients to reduce the risk of mortality.

Abbreviations

COVID-19: coronavirus disease 2019; SARS-CoV-2: severe acute respiratory syndrome coronavirus-2; CI: confidence interval.

Ethics Approval and Consent to Participate

This study has been approved by the Ethics Committee of the Education Installation Section of TK. II Moh Ridwan Meuraksa Hospital, Number Sket/321/VIII/2021.

Competing Interest

The authors declared no competing interests in this study.

Availability of Data and Materials

The participants of this study did not give written consent for their data to be shared publicly, so due to the research's sensitive nature, supporting data is unavailable.

Authors' Contribution

NP: conceptualization, data curation, formal analysis, methodology, supervision, writing – original draft, writing – review & editing. AG: supervision and review.

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Kesmas

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Article 3

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Systematic Review of Factors Related to PM2.5 Exposure on the Risk of Type 2 Diabetes Mellitus

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Systematic Review of Factors Related to PM_{2.5} Exposure on the Risk of Type 2 Diabetes Mellitus

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Abstract

Diabetes mellitus is a major public health problem in many countries, and most of them are type 2 diabetes mellitus (T2DM). Air pollution is thought to contribute to the T2DM incidence, and one of the most important pollutants is PM2.5. This study aimed to determine factors related to PM2.5 exposure and individual factors in increasing the risk of T2DM based on a systematic review. The PRISMA was used as a method of data collection and selection. Of 176 relevant articles identified and screened, 12 articles from various countries published in 2013-2021 were synthesized in this study. Results showed that long-term PM2.5 exposure, high PM2.5 concentrations, and living in densely-populated areas, close to roads, and in areas with industrial activity could increase the risk of T2DM. Population with an older age (>40 years) and a BMI of overweight or obese were more vulnerable. However, men and persons who stopped or never smoked were also at higher risk; thus, further studies need to be carried out along with other risk factors. A future study is recommended to determine the effects of PM2.5 exposure on the incidence of T2DM in Indonesian populations.

Keywords: air pollution, individual factors, PM2.5, systematic review, type 2 diabetes mellitus

Introduction

Noncommunicable diseases are the major cause of death and disability globally, one of which is diabetes, standing out as one of the most prevalent among them.¹ As of 2021, the International Diabetes Federation (IDF) reports that approximately 537 million adults aged 20-79 years are currently living with diabetes, and this number is expected to rise further.² Type 2 diabetes mellitus (T2DM) constitutes over 90% of these cases, with a consistent annual increase attributed to factors such as population aging, economic development, and escalating urbanization, leading to unhealthy lifestyles and increased consumption of food associated with obesity.³ Analyzing global diabetes prevalence in adults (20-79 years), the 2021 IDF data reveals that China (140.9 million), India (74 million), Pakistan (33 million), the United States (32.2 million), and Indonesia (19.5 million) have the highest numbers of diabetes cases.² The 2018 Indonesian Basic Health Research indicated a 2% prevalence of diabetes mellitus among individuals aged ≥15, signifying an increase from the 2013 rate of 1.5%.⁴ Furthermore, a primary risk factor for diabetes in 2017 was ambient air pollution, contributing to 13.4% of deaths and 15.4% of Disability-Adjusted Life Years (DALYs).⁵

Pollutants that play a major role in increasing the risk of T2DM include particles <2.5 μ m in diameter (PM_{2.5}), nitrogen dioxide (NO₂), particles <10 μ m in diameter (PM₁₀), and nitrogen oxides (NO_x).⁶ Ambient (outdoor) air pollution in cities and rural areas was estimated to cause 4.2 million premature deaths worldwide per year in 2016. These deaths were mostly due to exposure to fine particles 2.5 microns in diameter or less (PM_{2.5}). Due to its fine size, PM_{2.5} can penetrate the lung barrier and enter the circulatory system, which can increase mortality or morbidity over time.⁷

 $PM_{2.5}$ can enter the body through the respiratory system and then enter the lungs, and some can even enter the bloodstream. Concerning T2DM, $PM_{2.5}$ can penetrate the lung barrier and enter the circulatory system.⁷ At this stage, $PM_{2.5}$ in the air enters the body through the respiratory tract and enters the lungs until it penetrates the alveoli. Then, during the gas exchange process between the alveoli and blood vessels, $PM_{2.5}$ will diffuse into the blood vessels, causing oxidative damage, endothelial dysfunction, and inflammation, resulting in insulin resistance, which in turn causes T2DM.⁸

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Received: February 6, 2024 Accepted: July 8, 2024 Published: July 31, 2024 A study in South Korea in 2020 showed an increased risk of increased blood glucose levels with short and medium-term air pollution exposure that was more pronounced among 65-year-old diabetic men.⁹ Another study in India in 2019 identified an independent association between urban environment and insulin resistance in adults older than 20 years, in which those living in urban areas had higher levels of Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) assessments than those in rural areas. The largest increase was found for populations living within 20 km of the city center.¹⁰ A previous study conducted in 2019 in Indonesia showed a significant relationship between the incidence of T2DM in urban and rural communities; however, this difference is also due to other factors, such as individual factors, cultural and socioeconomic differences, and lifestyle patterns in urban and rural areas.¹¹

For its gradual onset, the impact of PM_{2.5} exposure on T2DM varies based on factors such as the duration of exposure, concentration levels, individual or population sensitivities, and other associated risk factors.⁶ Extensive studies on this matter, particularly in Indonesia, are limited. A systematic review was conducted to address this gap, analyzing literature from around the globe. This study aimed to explore how factors related to PM_{2.5} exposure and individual characteristics could contribute to an elevated risk of developing T2DM, drawing insights from various studies conducted in different countries. Compared with other systematic review studies, this study was carried out with a focus on studying a more specific relationship between environmental factors (PM_{2.5} exposure) and individual factors with T2DM.

Method

This study took place in 2022 and used a systematic review design with a qualitative approach (meta-synthesis). Systematic study or systematic review is a research method that implements studies, reviews, structured evaluations, classifications, and categorizations based on several evidence bases that have been produced previously. While, meta-synthesis is a data integration technique to obtain new theories or concepts or a deep and comprehensive level of understanding by narratively synthesizing previous study results. This study's analysis unit was secondary data from both national and international scientific journal articles published in 2013-2022. To access the literature, a database belonging to the Universitas Indonesia (UI) Library (remote-lib.ui.ac.id), was used and connected to various subscription literature databases. The database is free for the UI academic community to access.

The data collection and selection method were based on guidelines called Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocol (PRISMA) protocol.¹⁴ The PRISMA protocol is developed to facilitate transparent, complete reporting of systematic reviews and has been updated (PRISMA 2020) to reflect recent advances in systematic review methodology and terminology. The selection process with PRISMA 2020 is a checklist and flow diagram consisting of identification, filtering, and literature inclusion processes (Figure 1).

Identification

a. Literature Search

During the literature search phase, relevant keywords concerning $PM_{2.5}$ exposure and its correlation with the T2DM incidence were inputted into the search field of the UI library database (remote-lib.ui.ac.id). The keywords are T2DM, $PM_{2.5}$, and Fine PM. This search employed the Boolean Operator, utilizing both AND and OR codes to refine the search parameters. The keyword-based search yielded a total of 176 pieces of literature.

b. Duplicate Removal Before Filtering Process

During this phase, a deduplication procedure was conducted to eliminate redundant literature. This process was executed through a database automation engine or a reference manager application, specifically Mendeley, throughout the literature export process. Additionally, parameters such as the publication year, literature type, language, and file availability were incorporated as boundaries (Figure 1). By entering these limits, 73 pieces of literature were eliminated, and 103 were obtained. At this stage, the deduplication process or removal of duplicate literature was also carried out before the filtering process using database automation tools and through the literature export process to Mendeley. A total of 6 pieces of literature were deleted using automation tools and manually during the literature export process to Mendeley, bringing the total literature obtained at this identification stage to 97 pieces of literature.

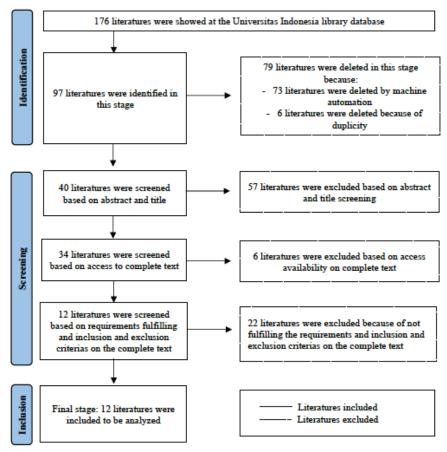


Figure 1. Literature Identification Results Using PRISMA 2020 Flow Chart

Screening

a. Title and Abstract Screening

Once identified, the next step was to screen the title and abstract (Figure 1). In this process, literature that still had duplicates was identified by screening the abstracts and titles obtained using an abstract checklist of PRISMA 2020.¹⁴ Apart from identifying the title or abstract, filtering was carried out based on the research topic and variables studied. If duplicate or inappropriate literature were found, the literature would be excluded. In this stage, 57 pieces of literature were eliminated because they did not match the research topic and variables. Next, a total of 57 pieces of literature were scanned again in their entirety for full text.

b. Literature Screening with Full-Text

After screening the title and abstract, the next step was screening the literature with full text (Figure 1). First, the amount of literature obtained in the initial screening process was reduced by the number of literature excluded from screening in the title and abstract. After that, the literature was filtered again by reducing literature that did not have complete text or could not be accessed. At this stage, elimination was done twice: eliminating six pieces of literature that did not have complete texts.

Fulfillment of Conditions

In the next process, the literature was selected for full text using the conditions made in the inclusion and exclusion criteria (Figure 1). Following the PRISMA protocol, inclusion criteria in this study were based on study and publication characteristics. The study characteristics include the Population, Intervention, Comparison, Outcomes, and Study (PICOS) framework: Population (the entire study population exposed to $PM_{2.5}$), Intervention (exposure to $PM_{2.5}$ along with other risk factors), Comparator (not included in this study), Outcome (the incidence of T2DM), and Study Design (all literature selected in the form of non-experimental quantitative research that could answer research questions). Publication characteristics included the year of publication within 10 years (2013 to 2022), the language used (English), and publication status in the form of journal articles and scientific research. The exclusion criteria were the literature in the

form of a literature review or book review, the literature used experimental studies, the literature documents were incomplete, and the literature did not cover the variables to be studied.

After reviewing all literature texts at this stage, the next step was to enter the total number of excluded literature and the reasons for the exclusion. At this stage, the literature eliminated consisted of 22 pieces that were unsuitable for research inclusion and exclusion criteria (study on population, exposure to $PM_{2.5}$, T2DM as health outcome, non-experimental quantitative research). In the final stage (inclusion), 12 pieces of literature were included for systematic review research.

Inclusion

In this final step, the amount of literature that had been selected and was ready for data analysis was entered (Figure 1). In this study, only one database was used: remote-lib.ui.ac.id. Therefore, no further stage was carried out to filter literature from other databases.

Results

A total of 12 pieces of literature were synthesized in this study (Table 1) obtained from several databases connected to the UI Library database. The oldest literature published was in 2013, and the latest was in 2021. The 12 pieces of literature synthesized were international journal articles with research locations in the United States, China, England, Canada, Mexico, Germany, Hong Kong, Chinese Taipei, and Denmark. In these pieces of literature, T2DM was discussed in terms of case prevalence and incidence. The case of T2DM in these pieces of literature was obtained with percentages ranging from 1.5%-12.9% for case incidence and 4.24%-14.9% for case prevalence. While the characteristics of subjects for each piece of literature also varied, on average, they were adults and elderly.

Table 1. Distribution of Individual Characteristics and Type 2 Diabetes Mellitus in the Literature

Literature	Author (Year)	Study	The Number			Individ	ual Characteristi	с			T2	DM
		Location	of Study	Age (years,	Sex	(%)	BMI (kg/m³,	Sı	moking (%)	Prevalence	Incidence
			Subjects	mean±SD)	F	M	mean±SD)	N	Q	С	•	
116	Liu et al. (2016)	China	11,847	59.3±10.6	53.5	46.5	21.5±2.1	63.8	9	27.2	14.9%	
217	Liu et al. (2019)	China	39,191	60.3±9.3	61.9	38.1	26.2±3.7	75.3	10.1	14.6	9.5%	
318	Dimakakou <i>et</i> al. (2020)	England	502,504	61.5±4.5	39.5	60.5	≥25		-		4.24%	
419	Park <i>et al</i> . (2015)	The United States	6,814	64.3±9.4	47	53	31±5.9	49.8	38.1	12.6	12.01%	12.1%
520	Qiu <i>et al</i> . (2018)	Hong Kong	61,447	72.4±5.5	65.5	34.5	27.5±2.5	65	20.7	14.3	13.5%	1.5%
621	Hansen <i>et al</i> . (2016)	Denmark	28,731	56.5±8.1	100	-	26±4.4	31.5	28.5	40		3.9%
722	Weinmayr <i>et al</i> . (2015)	Germany	3,607	60.5±7.5	44	56	29.8±4.7	39	40	21		9.1%
823	Lao <i>et al.</i> (2019)	Chinese Taipei	147,908	46.7±12	37.2	62.8	26±3.7	66.2	6.8	27		3.2%
924	Li <i>et al.</i> (2021)	England	449,006	56.6±8.1	54.3	45.7	27.4±4.8	55	34.6	10.4		4.06%
1025	Coogan <i>et al</i> . (2016)	The United States	33,771	38.7	100	-	≥25	53.5	40	5.5		12.9%
1126	Chilian-Herrera et al. (2021)	Mexico	2006: 2,275 2012: 2,297	51±13	60	40	≥25	47.2	22.8	30		8.3%-11.3%
1227	Chen <i>et al</i> . (2013)	Canada	62,012	54.9	48.7	51.3	≥25	7	76	24		10.1%

Notes: F = female, M = male, BMI = body mass index, N = never smoking, Q = already quit smoking, C = currently smoking, T2DM = type 2 diabetes mellitus.

Based on the results of identifying $PM_{2.5}$ risk factors in the literature (Table 2), the risk factors are $PM_{2.5}$ exposure duration and $PM_{2.5}$ exposure concentration, which were discussed in all 12 pieces of literature. In contrast, the risk factors for $PM_{2.5}$ exposure are discussed in five pieces of literature: Literature 1, 4, 6, 7, and 12. Individual risk factors, including age and body mass index (BMI), are discussed in all 12 pieces of literature. Risk factors for sex are discussed in 10 pieces of literature: Literature 1, 2, 3, 4, 5, 7, 8, 9, 11, and 12, and smoking behavior risk factors are discussed in 11 pieces of

literature: Literature 1, 2, 4, 5, 6, 7, 8, 9, 10, 11, and 12. The next step is synthesizing the analysis of the relationship of each risk factor from the significance of the relationship obtained from the results of statistical measurements in each literature.

Table 2 shows that $PM_{2.5}$ exposure (exposure duration and $PM_{2.5}$ concentration) has a significant relationship with T2DM, except in Literature 4. However, in Literature 4, T2DM has a significant relationship with the distance between population and source of pollutant. Among individual characteristics, T2DM has a significant relationship with age, sex, BMI, and smoking behavior, except in Literature 7, in which no significant relationship is found between T2DM and smoking behavior.

Table 2. Relationship between PM2.5 Exposure and Individual Factors with Type 2 Diabetes Mellitus

Literature		PM _{2.5} Exp	osure			Indivi	dual Charactei	ristic			T2	DM
	Exposure Duration	PM _{2.5} concentration	Distance between population and source	Age (years)	Sex	(%)	BMI (kg/m³,	Si	Smoking (%)		Prevalence	Incidence
	(Years)	(μg/m³)	of pollutant		F	M	mean ± SD)	N	Q	С		
116	1*	72.6*	Higher cases of study subjects living in rural areas*	>58*		46.5*	>25*			27.2*	14.9%	
217	3*	73.4*	No data	≥65*		38.1*	≥25*	75.3*	10.1*		9.5%	
318	1*	(per 1 µg/m³ yearly average increase of PM _{2.5} concentration)*	No data	>56*		60.5*			No data		4.24%	
419	3	17.3	27% of study subjects lived near the road**		47**		>30**	49.8**	38.1**		12.01%	12.1%
520	12*	35.8*	No data	≥65*	65.5**		25-30 and >30*	65*	20.7*		13.5%	1,5%
6 ²¹	5*	18.1*	Estimated incidence of cases in population living in urban areas: 3.5 per 1,000 persons per year**			-		31.5*	28.5*			3.9%
722	2**	16.7**	Living within 100 m of a main road has a >30% higher risk of T2DM*	≥65*		56*			lo significa relationshij			9.1%
823	2*	26.5*	No data	>46*		62.8*	<23*			27*		3.2%
924	1*	10*	No data	>56*		45.7*	25-30 and >30**			10.4*		4.06%
1025	9*	13.9*	No data	≤40**		-	<25*		46	.5*		12.9%
1126	6*	25.5*	No data	>64**		40*	25-30 and >30*	47.2*				8.3%-11.3%
12 ²⁷	6*	10.6*	17% of study subjects living in urban areas; 83% of study subjects living in manufacturing sector area**	<50 and >65**		51.3*	25-30 and >30**		lo significa relationshi			10.1%

 $Notes: F = female, M = male, BMI = body \ mass \ index, N = never \ smoking, Q = already \ quit \ smoking, C = currently \ smoking, T2DM = type \ 2 \ diabetes \ mellitus.$

Discussion

Description of T2DM in the Literature

The T2DM case in the 12 selected pieces of literature was obtained with percentages ranging from 1.5%-12.9% for case incidence and 4.24-14.9% for case prevalence (Table 1). The case prevalence rate in this literature was considered high because it was greater than the global case prevalence rate in 2021 (10.5%) and the estimated global case prevalence in 2030 (11.3%) and 2045 (12.2%), according to the IDF.² Among the 12 pieces of literature included, there were studies with a prevalence of T2DM cases above 10.5%: Literature 1 (14.9%) in China, Literature 5 (13.5%) in Hong Kong, and Literature 4 (12.01%) in the United States.^{16,19,20}

^{*} Significant relationship

^{**} No significant relationship

The Relationship between the Incidence of T2DM and Risk Factors for PM_{2.5} Exposure

The exposure duration factor in this study was identified through the duration of observation of air quality, especially $PM_{2.5}$. The duration of long-term exposure was considered to influence the incidence of T2DM, a chronic disease. This is in accordance with the definition of diabetes mellitus, a chronic metabolic disease that requires a long time to cause damage to organs or affect the body. Based on the results of the literature synthesis (Table 2), it can be seen that the 10 pieces of literature $^{16-18,20,21,23-27}$ taken show a significant relationship between the duration of $PM_{2.5}$ exposure and the incidence of T2DM. In these pieces of literature, long-term observations of $PM_{2.5}$ concentrations significantly associated with T2DM were observations with a minimum time span of 10 months (considered equal to one year) and a maximum of 12 years. A study conducted for ten months in China showed that long-term exposure to $PM_{2.5}$ was positively associated with a significant increase in the prevalence of T2DM, fasting blood glucose, and HbA1c levels, while, in this study, there was a 14.9% prevalence of T2DM. Furthermore, a study conducted over 12 years in Hong Kong shows that long-term high exposure to $PM_{2.5}$ can increase the risk of prevalence and incidence of T2DM in the population, which in this study had a T2DM prevalence of 1.5% and 13.5%. 20

Regarding the $PM_{2.5}$ concentration factor in influencing the incidence of T2DM, 10 pieces of literature^{16-18,20,21,23-27} indicated a significant relationship, with the average concentration of annual $PM_{2.5}$ ranging from 10 μ g/m³ – 73.4 μ g/m³. The average concentration of all these studies exceeded the threshold value for air pollution concentrations from the World Health Organization (WHO), in which annual average maximum concentration for $PM_{2.5}$ is 5 μ g/m³.²⁹ High concentrations of $PM_{2.5}$ exposure, especially with continuous intensity or long-term duration, would have an impact on individual health, including T2DM.⁶ For comparison with case prevalence data, the highest concentration of $PM_{2.5}$ exposure was in a study in China, in which the annual average was 73.4 μ g/m³ with a prevalence of 9.5%.¹⁷ The lowest $PM_{2.5}$ exposure concentration was in a study conducted in Germany, in which the annual average concentration was 16.7 μ g/m³ with a prevalence of 9.1%.²² Even though the difference in prevalence was small, a study in China had stronger results as it had a significant relationship, while a study in Germany showed no significant relationship.

Apart from the risk factors of duration and concentration, the risk factor of distance between the respondents and PM_{2.5} was also considered to play a role in influencing the T2DM risk. Several pieces of literature^{16,19-21,27} have been synthesized to discuss the distance between places. In those pieces of literature, all the study subjects were living with a primary source of exposure, such as roads (Table 2). In a study stating a significant relationship, Literature 1 discussed that location of residence was related to PM_{2.5} exposure in causing the incidence of T2DM. In this study, the cases were mostly identified in rural areas. Meanwhile, a study in Germany discussed the distance between the location of residence and the main road, where respondents who lived 100 meters from the main road had >30% higher risk of experiencing T2DM compared to respondents who lived >200 meters from the main road. Another study related but not significant stated that study subjects living in urban areas with a density of \geq 5,220 people/km² had a higher incidence of T2DM compared to the subjects living in rural and provincial areas. Then, Literature 12 stated that the T2DM risk was higher in study subjects living in Southern Ontario with higher PM_{2.5} concentration levels compared to urban areas because it was an area with a large manufacturing sector.

Individual Risk Factors

Literature 1 showed a significant relationship in the prevalence of T2DM in older individuals, which in this study was above the median age (>58 years). Literature 2 showed that individuals aged \geq 65 years had a significant association with increased fasting blood sugar levels and a higher prevalence of T2DM. Literature 3 stated that individuals aged >56 years had an increased risk of T2DM. Literature 5 showed that individuals \geq 65 years of age were associated with a significant increase in the prevalence and incidence of T2DM. Literature 8 and 9 showed that individuals older than the average population significantly increased the incidence of T2DM. These results aligned with previous theories related to age risk factors that changes in human physiology decrease after 40 years, and the increased risk of T2DM and glucose intolerance can be due to degenerative factors, which is decreased body function at the age of \geq 45 years. 30,31

Literature 1 showed a significant result: the risk of T2DM was 22%-135% higher in male respondents. Literature 2 showed a significant relationship between study subjects who were older and male. Literature 3, 8, and 9 also stated that males were more experienced with T2DM. However, different results were found in Literature 5, which showed a significant relationship in female study subjects. The results from the literature largely showed differences from

previous theories, showing that females likely have a higher risk of developing T2DM because their cholesterol was higher than males and the amount of fat in body weight was higher in females, which makes females at 2-3 times higher risk of suffering from T2DM.^{32,33}

Literature 1, 2, and 3 showed a significant relationship: subjects with higher BMI values had a higher risk of the impact of PM_{2.5} exposure on the risk of T2DM. $^{16-18}$ Literature 5, 6, 9, and 11 showed that the study subjects who were overweight (BMI 25 kg/m³-30 kg/m³) and obese (BMI \geq 30 kg/m³) had a higher risk of the impact of PM_{2.5} on T2DM. 20,21,24,26 In contrast, Literature 8 showed contradictory results in which long-term PM_{2.5} exposure had a stronger relationship with developing T2DM in study subjects with a BMI <23 kg/m³. 23 Literature 1, 2, 3, 5, 6, 9, and 11 show strengthening of the obesity risk factor statement that overweight (BMI 25 kg/m³-30 kg/m³) and obesity (BMI \geq 30 kg/m³) could increase risk of T2DM. $^{16-18,20,21,24,26}$

Several pieces of the literature showed a significant relationship between smoking behavior and the influence of $PM_{2.5}$ exposure on the risk of increasing T2DM. A significant relationship was shown in Literature 1, 8, and 9 among smoker respondents, 16,23,24 in Literature 2, 5, and 6 among respondents who had stopped and never smoked, 17,20,21 and in Literature 11 among respondents who had never smoked. Smoking behavior with the incidence of T2DM in the literature has mixed results but tends to be different from previous theories. The risk factors for smoking behavior can be a risk in increasing the incidence of T2DM in individuals who are or have consumed it, especially with frequent intensity. This is because insulin sensitivity can decrease due to nicotine and other dangerous chemicals contained in cigarettes, which, after some time, can potentially cause diabetes. Results that were not in line with this theory were identified due to other factors included in the statistical analysis, the study area tending to have high concentrations of air pollution, and the uneven number of respondents regarding smoking behavior characteristics.

Overview of the Relationship between PM_{2.5} Exposure and Individual Risk Factors in Increasing the Risk of T2DM

According to previous theories, T2DM was hypothesized to result from the interaction of environmental, biological, and behavioral risk factors.⁶ Air pollution as one of the environmental variables has been proven to disrupt the body's balance, such as insulin resistance, changes in endothelial function, inflammation, increased blood pressure, and changes in blood lipid levels, which, over time, could cause T2DM.⁶ Several previous studies also showed that this increased risk was related to pollutant concentration, duration of pollutant exposure, and location.^{9,10} Apart from that, the smaller particle size was also thought to increase its effect in causing the incidence of T2DM.

Previous theories and studies were proven through this systematic review study. Based on the analysis of relationship between each variable in risk factors for PM_{2.5} exposure in increasing the incidence of T2DM, 12 pieces of synthesized literature showed that the influence of PM_{2.5} exposure in increasing the risk of T2DM could be seen in long-term exposure, ≥ 1 year, with high exposure concentrations even above the WHO's threshold value ($>5 \mu g/m^3$), and within a distance or location with industrial activity or high mobility which could work together to increase the T2DM risk. In addition, individual risk factors were also analyzed on the population at risk. The individual risk factors in this study identified to increase the risk of exposure to PM_{2.5} in causing T2DM were older respondents (>45 years), male, with an overweight BMI (25 kg/m^3 - 30 kg/m^3) and obesity ($\geq 30 \text{ kg/m}^3$), and having a habit of never or quitting smoking showed an association in increasing the impact of PM_{2.5} exposure on T2DM.

The diverse result is because diabetes mellitus is a multifactorial disease, which means that many environmental and individual factors can influence it.³⁸ In addition, the incidence and prevalence of T2DM vary by geographic region because genetic and environmental factors influence the epidemiology of diabetes.³⁹ People of different ethnic origins have different specific phenotypes, which increases their risk of developing T2DM.⁴⁰ This is proven through systematic studies which use data from the research literature in various countries.

Limitations

This study used a systematic review method because the initial study was conducted during the COVID-19 pandemic, and large-scale social restrictions made it difficult to carry out in the field. The shortcoming of this study was the literature came from various countries, but not from Indonesia because of the keywords' limitations. Therefore, not all the literature in the database was identified. Besides, the variables could not fully describe the relationship between $PM_{2.5}$ exposure and the incidence of T2DM, and many other variables from the environmental and individual factors can still be studied.

Conclusion

Exposure to $PM_{2.5}$ has a relationship with the risk of T2DM through three interrelated risk factors: long-term exposure duration, exposure concentration, and location of residence. Individual risk factors related to the impact of $PM_{2.5}$ exposure on T2DM are age, sex, BMI, and smoking behavior. T2DM is a multifactorial and chronic metabolic disease, which, in this study, is proven to occur due to interactions between environmental and individual factors over time. Since no study has examined the relationship between PM2.5 exposure and T2DM in Indonesia, it is crucial to conduct a study to determine the effect of $PM_{2.5}$ exposure on the incidence of T2DM in the population in Indonesia. For systematic review studies, it is also recommended to use a larger database to capture more studies and produce better study results. Studies on other risk factors (compounds or other particulates) and individual factors (lifestyle, economics, and education) must be included to elevate the knowledge and prove previous theories.

Abbreviations

IDF: International Diabetes Federation; T2DM: type 2 diabetes mellitus; UI: Universitas Indonesia; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols; BMI: Body Mass Index; WHO: World Health Organization.

Ethics Approval and Consent to Participate

This study has been approved by The Research and Ethics Committee of the Faculty of Public Health, Universitas Indonesia, with Ethical Clearance Letter Number: Ket- 375/UN2.F10.D11/PPM.00.02/2022.

Competing Interest

The authors declare no conflict of interest.

Availability of Data and Materials

This study used secondary data from scientific journal articles published in 2013-2022, accessed from the Universitas Indonesia Library database (Remote-Lib UI).

Authors' Contribution

RPS conceptualized, designed, and interpreted the data. LF prepared the initial draft and editing.

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Not applicable.

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Ambient Particulate Matter with Blood Pressure in Adult Women Living in Urban City

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Abstract

Ambient air pollution, especially from fine particles, contributes to human mortality from cardiovascular and respiratory diseases, for which high blood pressure (BP) is a major modifiable risk factor. This study aimed to analyze the influence of ambient particulate matter ($PM_{2.5}$) on the risk of high BP leading to hypertension. This study used a cross-sectional design on 118 adult women living in Central Jakarta, Indonesia. Participants were selected from a 1-km radius of the nearest air quality monitoring station with available data $PM_{2.5}$. Linear regression was analyzed to examine the relationship between $PM_{2.5}$ and systolic and diastolic BPs adjusted for potential confounders. The annual means of $PM_{2.5}$ concentration was $36\pm5.74 \,\mu\text{g/m}^3$. The linear regression model showed that $PM_{2.5}$ exposure was associated with systolic BP after controlling with age and body mass index (r = 0.408; $R^2 = 0.167$). The second model showed that exposure to $PM_{2.5}$ concentration could explain about 10.9% variation of diastolic BP after controlling with age, length of stay, body mass index, smoking status, and diabetes mellitus record. Ambient air $PM_{2.5}$ has a risk of BP and hypertension among adult women in Central Jakarta.

Keywords: ambient air pollution, blood pressure, hypertension, PM_{2.5}, women

Introduction

High blood pressure (BP) is the leading risk factor for death and disability-adjusted life-years (DALYs).¹ High BP leading to hypertension is influenced by various elements, such as genetic, environmental, adaptive, nervous, endocrine, and hemodynamic factors.² Hypertension is a significant risk factor for the incidence of cardiovascular disease and a leading cause of premature deaths in the world. About 1.13 billion population in the world suffer from hypertension, and most of them live in low-middle-income countries.³ According to the 2018 Indonesian Basic Health Research, the prevalence of hypertension in the population aged 18 years and older based on a doctor's diagnosis was 8.4%, while the prevalence based on measurement was 34.1%. Central Jakarta is one of the cities with a high prevalence of hypertension in Indonesia. The prevalence of hypertension based on a doctor's diagnosis is about 12.16%, while the prevalence based on measurement is slightly higher than the national figure, about 39.05%. However, Central Jakarta is the municipality with the highest prevalence of hypertension in the Special Capital Region of Jakarta Province.⁴

High blood pressure is also influenced by environmental factors, one of which is air pollution.^{5,6} Ambient air pollution increases mortality and morbidity, shortens life expectancy, and is a major contributor to the world's disease burden.⁷ Particulate matter (PM), especially PM_{2.5}, is a pollutant resulting in public health problems the world concerns.^{8,9} The primary sources of PM from human activities include motor vehicle exhaust gases, industrial activities, agriculture, biomass combustion, and construction activities.^{7,9} These airborne particles can generate health problems depending on where a person lives.¹⁰ The microscopic size of PM_{2.5} allows these particles to be absorbed into the lower bloodstream when someone breathes, resulting in health effects such as asthma, lung cancer, and heart disease.⁹ In 2013, PM was classified as the cause of lung cancer by the International Agency for Research on Cancer.⁸ In 2016, PM_{2.5} contributed to the deaths of approximately 105.7 million DALYs and 4.1 million deaths in the world.¹¹ The increase in hypertension prevalence, along with the decrease in environmental quality, is characterized by an increase in the concentration of air pollutants in the environment.

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Over the past decade, several studies have found that exposure to air pollutants can affect BP. A previous study shows that long-term exposure to air pollutants is associated with increased BP and a high prevalence of hypertension in children and adults. Short-term exposure to $PM_{2.5}$ within 24 hours is associated with increased systolic blood pressure (SBP), and an increase in $PM_{2.5}$ concentration is associated with increased BP. Lang-term exposure to $PM_{2.5}$ is statistically associated with prevalence of hypertension. Several previous studies have also examined the relationship between long-term $PM_{2.5}$ exposure and the incidence of hypertension in a correlation analysis in urban populations, in which the results showed that increasing $PM_{2.5}$ concentrations in ambient air were associated with changes in the incidence of hypertension and increasing SBP. $P_{2.5}$ is $PM_{2.5}$ concentrations in ambient air were associated with changes in the incidence of hypertension and increasing SBP. $P_{2.5}$ is $PM_{2.5}$ concentrations in ambient air were associated with changes in the incidence of hypertension and increasing SBP. $PM_{2.5}$ is $PM_{2.5}$ concentrations in ambient air were associated with changes in the incidence of hypertension and increasing $PM_{2.5}$ is $PM_{2.5}$ in $PM_{2.5}$ in

Adult women were selected as participants in this study based on the intensity of staying at home compared to men. A previous study on ambient particulate air pollution in peri-urban India shows that women spend most of their time near home compared to men at 83% of the daytime vs. 57% for men.⁵ Results of the study show a positive association between long-term exposure to ambient $PM_{2.5}$ with BP and hypertension, with a stronger association found for SBP than diastolic blood pressure (DBP).⁵ A previous study in Indonesia shows that women aged over 60 years were more likely to have hypertension compared to the ones under 60 years.¹⁷

A previous study shows that every 5 μ g/m³ change in exposure to PM_{2.5} was associated with a 16% change in the incidence of hypertension (hazard ratio, 0.84; 95% CI, 0.82–0.86).⁵ Short-term exposures of SO₂, PM_{2.5}, and PM₁₀ are significantly associated with the incidence of hypertension.¹⁸ Air pollution due to exposures to PM_{2.5}, ultrafine (PM_{0.1}), ozone, nitrogen oxides, and transition metals potentially generate health effects through oxidative stress.¹⁹ Oxidative stress acts as a mediator against cell damage and inflammation to several systems that eventually affect BP.²⁰

There were various findings to understand the role of ambient air pollution, especially from PM exposure to cardiovascular disease and BP. However, the relationship in adult women is still limited. The difference from other studies is that, in this study, the sampling area of the subject used mapping from the nearest Air Quality Monitoring Station (AQMS) to the residence. This study aims to determine the effect of ambient air particulate pollutants on SBP and DBP to predict hypertension.

Method

An epidemiological study with a cross-sectional design was carried out among residents in Central Jakarta. This study was conducted from May to June 2023. A multistage cluster random sampling method was adopted as a representative sampling approach to minimize selection bias in large areas. Initially, mapping of the study location based on the three nearest AQMS in Central Jakarta as the first cluster area to the residence with a proximity of ≤1,000 meters was conducted (Figure 1). From the mapping, about five subdistricts and nine villages in Central Jakarta were around the ring and selected as the second cluster. The nine villages were Bendungan Hilir, Kebon Sirih, Senen, Kwitang, Gunung Sahari Selatan, Kemayoran, Gunung Sahari Utara, Kartini, and Pasar Baru. Of nine villages, about 21 community units were selected as sampling areas for this study.

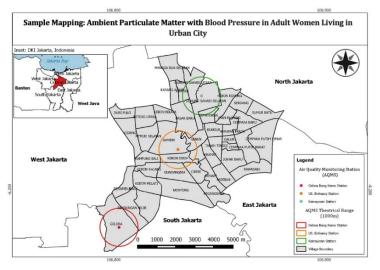


Figure 1. Mapping of the Study Location Based on the Three Nearest AQMS in Central Jakarta

The participants were selected using simple random sampling from the name list available based on the inclusion and exclusion criteria. Of the total population of 203,428 people, about 118 participants were obtained as the minimum sample, calculated using a hypothesis test comparing two means. The inclusion criteria for participants were adult women residents aged 18-65 years living or working at those nine villages in Central Jakarta for at least one year. Exclusion criteria were pregnant women and those who were rejected as study subjects.

There were three data collections in this study. First, PM_{2.5} concentrations were collected from three AQMS in Central Jakarta. Second, participant data measurements consist of measuring blood pressure to diagnose cases of hypertension and measuring body height (centimeters) and weight (kilograms) to calculate the human body mass index (BMI). Third, sociodemographic and health information data were collected by asking for a structural questionnaire from each participant. Prior to data collection, all participants were explained about the study by field staff and signed a consent form.

Ambient air pollution exposure in this study was defined as $PM_{2.5}$ -micron categorization in micrograms per cubic meter ($\mu g/m^3$). The data on $PM_{2.5}$ concentration in 2022 was collected from three AQMS in Central Jakarta and had received permission from the relevant agency. The three sources of air quality monitoring stations are stations belonging to the U.S. Embassy (open access data), Kemayoran Station belongs to Indonesia's Meteorological, Climatological, and Geophysical Agency, and Gelora Bung Karno Station belongs to the Indonesian Ministry of Environment and Forestry. The AQMS was a network of continuous ground-based air quality monitoring stations. From three AQMS data, the daily concentration data was obtained and calculated to get the annual concentration of $PM_{2.5}$ in 2022. The average number of $PM_{2.5}$ concentrations used in this study was obtained from the annual $PM_{2.5}$ concentration from the three AQMS.

Each participant's BP was measured at least twice by a professional nurse using a digital sphygmomanometer (Omron Automatic Blood Pressure Monitor HEM 7156, Kyoto, Japan). BP was measured in the sitting position, and the cuff was placed around 2 cm above the right or left arm elbow. Participants quietly sat in a reclined chair for at least five minutes with both feet flat on the floor and arms supported at heart level. At least 30 minutes before the measurement, participants avoided smoking, drank coffee or tea, and did exercise. The SBP and DBP were obtained from the average of at least two measurements. If the mean of two measurements were more than 10 mmHg, the third measurement was carried out. From the BP measurement, it was classified as hypertension cases if the SBP was 140 mmHg or higher or the DBP was 90 mmHg or higher. 11,15,16

To adjust for potential confounders, the following covariates were considered in the statistical analysis: age (continuous), duration of stay in the study area (continuous), employment status (employed, unemployed), BMI (continuous), smoking status (yes, no), family records of hypertension (yes, no) and diabetes mellitus (yes, no). The participants were also asked about current hypertension medication use and records of diagnosed high BP by a doctor.

A descriptive analysis was taken to illustrate the sample distribution based on various characteristics. Pearson's correlation and linear regression were used to determine the independent variable as a continuous variable. In contrast, t-test analysis was used to determine the independent variable as a categorical variable. Multivariate linear regression models were employed to estimate the association between the exposure of $PM_{2.5}$ with SBP and DBP by considering variables as potential confounders. In multivariate linear regression analysis, all potential confounders were carried out to the full model. Variables with a p-value of >0.05 were excluded one by one from the highest and got the final model. Effect estimates are presented as mmHg change for BP measurements per 1 μ g/m³ increase in $PM_{2.5}$ concentration.

Results

From the three AQMS in Central Jakarta, the average $PM_{2.5}$ concentration was $36.0 \,\mu\text{g/m}^3$. Among $118 \,\text{adult}$ women, the mean SBP and DBP from direct measurement were $120.1 \,\text{mmHg}$ and $80.3 \,\text{mmHg}$. The BP was also categorized and revealed that about 23.7% of adult women suffered from hypertension phase $1.0 \,\text{mmHg}$. The participants were adult women with an average age of $46 \,\text{years}$ who had lived in the study area for about $38 \,\text{years}$. The height and weight measurement showed that adult women had an average BMI of about $27.4 \,\text{(overweight)}$. From the structural interview, about 12.7% of adult women were taking antihypertensive medicine, and about 27.1% were diagnosed with hypertension by a doctor in the past. About 16.9% of adult women were smokers, and almost all of them started smoking when they were adolescents. Regarding genetic factors, about 42.4% of adult women had a family record of hypertension (from both parents), and about 9.3% had a record of diabetes mellitus (Table 1).

Table 1. Characteristics and Health Information of the Participants

Variable	Category	n=118	%
PM _{2.5} (mean±SD, μg/m ³)		36±5.74	
SBP (mean±SD, mmHg)		120.1±19.6	
DBP (mean±SD, mmHg)		80.3±11.5	
Age (mean±SD, years)		46.1±10.6	
Length of stay (mean±SD, years)		38.2±15.5	
BMI (mean±SD, kg/m²)		27.4±5.6	
Hypertension Category	Normal	42	35.6
	Pre-Hypertension	44	37.3
	Phase 1 Hypertension	28	23.7
	Phase 2 Hypertension	3	2.5
	Phase 3 Hypertension	1	8.0
Taking antihypertensive medicine	Yes	15	12.7
	No	103	87.3
Hypertension diagnosed by a doctor	Yes	32	27.1
	No	86	72.9
Employment status	Employed	36	30.5
	Unemployed	82	69.5
Smoking status	Yes	20	16.9
	No	98	83.1
Family history of hypertension	Yes	50	42.4
	No	68	57.6
History of diabetes mellitus	Yes	11	9.3
	No	107	90.7

Note: SD = standard deviation

There was a moderate correlation between age and length of stay in the study area with SBP (r = 0.341, r = 0.303), and it had a positive linear relationship. It suggested that increasing age or length of stay was accompanied by increasing SBP ($R^2 = 0.116$, $R^2 = 0.092$). The BMI had a weak relationship with SBP (r = 0.215), while PM_{2.5} concentration had a very weak relationship with SBP (r = 0.034). Both of them had a positive linear relationship with SBP. The statistical correlation between PM_{2.5} concentration, age, length of stay, and BMI with DBP had a low power (r = 0.011, r = 0.025. r = 0.129, r = 0.233, respectively) (Table 2).

Table 2. The Association of PM_{2.5} and other Covariates with Blood Pressure (continuous variable)

			•
Variable	R	\mathbb{R}^2	p-value
SBP			
PM ₂₅ concentration (μg/m ³)	0.034	0.001	0.715
Age (years)	0.341	0.116	0.001
Length of stay (years)	0.303	0.092	0.001
BMI (kg/m²)	0.215	0.046	0.019
DBP			
PM _{2.5} concentration (μg/m ³)	0.011	0.000	0.903
Age (years)	0.025	0.001	0.791
Length of stay (years)	0.129	0.017	0.165
BMI (kg/m²)	0.233	0.054	0.011

Notes: SBP = systolic blood pressure, BMI = body mass index, DBP = diastolic blood pressure

Independent t-test analysis showed there was no significant relationship between employment status, smoking status, family record of hypertension, and record of diabetes mellitus with SBP (p-values = 1.000; 0.192; 0.685; 0.356). When analyzed with DBP, the result was the same: there was no statistically significant relationship between employment status, smoking status, family record of hypertension, and record of diabetes mellitus with SBP (p-values = 0.403; 0.068; 0.664; 0.786) (Table 3).

Results showed that after controlling with age and BMI, the exposure of $PM_{2.5}$ concentration in a multivariate linear regression model could explain about 16.7% variation of SBP. It showed that the higher the $PM_{2.5}$ concentration, the lower the SBP level. With every increased $PM_{2.5}$ concentration of about 1 μ g/m³, the SBP level would decrease by about 0.45 mmHg after controlling with age and BMI.

Another model showed that exposure to $PM_{2.5}$ concentration could explain about 10.9% variation of DBP after controlling with age, length of stay, BMI, smoking status, and record of diabetes mellitus. Every increased $PM_{2.5}$ concentration of about 1 μ g/m³, the DBP level would decrease by about 0.049 mmHg. The higher the $PM_{2.5}$ concentration, the lower the DBP level. (Table 4).

Table 3. The Association of Other Covariates with Blood Pressure (categorical variable)

Tuble 5: The hisbellation of other covariates with blood i ressare (categorical variable)								
Variable	Category	Mean±SD	T (t-test)	p-value				
SBP								
Employment status	Employed	120.19	0.001	1.000				
	Unemployed	120.19						
Smoking Status	Yes	114.98	1.311	0.192				
	No	121.26						
Family record of hypertension	Yes	121.05	-0.407	0.685				
	No	119.57						
Record of diabetes mellitus	Yes	125.41	-0.927	0.356				
	No	119.66						
DBP								
Employment status	Employed	78.92	-0.839	0.403				
	Unemployed	90.86						
Smoking status	Yes	75.98	1.842	0.068				
	No	81.14						
Family record of hypertension	Yes	80.83	-0.436	0.664				
	No	79.86						
Record of diabetes mellitus	Yes	79.36	0.272	0.786				
	No	80.36						

Notes: SD = standard deviation, SBP = systolic blood pressure, DBP = diastolic blood pressure

Table 4. Final Linear Regression Model of PM25 with Blood Pressure

Variable	Coeff. β	p-value	r	\mathbb{R}^2
SBP				
PM _{2.5} concentration (μg/m ³)	-0.453	0.135	0.408	0.167
Age (years)	0.655	0.001		
BMI (kg/m²)	0.668	0.029		
DBP				
PM _{2.5} concentration (μg/m ³)	-0.049	0.793	0.330	0.109
Age (years)	-0.095	0.450		
Length of stay (years)	0.149	0.080		
BMI (kg/m²)	0.479	0.013		
Smoking status	-5.422	0.054		
Record of diabetes mellitus	-2.260	0.541		

Notes: SBP = systolic blood pressure, BMI = body mass index, DBP = diastolic blood pressure

Discussion

Air pollution has been an environmental health problem in Indonesia, especially in the metropolitan city of Jakarta. This study found that the annual mean concentration of $PM_{2.5}$ in 2022 around Central Jakarta was $36~\mu g/m^3$, greater than the national ($15~\mu g/m^3$) and the WHO's standard ($5~\mu g/m^3$). 21,22 In urban areas, motor vehicles are the major source of PM in ambient air, especially from gasoline and diesel vehicle emissions. 23 Central Jakarta is the location of the central government buildings, as well as being the center for finance and business with high traffic activity. In this study, the high concentration of $PM_{2.5}$ in participants' residences was revealed to be motor vehicle density. Data shows that the number of motorized vehicles in Jakarta is likely to increase from 2020 to 2022, dominated by two-wheeled vehicles. 24 In Jakarta, vehicle exhaust gas is the major source of air pollution, especially $PM_{2.5}$ in the dry and rainy seasons, contributing around 32-57%, followed by industrial burning activities around 43%. 25

The SBP and DBP results from the direct measurement categorized as hypertension category showed that adult women in Jakarta mostly had pre-hypertension and hypertension phase 1. The prevalence of all the hypertension phases in this study was 27.0%, lower than the national data in 2018 at 34.1% and slightly higher than in Central Jakarta at 39.5%.²⁶ Of the total hypertension cases in adult women, only 12.7% declared that they were taking antihypertensive medicine. This finding indicated that there was low awareness of the disease and low adherence to taking medication as they suffered from high BP.

In bivariate analysis, $PM_{2.5}$ concentration was not significantly associated with SBP or DBP, but other variables showed a significant relationship. Age and length of stay in the study area were positively associated with SBP, whereas only BMI status was significant with both SBP and DBP levels. In this study, most participants were at the age of 46 years on average. A previous study in Bekasi City, Indonesia, showed that there was a relationship between age and the occurrence of high BP. The participants aged \geq 40 years had a 9.3 times higher risk of hypertension than those aged <40 years.²⁷ Another study in Tokyo shows that the prevalence of hypertension grade 1 increased with age.²⁸ BP likely

increases with age, in which the high prevalence of hypertension is influenced by various health risks, and the incidence of the disease mainly occurs in older people.^{29,30} Aging is a continual process that decreases physiologic function across all organ systems and increases vulnerability to infection and disease. Transformation in arterial and arteriolar stiffness are primary factors contributing to hypertension in the elderly.^{30,31}

According to this study, high SBP occurred more often in people staying longer at the study location, indicating a greater possibility of $PM_{2.5}$ living in the body. The longer someone lives in a residence, the longer they get exposed to air pollutants. A previous study in five rural regions in China shows that the length of stay is related to long-term exposure to air pollutants ($PM_{2.5}$, PM_{10} , and NO_2), which increases BP and hypertension.³² This study also revealed that the participants living in the study area for 38 years were associated with SBP. However, these results differ from a previous double-blind crossover study stating that healthy adults and non-smokers aged 18-50 years who were exposed to $PM_{2.5}$ tended to increase DBP, not SBP.³³

In this study, BMI was associated with SBP and DBP. These results are similar to a previous study in two urban cities in Germany, stating that BMI and high BP had a significant relationship.³¹ The other study shows that the hypertension risk increases by about two to three times in overweight people compared with someone with a normal BMI.³² People with higher BMI status reflect increased body fat mass. Fat cells are characterized by being sensitive to lipolysis and producing high quantities of inflammatory cytokines. As the inflammatory process has an important role in the pathogenesis of hypertension, these processes could respond to BP elevation and end-organ damage.^{34,35}

Although the relationship between PM_{2.5} and hypertension in the bivariate analysis was not significantly related, but in the multivariate linear regression model, there was a risk of PM_{2.5} concentration with SBP and DBP after controlling with another confounding variable. This finding was consistent with the previous study among reproductive-age adults in China, which found that exposure to PM_{2.5} in a long-term period was associated with an increase in both SBP and DBP.³⁶ The mechanism of increased blood pressure from short-term exposure to PM_{2.5} concentrations is related to autonomic nervous system imbalance, generation, or release of endogenous biological mediators such as cytokines.

This study had several limitations. First, the research design was cross-sectional, and causal relationships on individual variables could not be attempted. A causal association was unlikely to be established after someone was exposed to $PM_{2.5}$. They had to have high BP. The inability to measure individual exposure to $PM_{2.5}$ and the use of secondary data led to incomplete or unavailable data. The second limitation was that there was less information on indoor air pollutants. Some potential influences on indoor $PM_{2.5}$ concentration, such as type of cooking fuel and home ventilation, could not be excluded. However, the study tried to include the effect of smoking as an important source of household air pollutants. Third, the number of samples in this study was insufficient to build a statistical association between each variable with SBP and DBP.

Despite those limitations, this study had several strengths. First, environmental health studies conducted regarding the influence of air pollutants on cardiovascular risk factors are still limited, especially in Indonesia. Second, this study tried to predict the influence of $PM_{2.5}$ on traffic activities with a simple spatial model based on the distance from the nearest AQMS with available data of $PM_{2.5}$ concentration to the study location. Future studies need to predict the spatiotemporal model of $PM_{2.5}$ or other air pollutants' exposure to estimate the exposure at each participant's residence.

Conclusion

Air pollution in Jakarta, Indonesia, is still an environmental problem faced by people living near sources of air pollution. Exposure to $PM_{2.5}$ in ambient air is associated with SBP after controlling with age and BMI. $PM_{2.5}$ concentrations explain variations in DBP after controlling for age, length of stay, BMI, smoking status, and record of diabetes mellitus. $PM_{2.5}$ ambient air has a risk of developing BP and hypertension in adult women in Central Jakarta. Further studies need to predict biological markers of exposure or effects that will be measured on the human body as an early predictor of high BP, which leads to hypertension and cardiovascular disease.

Abbreviations

DALYs: Disability-Adjusted Life-Years; BP: blood pressure; SBP: systolic blood pressure; DBP: diastolic blood pressure; AQMS: Air Quality Monitoring Station; BMI: body mass index.

Ethics Approval and Consent to Participate

This study was approved and reviewed by the Research and Ethics Committee of the Faculty of Public Health, Universitas Indonesia (letter number Ket- 36/UN2.F10. D11/PPM.00.02/2023).

Competing Interest

The authors declare no conflict of interest.

Availability of Data and Materials

The generated dataset is available to share with the corresponding author upon reasonable request.

Authors' Contribution

Conceptualization: NA, HK. Data curation: LF, BW. Formal Analysis: NA, LF. Funding acquisition: HK. Methodology: HK, BW. Project administration: NA. Visualization: NA, LF. Writing-original draft: NA, HK, BW, LF. Writing review & editing: NA, LF.

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Prevention of Tuberculosis Transmission Through Mycobacterium Tuberculosis Detection in the Air

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Prevention of Tuberculosis Transmission Through Mycobacterium Tuberculosis Detection in the Air

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Abstract

Tuberculosis (TB) is a dangerous and highly contagious disease. Global cases have increased since, and Indonesia is one of the countries with the highest number of TB cases. This study aimed to prevent TB transmission by analyzing air contamination. Air samples were taken from three primary health cares (PHCs) in Surabaya City, East Java Province, Indonesia, and cultured in Mycobacterium Growth Indicator Tube (MGIT) media. Of the 108 air samples collected, 36 came from the waiting room, 36 from the examination room, and 36 from the laboratory room. As a result, the waiting room (50%), examination room (16.7%), and laboratory room (2.7%) were declared positive. In short, the air in the three PHCs contained *mycobacterium tuberculosis*. There is a need for room management to prevent TB transmission.

Keywords: air, mycobacterium tuberculosis, primary health care

Introduction

Tuberculosis (TB) is a dangerous and highly contagious disease, posing a significant threat regarding mortality and morbidity, in which nearly one-quarter of the global population is infected by the bacteria. *1,2 Mycobacterium tuberculosis* (MTB) emerges as the causative agent of TB, leading to fatalities and representing a major infectious agent in humans. *3,4 TB remains a major health concern worldwide, persisting as a substantial public health menace with significant medical, social, and financial consequences, particularly in developing and tropical countries. *5 Rajasekaran et al.* assert that TB is a severe global burden often referred to as a disease of poverty. *6

World Health Organization (WHO) reveals that the number of people suffering from TB in 2021 reached 10.6 million cases, demonstrating an increase of around 600,000 cases from 10 million cases in 2020. Of 10.6 million cases, 6.4 million (60.3%) have been reported, and the patients undergo treatment; conversely, 4.2 million (39.7%) remain undiagnosed and unreported.⁷ The Southeast Asian region, primarily composed of tropical countries, contributes to 40% of global TB-related deaths. It has been assessed that 10% of patients with extrapulmonary TB exhibit musculoskeletal involvement, and 50% of these musculoskeletal TB cases manifest as spinal TB.⁸ Overall, TB-related deaths remain alarmingly high, with at least 1.6 million individuals succumbing to TB, representing an increase from the previous year's estimate of around 1.3 million deaths.⁷

Additionally, approximately 187,000 individuals die from TB in conjunction with human immunodeficiency virus (HIV).^{7,9} Around 90% of TB cases affect young adults, with a higher prevalence among males than females.^{10,11} More than half of TB patients are of productive age, according to WHO, and the age ranges between 25 and 44 years.^{12,13} This poses a serious concern, especially for developing countries like Indonesia, as the majority of TB patients are in their productive years.

Indonesia occupies the second position with the highest number of TB cases worldwide after India in which this position is followed by China, the Philippines, Pakistan, Nigeria, Bangladesh, and the Democratic Republic of Congo.¹⁴

Correspondence*: Eko Budi Koendhori, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia, Email : dr_eko@fk.unair.ac.id, Phone : +6287777265325 Received: February 29, 2024 Accepted: July 16, 2024 Published: July 31, 2024 Indonesia is ranked third with the highest number of TB cases in 2020, totaling 824,000 cases; in 2021, this number increased to 969,000 cases, representing an estimated 17% rise in cases.¹³ The TB incidence rate in Indonesia stands at 354 per 100,000 population, indicating that out of every 100.000 individuals in Indonesia, 354 are afflicted with TB.¹³

East Java is one of the provinces with the highest number of TB cases in Indonesia, with Surabaya City contributing the most, totaling 4,628 cases. This study selected three primary health care (PHCs) in densely populated areas where the Surabaya City Government recorded 184 TB cases. As population density increases, the dissemination of TB bacteria becomes more prevalent. Measurements were conducted at the PHCs because the government focused on TB patient care and monitoring at these nearby facilities.

A mode of transmission for pulmonary TB is through the dissemination of "droplet nuclei" from infected patients. However, in the post-pandemic era, there has been a lack of research regarding the presence of MTB in the air. Therefore, this study was carried out to prevent TB transmission by analyzing MTB contamination for management policies in waiting rooms, examination rooms, and laboratory rooms at three PHCs in Surabaya City, Indonesia.

Method

This descriptive observational study collected air samples from the waiting, examination, and laboratory rooms for general and TB patients in three PHCs in Surabaya City, Indonesia (Figure 1). These PHCs were located in the Eastern, Northern, and Western parts of the city. All the rooms utilized in this study met the standard size requirements for PHC, including a waiting room of $16 \, \text{m}^2$, an examination room of $12 \, \text{m}^2$, and a laboratory room of $9 \, \text{m}^2$.



Figure 1. (A) Waiting Room; (B) Examination Room; (C) Laboratory Room in Three Primary Health Care

Air sampling was conducted using the As82 PURIVA H1 device, with a suction rate of 200 m² per hour. Sampling was taken for one hour using HME Twinstar Drager virus and bacteria filters. The number of samples was determined based on the Federer formula. The study took 36 repetitions, resulting in each group comprising 36 samples, totaling 108 samples. The repetitions were made during active hours at selected PHCs.

After an hour, the device was turned off, and the filters were collected. The sampling underwent decontamination using 4% NaOH and was then cultured on Mycobacterium Growth Indicator Tube (MGIT) media. The cultures were incubated in MGIT machines until growth occurred or were declared negative after 40 days. Positive culture results were subsequently subjected to identification to differentiate between MTB and mycobacteria other than tuberculosis (MOTT) using SD TB Ag MPT64 Rapid test (Figure 2A, 2B, 2C).

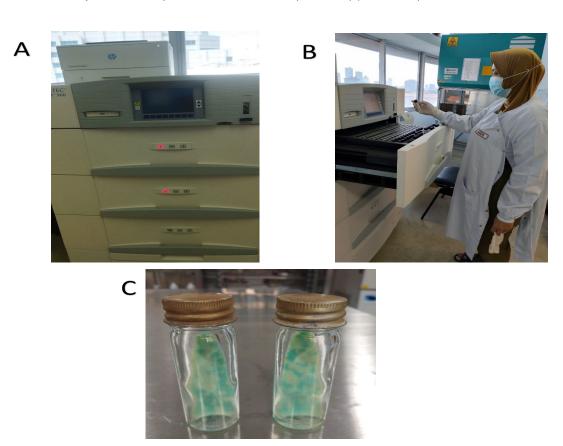


Figure 2. (A) MGIT instrument for automated MTB culture; (B) Analyst Observing the Culture Results in Tubes; (C) A positive TB Colony Result

Results

The waiting and examination rooms at the PHC were not separated between TB and non-TB patients, thus posing a significant risk of TB transmission. The waiting room was where patients queued to wait to be called into the examination room, while the examination room was for health personnel conducting patient interviews and examinations.

 ${\bf Table~1.~Results~of~\it Mycobacteria~\it Tuberculosis~\it Examination~in~the~Air~of~\it Primary~\it Health~\it Care~\it Car$

Area	The Number of Samples	Positive		
Waiting Room	36	18 (6 TB, 12 MOTT)		
Examination Room	36	6 (TB)		
Laboratory Room	36	1 (TB)		

Notes: TB = tuberculosis, MOTT = mycobacterium other than tuberculosis,

The result showed that, of 36 samples, 18 samples examined from the waiting rooms (50%) tested positive, and six samples from the examination rooms (16.7%) also tested positive. In contrast, only one sample from the laboratory rooms (2.9%) was tested positive.

Discussion

Pulmonary TB emerges as a disease transmitted through droplet nuclei from TB patients with acid-fast bacilli (AFB) positive status.¹⁷ When an infected patient coughed, respiratory droplets containing MTB bacteria were released into the surrounding air.¹⁷ If an individual is in the vicinity of these droplets, or if the wind carries them and an individual inhales them, then 10% of this group will develop active TB. At the same time, 90% will become latent carriers. However, those with a strong immune system can eradicate the MTB bacteria.¹

Individuals with weakened immune systems or those influenced by specific risk factors are more susceptible to TB. Several risk factors that can heighten vulnerability to TB include HIV infection, diabetes, the use of immunosuppressive drugs, malnutrition, prolonged exposure to tobacco smoke, crowded and poorly ventilated environments, contact with TB patients, and advanced age¹⁸ Given the high mortality rate associated with TB, and its transmission can be prevented.¹⁷

Preventing TB dissemination includes identifying and treating TB cases, utilizing masks, ensuring adequate ventilation, practicing good hygiene, administering preventive therapy, and promoting public education and awareness. 18

TB is not transmitted through activities such as shaking hands, sharing foods or drinks, touching bed linens or toilet seats, sharing toothbrushes, or kissing one another. When an individual inhales TB bacteria, the bacteria start settling in the lungs and commence multiplying. Afterward, the bacteria enter the bloodstream, and the bacteria start spreading to other body elements (e.g., kidneys, brain, and spine). TB attacking the throat or lungs will likely be transmitted to the surrounding environment. In contrast, TB affecting other body parts (e.g., spine or kidneys) will not be contagious. Those suffering from pulmonary TB have enormous potential to transmit the disease to people spending time together with the sufferers in their daily lives. TB transmission can occur in various settings, including households, workplaces, and health facilities such as hospitals, PHCs, and clinics.

A previous study stated that specific requirements were typically needed for outpatient pulmonary TB care facilities.²¹ First, the waiting room should provide comfortable seating for patients and their families, with ample space to accommodate the number of patients attending. Adequate ventilation is essential to maintain the fresh air and prevent disease transmission. Second, the examination room should have a sterilizable or easily cleanable examination table and essential tools such as stethoscopes, thermometers, and blood pressure monitors. It should also be equipped with a sink or handwashing station for sanitation purposes. Third, the consultation room should be furnished with a desk and chairs for doctor-patient communications. It should be stocked with paper and pens for recording patient medical information.²¹

Additionally, using a computer or electronic record-keeping system to maintain patient records is advisable. Fourth, the laboratory area should be equipped with necessary laboratory instruments like microscopes for examining patient sputum samples, as well as the required chemicals and reagents for conducting analyses. Fifth, the medication storage room should serve as a secure and locked medication storage area.²¹ It should include a working table or medication preparation area and a refrigerator for storing vaccines or medications requiring specific temperature control. Sixth, sanitary facilities should include clean and sterilized toilets and sinks. There should be safe disposal containers for contaminated medical materials and proper sanitation systems to ensure cleanliness and hygiene within the facility.²¹

The standard requirements for pulmonary TB clinics to prevent TB transmission to others include carrying valid identification, such as an ID card or driver's license, wearing a mask while in the pulmonary TB clinic area, cleaning hands with hand sanitizer or washing them with soap and water before entering the clinic, maintaining a safe distance from other patients in the waiting area, informing healthcare personnel if experiencing symptoms such as cough, cold, or other potentially contagious signs, completing and signing the informed consent form for pulmonary TB examination, undergoing sputum examination to determine the presence of MTB bacteria, and following instructions and procedures provided by the healthcare personnel during examination and treatment.⁴

In this study, one of the selected PHCs was located in a densely populated area and had inadequate facilities for its large patient population. All TB patient waiting rooms in three PHCs were shared with other patients, increasing the potential for faster transmission. The waiting room, being the most crowded, had the highest concertation of bacteria. Conversely, the examination room was more conducive to minimizing TB transmission since patients were managed individually, reducing contact. The laboratory with the lowest density had only one out of 36 samples tested positive for TB bacteria.

There was no separation for TB and non-TB patients at three PHCs in this study. This situation poses a considerable risk, as if a TB patient sneezes or coughs, there is limited awareness that MTB bacteria may spread into the surrounding environment, thereby increasing the risk of TB transmission. WHO has set Millennium Development Goals to make TB no longer a social or public health problem by 2030.¹³ However, the findings suggested that without improvements in spatial policies within PHCs, these PHCs could potentially become sources of TB transmission for those seeking care. This could result in a failure to meet the Millennium Development Goals and to eliminate TB as a public health concern.

A total of 12 samples were found positive for MOTT out of 25 positive samples. According to the Global Laboratory Initiative, the NSW Health, and the American Society for Microbiology, the diagnosis of TB involves various tests, including MTB culture, AFB staining, Tuberculin Skin Tests (TST), and rapid molecular tests.^{22–24} The current MTB detection program developed by the Indonesian Ministry of Health in 2020 involves the use of a rapid molecular test device.²⁵ These devices can detect MTB within two hours and determine whether the MTB strain is sensitive or resistant to rifampicin. However, a limitation of rapid molecular test is that it can only detect MTB and cannot identify MOTT. Further extensive study is necessary to confirm these findings, it is essential to consider that patients with MOTT may not receive appropriate treatment, potentially becoming transmission sources to other patients or individuals in their vicinity.

In future studies, reactivating AFB staining in conjunction with a rapid molecular test device could be examined. This approach would allow for a more comprehensive assessment. If the rapid molecular test results are negative but AFB staining is positive, it would strongly suggest that the cause of the patient's illness is MOTT rather than MTB.

Conclusion

The presence of MTB in the air of waiting rooms, examination rooms, and laboratory rooms at three PHCs in Surabaya City, Indonesia, necessitates effective management of these spaces to prevent the transmission of TB. First, it is imperative to establish a governmental policy that mandates separating waiting areas for patients with respiratory infections from those without. Such a measure is essential to achieving the WHO target for TB elimination. Second, given the rise in cases of MOTT infections, there is an urgent need for more comprehensive TB microscopic examinations to ensure timely treatment of MOTT patients. Third, a policy requiring all patients visiting a PHC to wear masks must be instituted.

Abbreviations

TB: tuberculosis; MTB: mycobacterium tuberculosis; WHO: World Health Organization; HIV: human immunodeficiency virus; PHC: primary health care; MGIT: Mycobacterium Growth Indicator Tube; MOTT: mycobacteria other than tuberculosis; acid-fast bacilli: AFB.

Ethics Approval and Consent to Participate

This study was approved by the Research Ethics Committee of dr. Soebandi Public General Hospital (No. 420/2453/610/2023).

Competing Interest

The authors declare no significant competing financial, professional, or personal interests might have affected the performance or presentation of the work described in this manuscript.

Availability of Data and Materials

The primary author can provide all data and materials from this study.

Authors' Contribution

NNJ, EBK, and INT contributed to the design and implementation of the research. NNJ was involved in the data analysis, while EBK provided supervision. NNJ, EBK, and INT were involved in manuscript preparation, content refinement, and administration. All the authors discussed the results and contributed to the final manuscript.

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Health and Environmental Pollution: A Literature Review

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Health and Environmental Pollution: A Literature Review

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Abstract

This study aimed to review various studies focusing on pollution that could adversely affect health, including sources, types, and mitigation efforts. The data used were obtained through a search on the Scopus website using the keywords "Health" AND "Pollution" from 2016 to 2023. Using these two keywords, 72 titles and abstracts of papers were successfully found. The results of this literature review were then analyzed with the assistance of NVivo 12 Pro, which grouped the findings based on their impact on health, reasons for pollution, types of pollution, and preventive measures. It was identified that the most common disease was respiratory disorder. One of the leading causes was vehicle combustion, emitting carbon monoxide due to the incomplete combustion of fossil fuels, such as petroleum and natural gas. This study also revealed that the dominant focus of those studies was on air and water pollution. These studies also indicated that solutions to pollution-causing diseases generally include using renewable fuels, waste management, public health literacy, and adopting electric vehicles.

Keywords: combustion fossil fuels, environment, health, pollution, respiratory diseases

Introduction

Rapid global economic growth and technological advances have modernized human lives, but it has a long-lasting impact on ecology and environmental sustainability. Over the past few decades, the world has experienced increasing emissions of toxic gases, severe global warming, and ambient air pollution. Mass reliance on internal combustion engine (ICE) vehicles has rightly been criticized for increasing air pollution, endangering public health, and facilitating the use of fossil fuels, all of which threaten sustainable development. Fossil fuels, such as petroleum and natural gas, remain the major energy sources that drive the economy and development worldwide. This has negative implications for public health and environmental pollution due to the intrinsic properties of the compounds in fossil fuels, especially petroleum, the most widely used fuel. The primary product in the process of refining petroleum through fractional distillation is gasoline containing aliphatic hydrocarbon compounds, especially n-heptane and isooctane, a few aromatic compounds such as toluene, and very little contains several organic compounds containing nitrogen and sulfur elements originating from anaerobic decomposition of biomolecules, in particular, proteins under sediments during the petroleum formation process.

Burning gasoline completely due to the abundance of oxygen (O₂) produces carbon dioxide (CO₂). The CO₂ can last in the atmosphere for 200 years, and increasingly thick deposits of carbon dioxide gas can cause a greenhouse effect because it can absorb and trap infrared wave heat from the sunlight, thus significantly increasing the earth's temperature, known as the global warming phenomenon. Climate change affects the quantity and quality of food produced, as well as its equitable distribution.⁵ Several lower-middle-income countries, especially those that still have dense forests, gain "benefits" from CO₂ emissions through carbon compensation funds because they contribute to reducing CO₂ emissions.⁶ However, when viewed from the perspective of the human development index, income in rich countries driven by transportation and industrialization produces enormous CO₂ emissions that have an impact on food security and human health, environmental damage, and carbon compensation received by low-income countries are

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very small, which is disproportionate to the tremendous impact caused by CO_2 emissions.⁵ An increase in gross domestic product per capita by 1% will decrease (inelastic) CO_2 emissions by 1.45%. In comparison, an increase in industrialization by 1% will increase CO_2 emissions (elastic) by 1.64% in the long term.⁷ Deteriorating environmental quality, global warming, and climate change pose serious threats to future population, health, and international development.⁷ Environmental pollution increasingly worsens its adverse impacts on human health.⁸

The increasing demand and use of diesel engines in various oil fields cause exhaust gas emissions, such as sulfur dioxide (SO_2), nitrogen oxide (SO_2), nitrogen oxide (SO_2), such as nitrogen monoxide (SO_2), and nitrogen dioxide (SO_2), and carbon monoxide (SO_2), causing severe environmental pollution and dangers such as respiratory problems. Incomplete gasoline combustion due to limited oxygen gas produces carbon monoxide gas. SO_2 0 gas can bind to hemoglobin 200 times stronger than SO_2 1 gas, causing cells and body tissues to experience a lack of oxygen (hypoxia), leading to death. Burning gasoline and diesel, which contain small amounts of organic compounds with a small amount of nitrogen in their composition, produces SO_2 1 gas, which can carry out photochemical reactions, with the final result being the compound peroxyacetyl nitrate (SO_2 1), which can cause eye irritation and respiratory problems. Apart from that, SO_2 2 gas can also carry out a series of reactions, the final result of which is nitric acid (SO_2 2) pollution from burning gasoline and diesel.

Global warming and air pollution due to non-renewable energy sources have long-term negative impacts on human health and the environment. Various solutions must be immediately made to ensure the survival of the next generations on earth. One method being intensively implemented is using eco-friendly renewable energy sources, such as solar energy or biodiesel, one of which is battery-powered electric vehicles. Therefore, they do not produce gas emissions that can pollute the air and damage the environment.¹² Preventive solutions to reducing pollution causing health and environmental problems can be provided through public health literacy. This can start from causes of pollution, household waste management, cultivating the behavior of throwing waste in its place, and greening movements through planting trees. Then, self-awareness emerges in each community member to be jointly responsible for environmental sustainability and a healthier and more prosperous quality of life.

Over the past decades, most researchers have paid much attention to ways to reduce environmental pollution in their regions. Therefore, this has culminated in several approaches and solution models being formulated, ranging from ordinary linear regression, multivariate regression, and Auto-Regressive Integrated Moving Average (ARIMA) to contemporary practices. The model environment was developed to achieve sustainable growth without destroying the environment. These environmental energy models can be classified as dynamic, static multivariate, univariate, or hybrid. Several researchers have investigated the development of energy environmental relations. This study aimed to bibliometric analysis of various studies of pollution having a negative impact on public health and environmental damage, including sources of pollution, types of pollution, the impact of pollution on health and the environment, as well as various solutions offered to overcome pollution problems to create a better life and healthier and more sustainable environment.

Method

This study used secondary data from several studies examining various perspectives on pollution based on impacts on health and solutions that had been attempted to prevent these impacts. The secondary data was obtained through a search on the Scopus website with the keywords "Health" AND "Pollution" from 2016 to 2023 on November 3, 2023. The year range was selected for the phenomenon of extreme air pollution in Jakarta in 2023; in addition, a study stated that Jakarta was the most polluted city in the world.¹⁴ Therefore, the authors are interested in exploring how to further study pollution as information for all parties who play an active role in preventing pollution. These two keywords obtained 72 titles and abstracts in English or Indonesian recorded in the Scopus database. As the primary source for this study, the review was carried out based on metadata information, and 36 pieces of literature were selected. The selection was made after looking at the entire content of the article and selecting based on the aim of this study. The object of this study is to know the various studies of pollution having a negative impact on public health and environmental damage.

In each group, a discussion was carried out, and a subdiscussion with the most literature was selected by linking the literature in that group with an NVivo label in the form of a "notepad," which had a code for the serial number of the literature and the year of publication. With the help of NVivo, the discussion of the results of this study became clearer in connecting each pollution category with health and the literature examining it.

Results and Discussion

Interpretation of the literature review results was mapped with the help of NVivo 12 Pro (v12.1.115-d3ea61) with groupings including impact on the health problem, prevention, reason, and types of pollution (Figure 1).

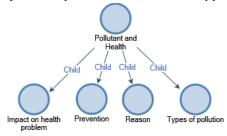


Figure 1. Interpretation of Pollution and Health Studies (Mapped with NVivo 12 Pro)

Based on Figure 1 above, there is a direct and strong correlation between pollutants resulting from various human activities and their negative impacts on human health and environmental damage. Burning fossil fuels is a major source of pollution which endangers health and causes environmental damage. The various types of pollution include land, water, and air pollution.

Types of Pollution

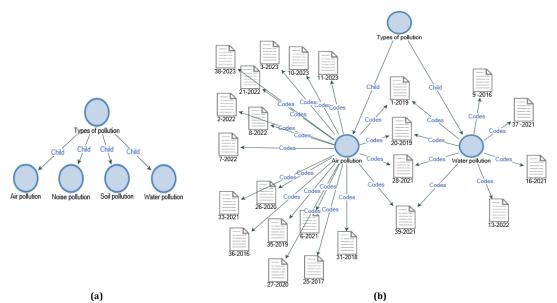


Figure 2. (a) Types of Pollution Impacting Human Health, (b) The Most Common Pollution Occurs and Impacting Human Health

In this study, various information was obtained about the types of pollution that could potentially be dangerous to human health, including air pollution, land pollution, water, and sound or noise. Various studies showed that the most dominant research focuses on air and water pollution (Figure 2). Figure 2 shows 20 studies on air pollution and 8 on water pollution. Studies on air pollution have been the focus of research since 2016 and will increase in number in 2023. These findings concluded that health problems from air pollution have not been completely resolved; in fact, they continue to grow. One of the major causes of air pollution is the rapid increase in the global population and demand for the energy sector. In the end, the use of fossil fuels continues to grow, even carelessly, resulting in greenhouse gases, air pollution, and global warming, which causes ecological imbalance and health risks.¹⁵

One of the potential causes of soil pollution was the occurrence of explosions at landfills caused by volatile organic compounds (VOCs) such as methane and acetone. As hazardous materials are released from landfills, VOCs have been increased to avoid serious health problems for operators, workers, and residents. Foil pollution from landfills has been proven to contain various dangerous organic compounds. Higher concentrations include benzene (3.7 ppm), followed by xylene (1.3 ppm), toluene (0.68 ppm), and ethylbenzene (0.61 ppm). Benzene emissions are the largest cause of concern at the landfills studied due to their carcinogenic properties and impact emissions exceeding acceptable limits. Given the

harmful effects of aromatic compounds such as benzene, toluene, and xylene, although their dangerous concentrations are not high compared to other gases in dump sites (less than 1% of the total volume), the most commonly observed VOCs in the air around the area are toxic, and in some cases carcinogenic, and will have a critical impact on air quality in the region.¹⁷ Air pollution is usually caused by chemical compounds resulting from burning fossil fuels. Chemical compounds like CO and NOx gas can harm human health. Chemical compounds, such as CO₂, SO₂, and NO₂, can cause environmental damage due to acid rain and global warming.¹⁸

Impact on Health and Environment Problems

This study found that the most common disease was respiratory disorder. Respiratory disorder is the most dominant cause and has been studied for a long time since 2016. They would still be the main notion of discussion on the impact of pollution until 2023 (Figure 3). Respiratory problems have also been a peak problem during the COVID-19 pandemic. Anthropological sources were responsible for respiratory and cardiovascular diseases; hence, restricting social activities was the solution taken when a pandemic occurred.¹⁹

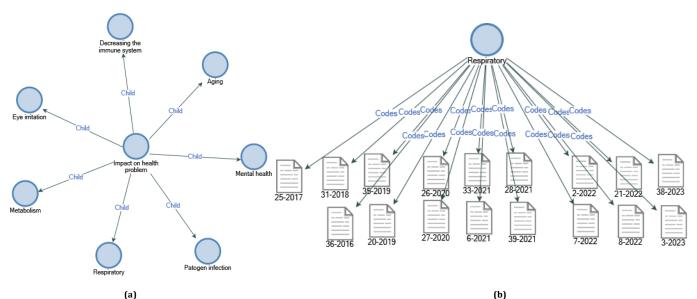


Figure 3. (a) Various Health Impacts of Climate Change, (b) The Most Common Diseases Caused by Environmental Pollution

 CO_2 gas can cause a greenhouse effect, and global warming can be understood through spectroscopic studies of the vibrational, rotational, and translational movements of CO_2 molecules. CO_2 molecules with asymmetric vibrations have one shorter and longer bond. Asymmetrical vibrations are active in infrared radiation because there is a change in dipole moment during vibration. Infrared radiation of 2,349 cm⁻¹ excites asymmetric vibrations. The asymmetric vibration of 2,349 cm⁻¹ is in the center of the absorption band (red, 2,100 – 2,400 cm⁻¹) as a heat radiation band, so it can act as a greenhouse gas that causes global warming and climate change.²⁰

Climate change has been proven to impact health, increasing pollution and stress.²¹ For the global warming concern in developed countries, the United States, for example, designs urban areas to include more plants to reduce heat-related deaths.¹⁵ This condition is due to the ocean heat waves associated with the urban heat island effect, which can increase environmental temperatures in urban areas and is exacerbated by higher population density and more pollution, thereby posing a severe threat to population health with an increased risk of death.²² Growing concerns about global warming, coastal pollution, and microbial contamination of live or raw seafood are known based on the detection of pathogenic bacteria *E. coli* in American oysters in South Texas waters, which humans then consumed.¹⁶ Pollutants in waters are caused, among other things, by the impact of pesticides and chemical fertilizers, which have severe implications for human health, as well as increasing concerns about environmental pollution originating from modern agricultural practices, such as increased greenhouse gas emissions and water contamination.²³

Climate change also impacts increasing volatile organic compounds (VOCs), which are most commonly observed in the air around these toxic locations, and in some cases carcinogenic, and would have a critical impact on air quality in the region. The most extreme effect of global warming is a determinant in the incidence of hematological malignancies among black anemia patients. Motorized vehicles and industrial activities are the largest contributors to carbon

dioxide (CO₂) gas emissions, which reduces the environment, health, and air quality.²⁴ One of the causes was vehicle combustion, which produces CO gas. The gas released by cars was caused by incomplete combustion of fossil fuels, such as petroleum and natural gas. Carbon monoxide is a deadly gas without color, smell, or taste. Inhaling carbon monoxide causes serious injury to the brain, heart, and other vital organs. Respiratory insufficiency due to carbon monoxide poisoning increases troponin-I, creatine kinase-MB fraction levels, and carboxyhemoglobin.¹⁸ CO gas can coordinate bonds with the central Fe atom in the porphyrin ring of hemoglobin 200 times stronger than the coordination bonds of the central Fe atom in the porphyrin ring with O₂ gas, which causes the supply of oxygen gas to cells and body tissues to be very limited so that symptoms of hypoxia can occur causing death.¹⁹

The combustion reaction of fossil fuels containing organic compounds, one of whose components is the element nitrogen, produces NO gas, which can be seen in the color of the leaves that turn brown. Furthermore, NO gas can undergo an oxidation reaction to produce NO_2 gas. The NO_2 gas undergoes a photochemical reaction with ultraviolet rays from the sunlight to produce NO gas and oxygen radicals. Oxygen radicals (0.) are very energetic and react very easily with O_2 to form ozone (O_3). The ozone formed then reacts with double bonds in unburned hydrocarbons in motor vehicle engines, NO and O_2 , to produce compound PAN, which can cause irritation and pain in the eyes as well as various respiratory problems, such as shortness of breath, asthma, coughing, and others.²⁰

 NO_2 gas can react with H_2O molecules to produce HNO_3 , which dissolves and falls with the rain, causing acid rain, which can cause groundwater to become acidic, causing plants to die. All biota that live in water also die because they cannot survive in acidic water, and iron corrosion accelerates, which causes massive damage to buildings and other infrastructure. Acid rain can also be contributed by SO_2 pollutants oxidized to SO_3 and then react with sulfuric acid to produce pyrosulphuric acid $(H_2S_2O_7)$, which dissolves in water and produces sulfuric acid (H_2SO_4) .

Reason for Health and Environment Problems

The literature review revealed industrial and motor vehicle pollution (Figure 4). Several studies even showed that both factors were the main disadvantages in one study. These findings indicated that industrial activities and various oil-fueled vehicles predominantly cause health-related pollution.

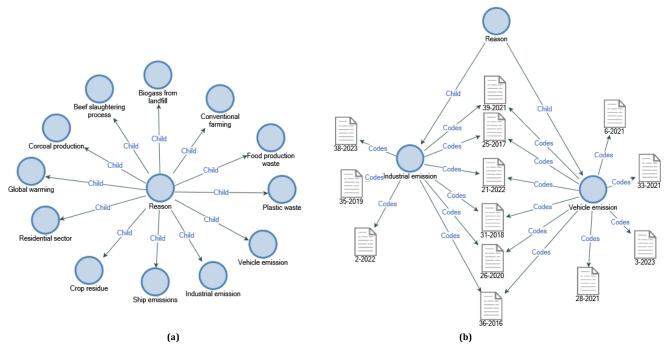


Figure 4. (a) Various Factors Causing Health Problems from Environmental Pollution, (b) The Most Dominant Source of Pollution Impacted Health Problems

Oil fields were found to be one of the factors resulting in the impact of disease on the community (Figure 4). Exhaust gas emissions, such as NO_x and CO, cause serious environmental pollution and dangers like global warming and respiratory problems. Many compounds in the form of greenhouse gases are also produced by water transportation. Used vehicle ships have the highest fuel consumption per ship, followed by general, cargo, and passenger ships.²² The most frequent cause was transportation activities using oil fuel.

Sea water pollution impacts increasing water temperatures, showing a positive correlation with the proliferation of *E. coli*, which implies the effect of global warming and heat waves on the development and severity of oyster disease worldwide.²³ The next factor of charcoal production in soil should be addressed because it significantly increases soil pH, base saturation percentage, electrical conductivity, exchangeable base cations, and available P at charcoal production sites compared to the surrounding soil. Not only does the addition of charcoal produced during production affect nutrition, but it also affects the population and activity of microbes in the ground, including microbial interactions and habitat modification.²⁴

Prevention and Solution of Health and Environment Problems

Studies stating solutions to disease-causing pollution mostly include renewable fuels, waste management, public health literacy, and the use of electric vehicles (Figure 5).

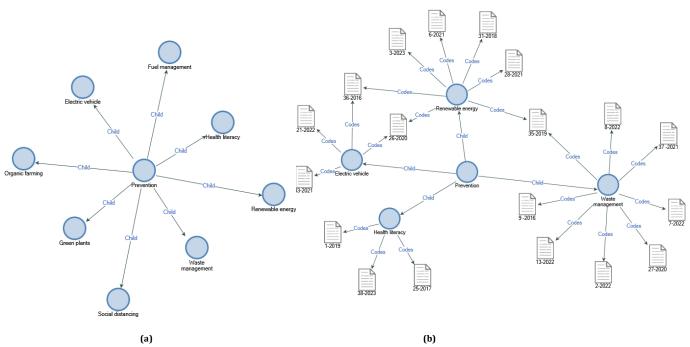


Figure 5. (a) Various Alternative Solutions to Prevent the Impact of Pollution on Health, (b) Most Discussed Solutions to Prevent the Impact of Pollution on Health

Waste management is an effort to reduce emissions, and increasing biogas to biomethane is technically exciting. Since then, biomethane has been intended to be injected into the national gas grid or used as vehicle fuel. Biomethane is a versatile renewable fuel which can replace fossil natural gas and be used in combined heat and power (CHP) systems, distributed over small local gas networks, dedicated to public transport, or converted into hydrogen. In addition, vehicle biofuel produced from waste meets the European Union's requirements to reduce greenhouse gas emissions by up to 60% compared to current fossil fuels. 18

One of the most appropriate solutions to overcome health problems and environmental damage caused by pollution from burning fossil fuels is eco-friendly renewable energy. The sunlight, which provides enormous energy, must be utilized using solar panels to store and distribute energy for industrial operations and household needs. Biodiesel or bioethanol obtained through the extraction of certain plants, such as sugar cane, can be explored to obtain an energy source that produces quite a lot of heat. Genetic engineering can also continue to be pursued by engineering the sucrose synthase enzyme so that microalgae can divert sucrose production to form more triglycerides that can be used as alternative fuel.² Mahua biodiesel blend is considered a safe renewable fuel for conventional engines because it increases energy efficiency. Mahua biodiesel mixed with n-butanol is used as test fuel in traditional engines. Mahua has a regular biodiesel-burning period. Mahua Biodiesel contains antioxidants, which makes it an environmentally friendly fuel.⁴

Solutions are starting to be developed in the form of electric vehicles (EVs). In addition to environmental benefits,

when compared with ICE vehicles, EVs have several advantages, including lower operating costs, less interior noise and vibration, low-speed acceleration, a convenient charging system, and zero exhaust emissions. They can also provide a great boost to the vehicle, economic, and industrial competitiveness by attracting investment in developing countries.⁶ In addition, electric vehicles are an environmentally friendly alternative to conventional vehicles with high emissions. The key is the success of encouraging the adoption and diffusion of electric vehicles in developing countries, which must continue to be identified and evaluated for efficiency and performance optimization.²⁰

Natural resources can be an important element in reducing various health risks. For example, increasing forestry activities can reduce environmental pressure by increasing forest capacity, thereby reducing health problems by providing cleaner air. Accordingly, a process consisting of three parts: increasing natural resources, reducing environmental pollution, and improving the quality of health is hypothesized to help reduce health spending and increase the efficiency of health spending.⁸

Organic farming systems can contribute to reducing production costs and increasing energy efficiency but are limited in reducing certain forms of environmental degradation. It is important to consider other alternatives to manage soil health and productivity, reduce environmental degradation, and mitigate global warming, ozone layer depletion, and climate change. This can ultimately play a significant role in overcoming the problem of climate change and its challenges.¹⁹

One of the advances in pollution prevention is technology-based, human-centered environmental design, including (1) using the core perspective of data mining, human-centered through AI, which investigates new visual phenomena occurring in the context of Web 4.0, as well as cross-border linkages and multidimensional characterized by graphic images; and (2) after correction, Web 4.0 shows that the same metric information can be found between exterior predictions and images correlated with pore structure, as shown in three-dimensional (3D) scenarios.⁷

An effort to avoid risks due to air pollution is made through sensitivity analysis by measuring the concentration of benzene in workers' breath, which is considered the most important factor for measuring carcinogenic and non-cancer risks. Therefore, active protective measures are important to reduce workers' exposure to risk factors. The implementation of personal protective equipment, specifically designed to eliminate the administration of inhaled VOCs and fit testing for each worker, is recommended. In addition, preventive steps to reduce the potential for workers to be exposed to carcinogenic compounds require reducing working hours or occasionally changing working hours, rotating workspaces from one location to another sequentially. Moreover, regular biological monitoring of metabolite compounds needs to be carried out in order to scientifically ascertain the level of danger that can be caused by exposure to these carcinogenic compounds.¹⁸

Conclusion

The use of fossil fuels is the main source of air pollution, which can cause health problems, especially respiratory problems due to CO, NO, NO_2 , and SO_2 gases, as well as environmental damage, especially global warming due to CO_2 emissions. Some solutions to eliminate pollution that causes health problems and environmental damage include using renewable fuels, waste management, public health literacy, electric vehicles, reforestation, and tree planting movements. As a policy recommendation, the government must provide an environment supporting clean and renewable energy technologies for residential, commercial, and industrial purposes to reduce environmental pollution and its impact on health.

Abbreviations

ICE: Internal Combustion Engine; VOCs: Volatile Organic Compounds; EVs: Electric Vehicles.

Ethics Approval and Consent to Participate

This research does not require approval by the ethics committee because it is a research study of secondary data (literature study)

Competing Interest

The authors declare that there is no conflict of interest.

Availability of Data and Materials

Data is available when requested

Authors' Contribution

Conceptualization, methodology, and data analysis, EY, ID, and FADN; writing—original draft preparation, EY; resources, writing—review and editing, EY, LASM, ID, FADN, and A. All authors have read and agreed to the published version of the manuscript

Acknowledgment

Not applicable.

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Capitation Management Through Performance-Based Capitation Mechanism of Primary Health Care in Malang, Indonesia

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Abstract

Primary health care (PHC) has one of the largest funding sources, capitation, which BPJS Healthcare Security transfers monthly. Capitation fund receipts were frequently insufficient due to failure to meet performance-based capitation/*Kapitasi Berbasis Kinerja* (KBK) targets, including for PHC in Malang City, Indonesia. This study aimed to examine the management and utilization of capitation funds through a KBK mechanism. This descriptive study used a qualitative approach supported by quantitative data. This study was conducted from July to August 2023 and purposely selected nine informants from BPJS Healthcare Security, the local health office, and PHC. The interviews were transcribed verbatim and analyzed using a thematic analysis approach. Three themes were identified from data analysis: revenue allocation, utilization allocation, and budget expenditure appropriateness. The use of capitation follows the Mayor's regulations, which allocate service and operational costs. However, remaining capitation funds always occur due to unavoidable conditions. Separating accounts between capitation and other funding sources is necessary to track capitation utilization. Therefore, BPJS Healthcare Security needs to participate in capitation reporting and monitoring.

Keywords: capitation, management, performance-based capitation, primary health care

Introduction

Indonesia is a middle-income country that has implemented reforms to achieve universal health coverage (UHC) through the National Health Insurance (NHI) since January 1, 2014.¹ The goal of UHC, according to the World Health Organization, is that countries must provide access to essential health services to the public without financial hardship, and strengthening primary health care (PHC) is the most effective way to address it.² PHC plays a role as the gatekeeper, which is the first-level health facility to control the referral system in healthcare.³ The fundamental duties of gatekeeping are regulating health expenditures, lowering the need for hospitalization and specialized treatments, and enhancing the quality of life and satisfaction of patients.⁴,5

Over half of the PHC budget was funded by the BPJS Healthcare Security, almost entirely through capitation.⁶ Prospective capitation payments for PHC providers and organized referral systems were intended to promote efficiency and effectiveness in service delivery as well as access to health care.⁷ Capitation payment is based on the number of patients registered to PHC without considering the type and amount of health services provided.⁸ BPJS Healthcare Security issues a regulation on instructions for implementing performance-based capitation/*Kapitasi Berbasis Kinerja* (KBK) payments to ensure PHC continues to perform optimally.^{9,10} The KBK mechanism is tied to three performance indicators: contact rate, non-specialist referral ratio, and controlled Chronic Disease Management Program/*Program Pengelolaan Penyakit Kronis* (Prolanis) participant ratio, with targets of $\geq 150\%$, $\leq 2\%$, and $\geq 5\%$ respectively, affecting the amount of capitation.⁹

The contact rate reflects the proportion of NHI enrollees who receive individual services and community health appointments outside the PHC, and the number must be at least 150 per million people in a month. The non-specialist

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Received: February 5, 2024 Accepted: July 3, 2024 Published: July 31, 2024 referral ratio determines the percentage of patients referred for non-specialistic cases. This indicator means to ensure that the referral system is implemented according to medical indications and competence. The threshold of the non-specialist referral ratio was a maximum of two non-specialist referral patients per month. The last indicator, the controlled Prolanis participant ratio, depicts the number of patients involved in the program with stable conditions according to the medical examination. Prolanis addresses NHI enrollees with hypertension and type 2 diabetes mellitus, as these two diseases are considered the major causes of mortality and disability in Indonesia and have the largest burden of disease covered in the NHI. 11,112 The threshold of this indicator was at least 5 per 100 patients.

A previous study found that PHC in Malang did not consistently meet the KBK performance indicator targets. Consequently, the capitation rate was lower than the stated minimum standard capitation rate. In contrast, granting higher capitation payments did not compensate the First Level Health Facilities/*Fasilitas Kesehatan Tingkat Pertama* (FKTP) for exceeding the targets. Lech PHC received a different amount of capitation funding. According to the financial data from Malang City Health Office, the amount of capitation funding for each PHC varies substantially, with the difference between the PHCs getting the lowest and greatest capitation being nearly two to three times bigger. However, the realization of capitation fund expenditure in 2021 was only around 34 to 78% based on PHC financial data obtained from preliminary interviews.

A prior study regarding capitation management only discussed the comparison of capitation management between PHC, private general practitioners, and private primary clinics. However, no qualitative study has been conducted on managing capitation funds associated with the KBK mechanism, especially using PHC-level data. To fill this gap, this study aimed to examine the capitation fund management and utilization through the KBK mechanism on PHC in Malang City, Indonesia.

Method

This study was conducted in July–August 2023 and selected purposively three PHCs: Janti, Dinoyo, and Cisadea PHCs, to represent PHCs in different subdistricts in Malang City, Indonesia. Qualitative data were collected through semi-structured interviews. Two key informants from Janti PHC were the assistant expenditure treasurer and the NHI treasurer. Three informants from Cisadea PHC were interviewed: the assistant reception treasurer, assistant expenditure treasurer, and Technical Activity Executive Officer/*Pejabat Pelaksana Teknis Kegiatan* (PPTK). PPTK is a position at the PHC responsible for controlling the implementation of activities, reporting the progress of implementing activities and preparing budget documents for the costs of implementing activities. Two informants from Dinoyo PHC, the assistant reception treasurer and PPTK, were interviewed. Quantitative data were collected from BPJS Healthcare Security regarding the achievement of the KBK among the three indicators from 2021 to 2022. Realization of capitation income, expenditure (service and operational cost), and excess of budget calculations/*sisa lebih penghitungan anggaran* (SiLPA) were also gathered from PHC. Since this study examined the use of capitation funds during the COVID-19 pandemic, the contact rate indicators were seen based on face-to-face services and telemedicine.

Results

This study included nine informants involving the Head of the Benefit Guarantee and Utilization Section of BPJS Healthcare Security of Malang City (Informant-1), the Head of the Finance Sub-division of the Malang Local Health Office (Informant-2), the Activities Technical Implementation Officer of Cisadea PHC (Informant-3), Expenditure Treasurer of Cisadea PHC (Informant-4), Revenue Treasurer of Dinoyo PHC (Informant-5), Expenditure Treasurer of Dinoyo PHC (Informant-6), Activities Technical Implementation Officer of Dinoyo PHC (Informant-7), Expenditure Treasurer of Janti PHC (Informant-8), Revenue Treasurer of Janti PHC (Informant-9). All informants were engaged in managing capitation funds from diverse stakeholders. Therefore, the information acquired was sufficiently thorough to determine how capitation funds were managed. Three themes emerging from in-depth interviews included revenue allocation, utilization allocation, and budget expenditure appropriateness.

Theme 1: Revenue Allocation

Registered Participants

The number of participants registered at the PHC varied from one to another. The size of the population in coverage areas of the PHC influenced the number of registered participants, impacting the amount of capitation received. The PHC

stated they could not determine the number of participants, especially for the non-subsidy beneficiaries' membership, because they could change their FKTP every three months. Therefore, the quality of services the PHC provides could influence participants to move their FKTP to attain a greater volume of capitation revenue.

"We actually cannot determine the number of participants... We ask for a lot, it's impossible because it's the patient's rights. Patients can move every three months..." (Informant-4)

Capitation Rates

The availability of doctors influenced the capitation, with a doctor-to-participant ratio of 1:5000. The fewer doctors, the lower capitation rates would be received, and vice versa. Problems arose due to frequent transfers of doctors. Malang City Health Office redistributed doctors to meet the need for the number of doctors in every PHC.

"Now it has been balanced, according to the position map. If the primary health care lacks the number of officers, at least it has been filled with the position map. Oh, this is not enough [of officers], oh it needs [some officers], oh this also needs [some officers], we are then rolling [their position]. Besides, one of them wants to be promoted [to a higher position]. The rolling [is done] to those who need it. Well, now almost all of the PHCs have completed their accreditation; so, at least, administratively, they are in compliance." (Informant-2)

Performance-Based Capitation

BPJS Healthcare Security has amended the regulations governing capitation. The interviews revealed that the PHC treasurer did not know how to calculate the results of the indicators in detail. The degression of capitation funds mattered for PHC, especially for them with high capitation funds. For example, if the contact rate indicator was not achieved, it could lose more than 10 million in capitation revenue.

"KBK will encourage each FKTP to have optimal KBK performance so that the capitation obtained is greater than FKTPs that have fewer performance reports. The Performance Report will improve the quality of FKTP services for National Health Insurance participants" (Informant-1)

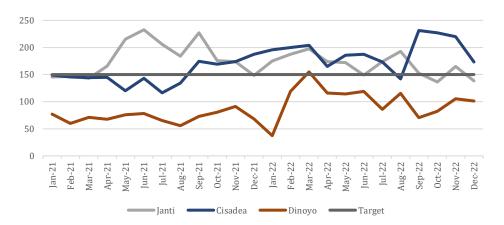


Figure 1. The Achievement of the Contact Rate Indicator in 2021 and 2022

To better understand the contact level indicators, Figure 1 shows the achievements of three PHCs from 2021 to 2022. Janti PHC mostly exceeds targets but experiences a decline at the end of the second year. This was also a reason why the Janti PHC's capitation revenue was reduced in December 2022. The Cisadea PHC tends to be below the target at the start of the first year but then increases. Meanwhile, the Dinoyo PHC has not achieved its target, especially in the first month of the second year. However, it starts to increase until it exceeds the target in March 2022 and falls.

"Yes, services [provided] outside the building [is] like integrated health care. We do input the BPJS Healthcare Security numbers. That is why we get a lot from integrated health care. Every time we have an activity or a home visit, we note down the BPJS Healthcare Security guarantee program." (Informant-4)

According to all PHCs, the contact level indicator was intended to provide services to participants, even if they did not visit the PHCs. Services can be provided through home visits, community group activities, and online consultations. If the contact rate indicator is only measured in the form of patient visits, then the indicator target will be difficult to achieve.

To improve service delivery in the building, the PHCs carry out internal referrals, such as visits to pregnant women and nutritional counseling.

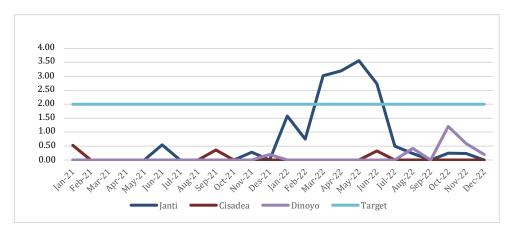


Figure 2. The Achievement of Non-specialist Referral Ratio in 2021 and 2022

In contrast to the previous indicators, Figure 2 illustrates the achievement of a non-specialist referral ratio below the target. All the PHCs tended to maintain their performance within two years. They were aiming for a zero non-specialist referral ratio within a few months. Even though there had been an increase, it was still below the threshold. Janti PHC exceeds the threshold from March to June 2022 but can still pass the limit.

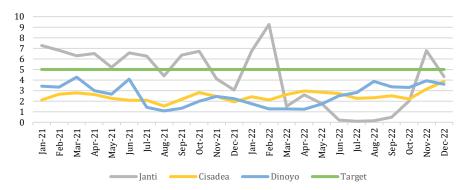


Figure 3. The Achievement of the Last Indicator of Performance-based Capitation in 2021 and 2022

Cisadea and Dinoyo PHCs did not reach their targets for two years, resulting in them not reaching 100% of capitation income. Janti PHC experienced fluctuations in achieving a controlled ratio of Prolanis participants. Apart from not achieving the contact rate indicator, the controlled ratio of Prolanis participants is also the reason why Janti did not receive full capitation in December 2022. In their interview, they said that deflation at the end of the year was due to busy activities.

Theme 2: Utilization Allocation

The three PHCs in this study have been registered as Regional Public Service Agency for Primary Health Care (RPSAPHC) since 2019, and their capitation payments are referred to funds because capitation is one of their funding sources. Following Malang Mayor Regulation Number 4 of 2016, capitation income is combined with other levy funds in one account.¹⁶

"It is not purely for capitation itself. It is because capitation is one of the sources of the Regional Public Service Agency for Primary Health Care funding." (Informant-4)

"...what is capitation called, it is recognized as Regional Public Service Agency for Primary Health Care income, so it is spent for activities under the Regional Public Service Agency for Primary Health Care." (Informant-6)

Utilization Allocation for Service Cost

The use of capitation funds for service costs is regulated in the Indonesian Ministry of Health Regulation Number 6 of 2022.8 The service payment quota is at least 60% of the capitation fund receipts. The allocation of costs for PHC services for the current year is based on capitation estimates for the previous two years. Service fees for each officer vary. Factors determining the amount of service include the type of staff or position and their presence.

"So, this is a bachelor's degree, [this is] a master's degree, each has its own points. The head of PHC owns points, the treasurer owns points, new civil servant owns points. Later, there will be a period of work. There is also a presence there. It is all there, at that service cost point" (Informant-2)

Table 3. Utilization Allocation for Service Cost of the Primary Health Care in 2021-2022

РНС		2021		2022			
	Revenue	Service Cost	%	Revenue	Service Cost	%	
Janti	USD 174,475.89	USD 74,048.61	42	USD 155,269.91	USD 166,896.50	75	
Cisadea	USD 87,768.52	USD 48,059.60	55	USD 82,010.42	USD 51,140.42	62	
Dinoyo	No record			USD 132,585.73	USD 76,510.75	58	

Notes: PHC = primary health care, USD = United States Dollar (1 USD = IDR 16,230.20)

In accordance with the Indonesian Ministry of Health Regulation Number 6 of 2022 concerning the use of capitation funds, a PHC allocates a minimum of 60% of capitation revenue.⁸ The table above shows that the PHCs used capitation funds under the provisions in 2021. However, the use of capitation funds at the Janti and Cisadea PHCs exceeded the threshold (\geq 60%) in 2022. The variables of officer's type and attendance influence the increase in the use of capitation funds for service costs. The transfer and addition of health personnel at the PHC affect the cost of services.

Utilization Allocation for Operational Cost

Allocation of capitation funds to support operational costs for health services, including medicines, medical devices, consumables, and health service operational activities. The allocation for operational cost support was a maximum of 40% of capitation revenue. PHC allocated more of these funds to operations and maintenance. Expenditures in this allocation were divided into expenditure on goods and services for purchasing current assets and capital expenditure for purchasing fixed assets. Promotional and preventive activities did not use capitation funds because they were limited.

"[It takes] 40% for operations. There are various operations for routine payments, electricity, water, and telephone. Specifically for cleanliness, we use cleaning service; and for security, we also use a professional third party with the same staff. Since we did not have a driver with civil servant status, we finally recruited one person from a third party. The biggest expense is for maintenance. Our pharmacy turned out to be no longer suitable for us to maintain, so we finally moved it. This means it already exists. You just have to repair it according to pharmacy standards. Then, in the end, I could not buy anything." (Informant-7)

Table 4. Utilization Allocation for Service Cost of the Primary Health Care in 2021-2022

	2021				2022				
	Medical device,				Medical device,				
PHC	Revenue	medicine,	Operational Cost	%	Revenue	medicine, consumable	Operational Cost	%	
	a	a consumable goods c		(b+c)/a	a	goods	C	(b+c)/a	
		b				b			
Janti	USD 174,475.89	USD 79,897.28	USD 79,897.28	92	USD 155,269.91	USD 61,294.42	USD 61,294.42	79	
Cisadea	USD 87,768.52	USD 8,123.22	USD 16,215.43	28	USD 82,010.42	USD 9,895.72	USD 3,988.34	17	
Dinoyo	No record				USD 132,585.73	Other funding sources	USD 37,405.65	28	

Notes: PHC = primary health care, USD = United States Dollar (1 USD = IDR 16,230.20)

Cisadea PHC expenditure allocation was in accordance with provisions (<40%) in 2021 and 2022. Dinoyo PHC used capitation payments solely for operational purposes (i.e., 28% of the total money allocated); additional funding sources were used to cover costs associated with consumables, medications, and medical equipment. Janti PHC spent much more than the maximum amount on medical equipment, medicines, consumables, and operations.

Obstacles

There were several obstacles to the use of capitation funds at PHCs. The first was related to human resources. PHC lacked human resources as they also carried out service duties to patients. Second, in carrying out procurement, the PHC

must go through a procurement service agency. The agency recommends prioritizing domestic purchases. Meanwhile, more medical goods are being produced overseas. PHCs were uncertain about taking risks and worried about the quality of service. Therefore, they continued to try to buy foreign products even though it takes a long time.

"The problem is that [the number of] our team is insufficient since we also provide care to patients. Our main task is [all about] services. From medical personnel, from finance [staff], we lack the human resources." (Informant-9)

Third, PHC still used one account for several RPSAPHC funding sources. Using one account made it difficult to track the realization of expenditures. Last, regulations of Malang Mayor concerning the use of RPSAPHC funds are still limited. While the scope of RPSAPHC funds is quite broad, several areas have yet to be regulated. 16

"We have one obstacle: we do not have all the Regional Public Service Agencies for Primary Health Care requirements yet. There is only one thing: the use of Regional Public Service Agencies for Primary Health Care funds. Even though there are around 13 regulations that have to be made this year, starting last year, we have started making them in installments." (Informant-7)

Theme 3: Appropriateness of Budget Expenditures

The use of capitation funds does not always conform with initial plans. The flexibility of RPSAPHC enables changes in budget use. However, the use of capitation invariably left SiLPA behind.

The Flexibility of Regional Public Service Agencies for Primary Health Care

All PHCs in Malang have been registered as RPSAPHC. The funding cannot be differentiated, making it easier for the PHC to manage it. In accordance with existing regulations, PHC can choose which activities or expenses will be paid for and which financial sources will be used. Even though they are flexible in handling finances, all the PHCs stated that they had not completely switched to the RPSAPHC since some expenses were still borne by the local Health Office and were reported. Meanwhile, BPJS Healthcare Security advised that capitation should be used to improve the quality of services through improving infrastructure and adding medical personnel.

"So, that is why we say it is not yet full because there are some costs still covered by the local Health Office." (Informant-8)

SiLPA

SiLPA is the excess difference between the realization of budget income and expenditure during one budget period. The first reason SiLPA ended was that health facilities had to provide medical equipment and medicines to treat health problems that had not arisen for a long time, so the planned medicines and medical devices could not be absorbed. The second reason was the difference in market prices. Market prices are usually lower than those budgeted by the Regional Government Information System. Purchases of goods and services can still be used to increase the number of goods, but not for purchasing capital goods. The use of SiLPA funds must follow the allocation in the previous year.

"Once the budget absorption process begins, suppliers may get offers, and the price will undoubtedly fall. It is impossible to buy above price. You can still buy goods and services in large quantities. Yes, the volume can be increased a little, but not for capital expenditure. That is what SiLPA is asking for." (Informant-3)

Discussion

Capitation is the monthly payment paid in advance to PHC based on the number of registered participants without considering the type and amount of health services provided. The amount of payment to the PHC is determined based on an agreement between BPJS Healthcare Security and regional health facility associations regarding standard rates set by the Health Minister.⁸ If no agreement is reached regarding the amount of payment as intended, the Health Minister shall determine the amount of payment for the health insurance program provided.

By implementing a capitation payment system at PHCs, the health service system aims to promote cost-effective services, improve preventive and proactive management, advance coordination for services, and optimize public health outcomes. The system encourages health professionals to take a holistic approach to patient care and manage resources efficiently to achieve better health outcomes for the enrolled population. However, capitation has weaknesses that could be detrimental to participants, leading to underhandling of primary services, underutilization, and referral of non-specialist cases to hospitals.¹⁷

KBK has a domino effect on the progress of PHC. Quality is demonstrated by comparing the quality index values achieved by the PHC group with and without CBC. The performance of PHCs implementing the KBK is superior to that of non-KBK PHCs in increasing participant access. In 2016, the number of registered participants per mile at the KBK PHCs who made contact was 54 people; while, at the non-KBK PHCs, it was only 44 per mile. This study showed a difference in contact rates between Janti and Cisadea PHCs that reached 10 per mile. In addition, there was efficiency due to a decrease in referral rates by 1.4%, thereby reducing outpatient and inpatient admissions. BPJS Healthcare Security data for 2019-2020 also shows an increase in primary service performance after the implementation of the KBK. Compared to 2017, there was an increase in the utilization rate of primary health services by 12.5% in 2019. In addition, there was an improvement in the referral system, as seen by a decrease in the number of referrals to hospitals by 2.3% from 2018 to 2020.¹⁹

The contact rate is an indicator showing a commitment and concern for PHC for the NHI participants' health. The contact rate was measured based on the ratio of registered participants contacting PHC, with the total number of registered participants in PHC multiplied by 1,000. Actions to increase the number of contacts between primary services and NHI participants can be carried out in various activities, both outside and inside the building, offline and online.⁹

The success in achieving contact numbers at the Janti and Cisadea PHCs was due to the availability, commitment, and innovation of their human resources. The availability of human resources has an important role in achieving contact rates since most contact rate activities are carried out outside regular medical services. Human resources must also be supported with adequate facilities, such as transportation and field equipment. ²⁰ Innovation by the Janti and Cisadea PHCs to increase the number of contacts in the building is by making internal referrals for participants deemed to need other services.

Meanwhile, to increase the number of contacts outside the building, the PHCs actively contacted participants through Integrated Health Care activities, home visits, and school visits. The digital technology also enabled telemedicine services for participants with limited PHC access. The role of administrative staff was also crucial in increasing the contact rate because, without good data collection, the contact rate would not be recorded in the P-care system. Therefore, officers who understand the P-Care system well and carried out regular records will greatly contribute to achieving contact rates.

The influential factor in the failure to achieve the contact numbers was the use of capitation funds for operational costs on health services, which did not fully support outside-of-the-building services. Also, they were part of small and medium enterprises, including promotional and preventive activities.²¹ This was experienced by the Dinoyo PHC, which did not reach the contact number target since the operational funds originating from capitation were used for pharmacy maintenance, making them unable to buy other needs.

Several factors cause a high ratio of non-specialist referrals in PHC.²² The first factor was the lack of PHC efforts to foster confidence in PHC's competence in handling non-specialist cases and participants coming to ask for hospital referrals. Support for doctors to handle non-specialist services optimally also influenced the number of non-specialist referrals. Due to a shortage of human resources, a PHC often assigns doctors to other services. Therefore, doctors could not fully focus on providing non-specialist curative services. Procurement of medicines and medical equipment for non-specialist services is also affected because patients prefer to ask for hospital referrals if medicines and medical equipment for non-specialist services are unavailable.

The three PHCs were able to meet the non-specialist referral ratio below the maximum limit required by BPJS Healthcare Security because they could resolve the above obstacles well. This obstacle could be resolved by special team monitoring programs that could reduce non-specialist referrals. Hence, communications with the community, human resources, and the availability of medicines and medical equipment can be fulfilled and carried out well.

Based on BPJS Healthcare Security data, most PHC services in Indonesia have not reached the target indicator of controlling the ratio of Prolanis participants, as experienced by the three PHCs in this study. Based on a study by the Bantul District Government, the target of controlled Prolanis participants that was not achieved was the participants' discipline in carrying out routine treatment and taking medication regularly. Indiscipline in routine control and treatment is caused by not feeling the symptoms and being busy with work. As a service in Indonesia have not reached the target indicator of controlling the ratio of Prolanis participants, as experienced by the three PHCs in this study. Based on a study by the Bantul District Government, the target of controlled Prolanis participants that was not achieved was the participants' discipline in carrying out routine treatment and taking medication regularly. Indiscipline in routine control and treatment is caused by not feeling the symptoms and being busy with work.

Seeing these obstacles, it is necessary to have a different approach to encourage participant discipline in carrying out consultations and taking medication regularly. One of the successful efforts made by the Mlati III PHC in Sleman District is by providing a special waiting room and integrated services from patient entry to exit, providing advice on consultations

outside of working hours and reminder notifications for participants to carry out monthly consultations and take medication reminder.²⁴

However, the importance of the controlled Prolanis participant ratio is that participants had stable conditions. This was proved by the result of monitoring health status.²⁵ Accordingly, PHC should be more thorough in putting the data into the P-care system.²⁵ However, the problem was the lack of staff for data entry into the P-care system. Another study showed that entering the data was hindered by a server that frequently had errors and was slow.²⁶

Three main obstacles were found in the utilization of capitation funds. First, the capitation account was the same as other fund accounts, making it difficult to track the allocation of fund flows. Second, providing capitation objects with civil servant status was detrimental to PHC due to limited human resources. Third, procurement of goods must prioritize domestic purchases, while most health products needed were produced abroad. Separation of accounts between capitation funds and other funds must be carried out immediately so that recording and reporting of capitation funds can be done better.

The use of capitation funds and Health Operational Assistance must not overlap. Referring to the implementation of capitation fund management at the Bajulmati PHC, Banyuwangi District, not only are the accounts separate, but the treasurers are also differentiated based on their funding sources.²⁷ Therefore, each treasurer can focus on recording and reporting their own funds. This can be done by fulfilling financial and accounting human resources in accordance with the needs of the PHC. The obstacles faced in managing capitation funds are limited resources, inadequate understanding of planning, less guidance support from the local Health Office, and the absence of applicable implementation instructions.²⁸

The policy for using domestic medical devices must be supported by the availability of domestic medical equipment providers. Currently, 70% of the medical equipment supply in Indonesia is still filled with imported medical equipment, and the domestic industrial market currently only reaches 10%.²⁹ Flexibility in regulations regarding the procurement of medical equipment needs to be implemented to optimize capitation funds to improve health services to the community. The utilization of capitation funds has not been maximized due to the unclear regulations that need to be developed.³⁰

Conclusion

The capitation funds vary due to various factors, such as the number of registered participants, doctor-patient ratio, and performance-based capitation outcomes. However, the absorption of capitation funds each year is not optimal due to unavoidable conditions which cause the SiLPA to occur. Budget absorption is an indicator of health facility performance. This study implies that BPJS Healthcare Security, as the sole purchaser, needs to be more involved in reporting and monitoring capitation funds. The management of capitation funds is still hampered by regulatory limitations, so further regulations are needed to regulate the capitation management.

Abbreviations

UHC: universal health coverage; NHI: National Health Insurance; PHC: primary health care; KBK: Kapitasi Berbasis Kinerja/Performance-based Capitation; Prolanis: Program Pengelolaan Penyakit Kronis/Chronic Disease Management Program; FKTP: Fasilitas Kesehatan Tingkat Pertama/First Level Health Facilities; PPT: Pejabat Pelaksana Teknis Kegiatan/Technical Activity Executive Officer; SiLPA: sisa lebih perhitungan anggaran/excess of budget calculations; RPSAPHC: Regional Public Service Agency for Primary Health Care.

Ethics Approval and Consent to Participate

Ethical approval for this study was obtained from the Health Research Ethics Commission of Poltekkes Kemenkes Malang (No.DP.04.03/F.XXI.31/1086/2023). Informed consent was acquired prior to data collection and guaranteed confidentiality.

Competing Interest

The authors declared no conflict of interest to be disclosed.

Availability of Data and Materials

The availability of data and materials are available upon request.

Authors' Contribution

ATP designed the study. ATP, HDN, and AA conducted data collection. ATP and AHZ interpreted the data and wrote the manuscript.

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Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal)

Environmental Health Risk Analysis of SO₂ and NO₂ in Kemiri Muka Village, Depok City, Indonesia

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Abstract

Kemiri Muka is a village in Beji Subdistrict, Depok City, Indonesia. Based on a preliminary survey conducted in one of the neighborhood units of Kemiri Muka Village, the residential had a high density of houses and was close to traditional markets, toll roads, the main road of Depok City, and landfills. This caused the air quality in the village area to decline. This study aimed to analyze risks to public health and the environment from exposure to toxic substances, SO₂ and NO₂, which are high in the air due to transportation on the highway and population density. The sample from this study consisted of three age groups: 15 adults, 3 school-age children, and 5 toddlers. This study used the Environmental Health Risk Analysis to analyze the data. Based on the results, the risk quotient (RQ) of non-carcinogenic effects by exposure to inhalation of chemical agents, NO₂ and SO₂, were also included in safe risk because all RQ values were <1. The public should remain alert to their health conditions and continue to take preventive measures.

Keywords: Depok, Environmental Health Risk Analysis, NO2, risk quotient, SO2

Introduction

The transportation sector largely contributes to the air pollution in cities, mostly from emissions it produces, particularly SO_2 and NO_2 , which contribute to air pollution in Depok City, Indonesia. Regarding pollution issues, temperature, and rainfall trends in this city basically can be seen from an analysis of the same trends within the last ten years in Bogor City and small waterfall areas directly bordering Depok City.¹ Observing types of pollutants is then necessary as a preventive measure to determine the pollution levels.

Environmental Health Risk Analysis (ERHA) is a scientific framework for solving environmental and health problems. The United States Environmental Protection Agency defines the ERHA as a scientific evaluation of the potential health effects that may result from exposure to a particular substance or mixture thereof under specified conditions. Apart from having a direct impact on human or individual health, air pollution also has an indirect impact on health. The effect of SO_2 on vegetation is known to cause blanching in the areas between veins or leaf edges. Emissions of Fluorine (F), Sulfur Dioxide (SO_2), and Ozone (O_3) interfere with the assimilation process in plants. Vegetable plants are exposed to/contain Pb pollutants, which ultimately have the potential to pose a public health hazard to vegetable plants.

From monitoring via IQAir, the air quality status of Depok City is unhealthy, with an air quality index of 176 AQI US; hence, a public health risk analysis needs to be carried out to estimate health impacts resulting from exposure to environmental media contaminated with hazardous substances.⁴ Depok City has some environmental problems, specifically in Kemiri Muka Village. Based on a preliminary survey conducted in the village, the residential location had a high density of houses and was close to traditional markets, toll roads, the city's main roads, and landfills.

One of the traditional markets in the subdistrict is Kemiri Muka Market. Based on the 2020 data on market hygiene and sanitation inspection in Depok City, Kemiri Muka Market received a score of 3604 with a percentage of 38.8%, below the scores for Sukatani Market and Cinere Fresh Market.⁵ This shows that Kemiri Muka Market does not meet cleanliness and health requirements, which relates to the market's environmental conditions. This study aimed to carry out an environmental health risk analysis related to the toxic substances, SO₂ and NO₂, in Kemiri Muka Village, Beji Subdistrict, Depok City, West Java Province, Indonesia.

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Method

This study used ERHA, an approach to quantify or estimate risks to human health, including identifying the presence of uncertainty, tracing specific exposures, and taking into account the inherent characteristics of the agent of concern and the characteristics of a particular target to analyze the data. The ERHA includes four steps: hazard identification, doseresponse analysis, exposure assessment, and risk characteristics to estimate health risks to monitor carcinogenic and non-carcinogenic effects.²

The population was 120 households living in Kemiri Muka Village, specifically in Neighborhood Unit 001, Community Unit 10. Random sampling was carried out with inclusion criteria, including residents staying at home for a minimum of 12 hours per day and living in the area for at least six months. While, exclusion criteria were residents of Kemiri Muka Village but were not based in the area. The number of respondents obtained was 23 people, consisting of five children aged 6-12 years, three adolescents aged 13-18 years, and 15 adults older than 19 years. In measuring air parameters, the air sampling location was determined at a point where the public frequently passes by either using vehicles or on foot.

This study measured the air quality of Kemiri Muka Village, which was close to the market area. Kemiri Muka Village has a traditional market with many environmental problems, including poor sanitation facilities.⁵ The poor condition of Kemiri Muka Market would directly impact the health of residents living around, specifically residents at Neighborhood Unit 001, Community Unit 10. Therefore, a survey was conducted on anthropometric exposure factors, especially regarding activity patterns in the area.

Air chemical parameters were then examined by taking samples of SO_2 and NO_2 compounds. Besides, a physical inspection of dust was carried out using a dust track for one hour. The air samples were explained in the accredited Environmental Health Laboratory, Faculty of Public Health, Universitas Indonesia. Data on anthropometric exposure factors, activity patterns, and community health profiles were processed, analyzed, and collected in December 2023. Doseresponse analysis was carried out to determine the quantitative value of the toxicity of a risk agent according to each form of chemical species listed in the RfC (for air/inhalation).

Table 1. Dose-Response to Inhalation Exposure Risk Chemical Agents⁶

Dose-Response Agent	Critical and Reference Effect
NO ₂ 0.02	Respiratory tract disorders
SO ₂ 0.21	Respiratory tract disorders

Exposure analysis is a step to determine the exposure route of a risk agent into the body, whether through inhalation, ingestion, or absorption so that the amount of intake received by the at-risk population can be calculated. The intake of each risk agent (chronic daily intake (CDI) and lifetime average daily dose (LADD)) must be calculated for all exposure routes according to the anthropometric characteristics and activity patterns of the population at risk. When determining the inhalation of SO_2 and NO_2 in air, anthropometric parameters (body weight and inhalation rate) and activity patterns (time, frequency, and duration of exposure) were also needed. The level of risk can be calculated by the following equation:

$$I = \frac{C x R x tE x fE x Dt}{Wb x tavg}$$

Here is the explanation of the equation above: I was to describe the inhalation intake (mg risk agent/kg individual body weight/day), C means the concentration of risk agent in the air (mg risk agent/m³ of air), R means the inhalation rate (m³ air/hour), tE means the duration of exposure (hours/day), fE means the exposure frequency (350 days/year), and Dt means the duration of exposure. Meanwhile, Wb means individual body weight (kg), and tavg means the average time.

Health risk characteristics were expressed as the risk quotient (RQ) or hazard index (HI) for non-carcinogenic effects. The RQ was calculated by comparing or dividing the non-carcinogenic intake (CDI or LADD) of each risk agent by its reference dose (RfD). Health risk and the need for risk management are measured on water or air parameters if the RQ >1 for non-carcinogenic effects, which also means that the CDI exceeds the RfD/RfC.

Characterization of exposure risks to inhaled chemicals, particulates, and probability of pathogen microbiological illness. The health risk characteristics of exposure to SO_2 and NO_2 , PM_{10} , and $PM_{2.5}$ to air were estimated as the RQ for non-

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carcinogenic effects. The RQ was the division between inhalation intake (I) and RfC, with the following formula:

$$RQ = \frac{1}{RfC}$$

The results of the RQ calculation showed the level of public health risk due to inhaling air containing SO_2 and NO_2 . If the RQ>1, the exposure inhaled by the public is dangerous, contains toxic gases, and can cause health problems if inhaled for a long time.

Results

Measurements of the characteristics of anthropometric exposure factors were carried out on 23 respondents from six households at Neighborhood Unit 01, Kemiri Muka Village. The household selection was based on inclusion criteria, including households whose family members were in the categories of adults (>=19 years), adolescents (13-18 years), and school-age children (6-12 years).

Table 2. The Respondents' Characteristics

Variable	Adult (n=15)	Adolescent (n=3)	Children (n=5)	
Anthropometry				
Wb	53.67	50.33	23.8	
fE	365	365	365	
tE	21	13	8	
Consumption rate				
Drinking water	1.5	1.5	0.9	

Notes: Wb = individual body weight (kg), fE = exposure frequency (350 days/year), tE = duration of exposure (hours/day)

The hazard identification stage identifies the type, characteristics, and capabilities inherent in a risk agent that can negatively impact an organism, system, or sub/population. The results of the SO_2 air contaminants were 750 mmHg of average air pressure and 29.6°C of average temperature, with 15 motorcycles passing by during 1 hour of measurement. In the Indonesian Regulation Number 22 of 2021 concerning Environmental Management and Protection, SO_2 per hour is 150 μ g/Nm3; thus, the SO_2 air sample results still met quality standards.

Meanwhile, the results of NO_2 air contaminants were 996.6 mmHg of average air pressure and 25°C of average temperature, with 15 motorcycles passing by during 1 hour of measurement. In the Indonesian Regulation Number 22 of 2021 concerning Environmental Management and Protection, NO_2 per hour is 200 μ g/Nm3; thus, the NO_2 air sample results still meet quality standards.⁷

Characterization of exposure risks to inhalation of SO_2 and NO_2 chemicals. Air chemical parameter measurements were carried out by involving two compound elements, NO_2 and SO_2 . The RQ value was calculated by dividing CDI by the RfD. The measurement results are shown in the table below:

 $Table\ 3.\ Estimated\ Chronic\ Daily\ Intake\ and\ Total\ Risk\ Quotient\ of\ Non-Carcinogenic\ Air\ Chemicals\ NO_2\ and\ SO_2\ and\ SO_3\ a$

Chemical Compounds	С	R		Fe	Wb	Dt	tavg	CDI	RfC	RQ	
NO ₂	0.0002032	0.83	365	53.67		21	7665	3.1x10 ⁻⁶	0.02	1.5x10-4	
SO_2	0.000216	0.83	365	53.67		21	7665	3.3x10-6	0.21	1.5x10-4	

Notes: $C = \text{concentration of risk agent in the air (mg risk agent/m}^3 \text{ of air})$, $R = \text{inhalation rate (m}^3 \text{ air/hour})$, tE = duration of exposure (hours/day), tE = exposure frequency (350 days/year), tE = duration of exposure, tE = duration of exposure.

Based on the table above, the RQ value for the chemical parameters NO_2 and SO_2 shows an RQ value of <1. This showed that no health risks were found from NO_2 or SO_2 compounds. Therefore, there was no need for control except to maintain SO_2 and NO_2 concentrations and activity patterns as they were at that time.⁸

Discussion

A previous study in the Kalianak Area of Surabaya City, Indonesia, using the ERHA, found that the risk agents NO₂ and SO₂ had non-carcinogenic effects, especially on breathing. The major source of chemical compound pollution comes

from mobile emission sources: transportation exhaust gases and motor vehicles. These exhaust gas emissions are often closer to the community, especially those living on the side of the main road with high traffic density. Such conditions make people living in these areas more likely to be exposed to the risk agents NO_2 and SO_2 from the combustion of motor vehicle engines. NO_2 is a reddish-brown chemical compound with a sharp odor and is very toxic to the respiratory tract. Exposure to this gas in the human body will cause swelling of the lungs, resulting in shortness of breath, convulsions, and even death. O(2)

The toxicity of NO_2 gas is four times stronger than the toxicity of NO gas. The body organs most sensitive to NO_2 gas pollution are the lungs. Lungs contaminated with NO_2 gas will swell so that sufferers have difficulty breathing, which can cause death. Air containing NO gas within normal limits is relatively safe and not dangerous, except for NO gas in high concentrations. High concentrations of NO gas can cause disturbances in the nervous system, resulting in seizures. If this poisoning continues, it can cause paralysis. NO gas will be more dangerous if the gas is oxidized by oxygen to become NO_2 gas. NO_2 is also highly reactive and has been reported to cause bronchitis and pneumonia, as well as increasing susceptibility to respiratory tract infections.

 SO_2 is a chemical compound that is colorless and has a sharp odor. When this gas accumulates in the body, it can cause respiratory problems, especially lung function, irritation, and asthma. A dose-response assessment is used to determine the toxicity value of a risk agent and is the most important step because the ERHA study can only be carried out if the toxicity value is known. So₂ is a toxic sulfur oxide compound and a pollutant that is dangerous for health, particularly for the elderly and those suffering from chronic diseases of the respiratory and cardiovascular systems.

This is because SO_2 gas, which easily turns into acid, attacks the mucous membranes in the nose, throat, and respiratory tract, some of which reach the lungs. SO_2 gas attacks cause irritation to the affected body parts. If irritation occurs in the respiratory tract, SO_2 and its particulates can cause swelling of the mucous membranes. The formation of mucosa creates obstacles to airflow in the respiratory tract. This condition will be more severe in sensitive groups, such as people with heart or lung disease, and the elderly.¹⁴

In urban areas, especially big cities in Indonesia, air pollution has become a serious problem. Without realizing it, the air quality in urban areas has reduced the citizens' quality of life, especially in the transportation and industrial areas. ¹⁵ The primary source of SO_2 is the burning of fossil fuels, such as motor vehicles, coal-fired power plants, and others.

Conclusion

The public should remain alert to their health conditions and continue to take preventive measures, such as using masks, doing activities outside the home as necessary, and planting more plants that can absorb pollutants from toxic substances in the air. Future studies and follow-up actions by relevant stakeholders are needed, specifically the Depok City Government, to pay attention to the population density and reduce the air pollution problem by providing more open green space.

Abbreviations

ERHA: Environmental Health Risk Analysis; SO_2 : sulfur dioxide; NO_2 : nitrogen dioxide; RfC: reference concentration; CDI: chronic daily intake; LADD: lifetime average daily dose; RQ: risk quotient; HI: hazard index; RfD: reference dose.

Ethics Approval and Consent to Participate

This study protocol was approved by the Ethics Committee of the Faculty of Public Health Universitas Indonesia number 706/UN2.F10.D11/ppm.00.02/2023. Before the survey, written informed consent was obtained from individuals aged 18 years or older. For individuals between 1 and 17 years, consent was obtained from caregivers.

Competing Interest

The authors declare that no significant competing financial, professional, or personal interests might have affected the performance or presentation of the work described in this manuscript.

Availability of Data and Materials

Data were available upon request.

Authors' Contribution

NDA performed data collection, data analysis, and interpretation, as well as manuscript writing. BH provided scientific input on manuscript writing.

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Economic Loss of Leptospirosis: Is It Still Appropriate to be **Tropical Neglected Zoonosis Disease?**

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Economic Loss of Leptospirosis: Is It Still Appropriate to be Tropical Neglected Zoonosis Disease?

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Abstract

Leptospirosis is a tropical endemic disease that can reduce the productivity of sufferers. However, research on economic and productivity losses due to leptospirosis is rare. This study aimed to determine economic and productivity losses due to leptospirosis in the Banyumas District, Indonesia, as an endemic area. This study used a cross-sectional design and quantitative methods conducted in October 2022. Secondary data of medical records and billing information from 73 inpatients receiving treatment at a Public Hospital in the Banyumas District from February 2021 to September 2022 obtained from the hospital's archives were used. This study examined the actual costs (direct and indirect costs) of treatment, average length of stay, and patient characteristics. Statistical tools were carried out to check the results. The results showed that over half of leptospirosis patients used insurance with an economic loss of USD 289.64 and a productivity loss value of USD 388,499. Patients infected with leptospirosis vary in age. Leptospirosis results in loss of patient productivity during treatment. Increasing prevention and control to prevent deaths and economic burdens on society and local governments is proposed to local governments.

Keywords: economic loss, leptospirosis, productivity loss, tropical zoonosis disease

Introduction

Leptospirosis is a significant zoonotic disease because it can reduce the patient's productivity.¹ *Leptospira interrogans* bacteria cause leptospirosis. *Spirochaeta* bacteria are obligately aerobic and exhibit flexuose movement, i.e., they move about in the cell membrane.² This disease is prevalent in the tropics, such as Southeast Asia and Latin America³, as the bacteria which causes it thrives at tropical temperatures.² The brown rat (*Rattus norvegicus*)⁴ and mouse house (*Ratus tanezumi*) are reported as the main reservoir. However, it is also found in reservoirs such as foresail⁵ cows, buffaloes, horses, sheep, goats, pigs, dogs, and other rodents.⁶ Leptospirosis significantly impacts the sufferer and cattle's lost income production. In humans, this disease is frequently associated with organ damage that leads to death and high maintenance costs. In contrast, in cattle, it includes reproductive disturbances such as embryonic resorption, fetus mummification, stillbirth, and neonatal death that result in a significant economic loss.⁵

A study quantifying the global disease burden showed that the global productivity cost of leptospirosis in 2019 was USD 29.3 billion.8 A study in New Zealand found that the median number of Disability-Adjusted Life Years (DALYs) of patients with leptospirosis was 0.42 per 100,000 people in the population.9 The costs incurred by the state due to Leptospirosis on community farms in New Zealand are estimated to be USD 12.63 million.9 A study in China indicated that the number of DALYs decreased concurrently with the total incidence of leptospirosis, and the productivity of the young age group increased.10 The study carried out at a hospital in Semarang City, Indonesia, reported the amount number of economic loss due to leptospirosis was USD 40,130 (IDR 651,317,284) in 2020.11

Leptospirosis is endemic in some provinces in Indonesia, such as Central and East Java.¹² In Indonesia, the incidence, incidence rate, and prevalence of disease have continued to rise over the past five years (2018-2022).¹³ In

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Received: February 10, 2024 Accepted: July 15, 2024 Published: July 31, 2024 2021, there are 734 new cases of leptospirosis were reported in Indonesia, 84 of which are fatal. Moreover, this case fatality rate (CFR) due to leptospirosis in 2021 increased by 2.4% compared to 2020 (9%) levels. The Central Java Province ranks the highest in the total leptospirosis number in the 2021 National Reports. Kebumen, Demak, and Banyumas are three districts with a high number of leptospirosis patients. In particular, Banyumas District, with 159 cases of leptospirosis, is one of the districts with the highest incidence of new cases and deaths in Central Java in 2021. Undiagnosed and unreported cases of leptospirosis contribute to the CFR in patients. In patients.

Leptospirosis diagnostic examination requires comprehensive, laboratory-based, and expensive examination tools, thereby increasing the risk of problems occurring. The large amount of health spending, reflecting economic losses of leptospirosis sufferers, forms the basis of evidence for the authorities to propose a policy. However, studies focusing on calculating economic losses due to leptospirosis are rarely carried out in Indonesia. Therefore, this study aimed to determine economic and productivity losses due to leptospirosis in the Banyumas District, Central Java Province, Indonesia.

Method

This study was a cross-sectional quantitative-methods study conducted in Banyumas District, Central Java Province, Indonesia. This study was conducted in October until December 2022. Due to the resource constraint, this study examined the economic loss from health facilities. The study included a total population of 73 leptospirosis patients treated in inpatient and outpatient care in two B-type public hospitals in Banyumas District and complied with the inclusion criteria. The inclusion criteria were patients completing the treatment in February 2021 until September 2022, being diagnosed with leptospirosis, and being alive until completing the treatment. Meanwhile, the exclusion criteria were patients who terminated the treatment or patients who died during the treatment. The data was obtained from the public hospital's archives. The hospital medical records and billing information of leptospirosis patients were collected retrospectively from February 2021 to September 2022 (20 months) for this study.

This study's variables included the actual costs of treating leptospirosis, the average length of stay, the prevalence rate (PR) of leptospirosis, the population of Banyumas District in 2021, and Banyumas District minimum wage in 2021. Leptospirosis inpatients were charged fees for registration, laboratory, doctor services; as well as action, medical supports, non-medical supports, consumables, nursing care, medicine, accommodation, food service, and support costs. In addition to the patient's characteristics, such as age, sex, distance from the hospital, length of stay, and payment method, research data also included patient demographics.

This study divided age into five categories: a) 20 years, b) 21-35 years, c) 36-50 years, d) 51-65 years, and e) > 65 years. The respective age groups performed the patients that had a productivity activity. Sex was categorized as male and female. The distance between the residence and the B-type public hospitals where the leptospirosis patient was treated was classified as either close (10 kilometers) or far (>10 kilometers). The treatment classification was three categories: a) first class, b) second class, and c) third class. There were two categories for length of stay: seven days and more than seven days.

The sampling method consisted of collecting all inpatient data from the hospital information and management system using the International Code of Disease (ICD) code for leptospirosis. Patients with leptospirosis were categorized according to their payment method: insurance and out-of-pocket. The actual cost data was processed, cleansed, and tabulated using Excel tools for descriptive analysis. Processes of editing, coding, processing, cleaning, and tabulation were used to generate characteristic data. A descriptive analysis of actual costs was conducted to calculate economic and productivity losses due to leptospirosis.

The formula of economic loss or cost of illness, adding all components of the actual cost of leptospirosis treatment, was performed to figure the number of economic losses. Productivity loss analysis used a multiplication formula between the average length of stay (ALOS), the leptospirosis PR, the total population in Banyumas District in 2021, and the total of Banyumas District minimum wage in 2021. A statistical tool for descriptive data analysis was used to determine the frequency and percentage of each category. The geospatial tool was performed to show the distribution of rats containing leptospirosis bacteria in the Banyumas District.

Results

This study was conducted in the lowland area of Banyumas District, with an average elevation of more than 108 meters above sea level. Banyumas District has a land area of $1,327.59 \, \mathrm{km^2}$ and $27 \, \mathrm{subdistricts}$. In terms of elevation (height

above sea level), the plains in Banyumas consist of 0 to 100 meters (54.86%) and 101 to 500 meters (45.14%). This district is a tropical region with distinct dry and wet seasons. The population of Banyumas District in 2021 was estimated to be 1,789,630, with 900,919 male and 888,711 female residents. Most leptospirosis cases in Banyumas were reported in the hill area and increased significantly in the middle and the end of the year.

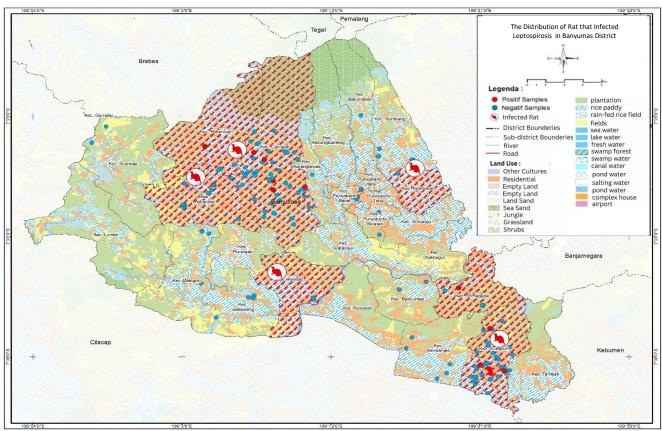


Figure 1. Distribution of Rat that Infected Leptospirosis in Banyumas District, 2018-2021

Figure 1 shows that rats with positive leptospirosis bacteria live in rice paddy, plantation, and residential areas. This study's population consisted of 73 leptospirosis patients in Banyumas District from February 2021 to September 2022, or in a period of 20 months. This study's samples comprised the entire case population, or all leptospirosis patients in the Banyumas District, totaling 73 inpatients. The distribution of leptospirosis patients based on patient characteristics is shown in Table 1.

This study involved leptospirosis patients receiving inpatient and outpatient care. Most samples consist of patients between aged 36-50 years (28.77%) and 51-65 years (27.00%), and male was dominant (57.53%). Most patients (57.53%) fell into the close category (10 km) between their home and the advanced health facility (General Hospital), and more than half of inpatients belong to first class (47.32%), second class (47.32%), and third class (43.84%). Patients receiving leptospirosis treatment mostly stayed less than seven days (79.45%). Most inpatients in this study (82.19%) paid with insurance. The cost of leptospirosis in Banyumas District was determined by calculating the amount of money spent on leptospirosis treatment. Table 2 outlines the results of the analysis.

The economic losses associated with leptospirosis were the sum of inpatient and outpatient costs. This amount produced an average of USD 289.64 (IDR 4,701,074) per period of illness. The average result exceeded the Banyumas District minimum wage of USD 121.37 (IDR 1,970,000). Leptospirosis, a zoonotic disease, is a financial burden for the Banyumas District. The components of leptospirosis hospitalization costs were analyzed using cases selected based on predetermined criteria, namely patient payments. The results of the analysis are depicted in Figure 2 below.

Table 1. Distribution of Leptospirosis Patient's Characteristics

Patient Characteristics	Frequencies	Percentage
Ago (vegage)	(n)	(%)
Age (years)		
<20	2	2.74
21-35	19	26.03
36-50	21	28.77
51-65	20	27.04
>65	11	15.07
Total	73	100
Sex		
Male	42	57.53
Female	31	42.47
Total	73	100.00
Distance to Health Facilities		
(<=10 km)	42	57.53
(>10 km)	31	42.47
Total	73	100.00
Treatment Classification		
First Class	35	47.32
Second Class	5	6.85
Third Class	33	45.21
Total	73	100.00
Length of Stay		
≤7 Days	58	79.45
>7 Days	15	20.55
Total	73	100.00
Payment Method		
Out-of-Pocket/General Patient	13	17.81
Health Insurance	60	82.19
Total	73	100.00

Table 2: Economic Loss Due to Leptospirosis in Banyumas District

Payment Method	N	ALOS patient	Minimum (USD)	Maximum (USD)	Average (USD)
Out-of-Pocket	13	3	74.26	372.37	200.87
Health Insurance	60	6.01	82.11	1,361.83	308.88
Economic Loss of patient's leptospirosis	73	5.04	74.26	1,361.83	289.64

Notes: ALOS = average length of stay, USD = United States Dollar (USD 1 = IDR 16,230.20)

Figure 2 shows that leptospirosis patients with full coverage who receive inpatient treatment tend to have higher maximum costs than patients who pay standard rates. The average cost of hospitalization for leptospirosis for those with insurance was greater than for those without insurance. The cost of inpatient care for leptospirosis patients consisted of several components: registration, laboratory, consultation, doctor service, service, medical support, non-medical support, disposable stuff, accommodation, food service, medicines, and other fees. The highest components on average and considered out-of-pocket were medicine, accommodation, procedure, and laboratory costs. Meanwhile, the highest average component covered by insurance was medicines, laboratory, medical support, and accommodation costs.

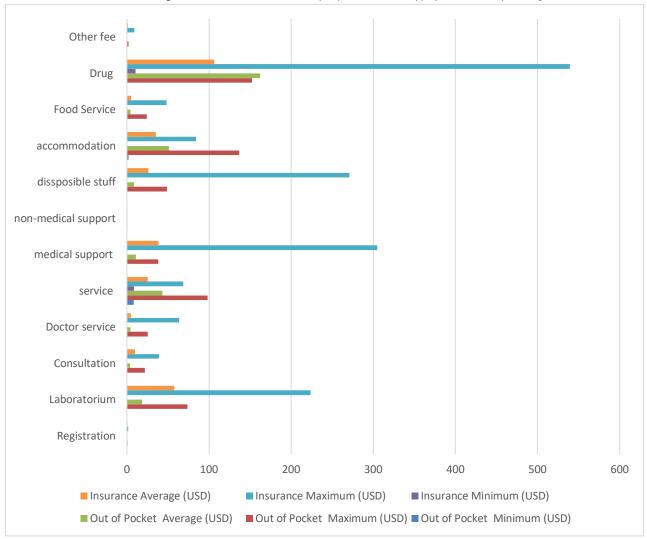


Figure 2. Cost Components for Leptospirosis Patient Care Based on Payment Method

 ${\bf Table~3.~Cost~of~Productivity~Losses~Attributable~to~Leptospirosis~in~Banyumas~District}$

Leptospirosis	Prevalence Rate	Population Number of Banyumas District (2021)	Average Length of Stay of Leptospirosis Patient	Minimum Wage of Banyumas District in 2021 (USD)	Total Productivity Loss (USD)
Icteric	2.76‰000	1,789,630	5.4	121.37	388,499

Notes: USD = United States Dollar (USD 1 = IDR 16,230.20)

Table 3 shows the costs of productivity losses due to leptospirosis in Banyumas District since this study also examined its impact. The proportional loss of productivity due to leptospirosis in Banyumas District was USD 388,499 (IDR 6,305,413,401) in 2021. The formula for productivity loss was the multiplication of the prevalence rate for Banyumas District in 2021, the average length of stay for leptospirosis sufferers, and the minimum wage for Banyumas District in 2021. The productivity loss represented the proportion of costs related to lost productivity due to Leptospirosis and hospitalization in Banyumas District.

Discussion

Based on the findings, there were 128 cases of leptospirosis in Banyumas District in 2021. Compared with the national number of leptospirosis cases in 2021, of 555 cases, 77 people died; this number is relatively high. In 2021, the incidence of leptospirosis in Banyumas District was 2.76 per 100,000 population, with a case fatality rate of 4.17%. In contrast to Surakarta City (CFR 100%), Kebumen District (CFR 39.13%), and Karangayar District (CFR 33.33%), the CFR was relatively low (the data was taken by one of the authors from the unpublished reports of Central Java Provincial

Health Office). This is because medical personnel in Banyumas District have been trained to detect cases of leptospirosis, but deaths still occur every year. This is a factor that must be considered when reviewing leptospirosis control programs in the field. Leptospirosis is a zoonotic disease with mild to severe symptoms (damage to the kidneys, lungs, heart, liver, and brain). Leptospirosis can potentially be fatal, and its eradication is impossible because *Leptospira* bacteria containing various pathogenic serovars can live freely in the environment. Moist soil and water, and almost all mammals are potential reservoir hosts. The main reservoir host for leptospirosis is rats, a source of serovars that are highly lethal to humans. The

This study showed that rats infected with leptospirosis live in rice fields, plantations, and residential areas. The area is at risk of being flooded if rainfall is heavy.²⁰ Heavy rainfall may diffuse *Leptospira* from the soil, resulting in higher concentrations of bacteria in the media to which humans are exposed (sewer water) and so to a higher inoculum dose, thus increasing hospitalized disease incidence and perhaps decreasing the environmental exposure risk in and around households (mud and exposed soil) and decreasing infection risk.²¹ The significant environmental factor that is associated with leptospirosis transmission is flooding.²² Climate change or extreme weather events should also be modeled to predict the severity of future leptospirosis outbreaks. The leptospirosis outbreaks impacted the number of economic losses.

This study attempted to quantify Leptospirosis incidence and monetary burden in the Banyumas District by calculating the average cost of hospital treatment and lost productivity due to leptospirosis. The primary findings of this study indicated that leptospirosis imposes a substantial economic burden on patients and governments that provide health services. Based on hospital billing data and medical records, it was determined that the average cost of hospitalization for leptospirosis patients was USD 289.64 (IDR 4,701,074). When the cost of treatment was differentiated between general patients and those with insurance, the cost of treating leptospirosis in the hospital was significantly higher, amounted USD 62.45 (IDR 1,013,265). In detail, the average cost for insured patients was USD 308.88 (IDR 5,013,265), and for non-insured patients or out-of-pocket payment was USD 200.87 (IDR 3,260,190).

Given the high cost of care for insured patients compared to non-insured patients, it can be assumed that most insured patients in this study were leptospirosis patients with comorbidities. Leptospirosis patients who experience tissue damage, organ damage, and comorbidities are categorized as having a severe form of the disease.²³ Similarly, a study in Bulgaria found that patients with severe leptospirosis incurred the highest average service costs, at USD 952.09 per day, compared to moderate and low leptospirosis patients, who incurred an average fee of USD 216.06 and USD 186.60, respectively.²⁴ In New Zealand, patients with severe leptospirosis incur average out-of-pocket expenses of USD 8,330 per disease period covered by insurance. In cases of mild leptospirosis, patients spend an average of USD 35 per period of illness for which they file an insurance claim.⁹

Several complications, such as disease complications, length of stay, number and type of medicines and medical devices consumed, and the number of supporting examinations performed while hospitalized, influence the magnitude of the cost factor for hospitalization of leptospirosis patients.²⁵ This study revealed that most leptospirosis patients (79.45%) were hospitalized for less than seven days. The total cost of leptospirosis treatment was directly proportional to the duration of treatment. According to a study in Jamaica, the number of days spent in a hospital significantly impacts the costs incurred by patients. Accessing services and laboratory results show that mild leptospirosis patients spend approximately three to five days receiving the medicine, incurring costs of USD 122 and 49 cents per day. Treatment for patients with severe leptospirosis lasts longer than five days and costs USD 535.3127.²⁶

The second economic impact of leptospirosis is the loss of patient productivity resulting from the condition. This study showed that the average patient hospitalized due to leptospirosis will lose productivity for five days. Patients could not work or carry out other productive activities. The average length of stay was determined by tracing the medical record data of 73 people in two hospitals in Banyumas District. In 2021, leptospirosis caused Banyumas District to lose productivity of USD 388,499 (IDR 6,305,413,401). This amount is quite large compared to the total health budget for Banyumas District in 2021, USD 6.93 million (IDR 112,507,053,384).²⁷ Considering the large decline in productivity due to leptospirosis in the Banyumas District, an immediate evaluation is needed to accelerate leptospirosis control and reclassify leptospirosis as a zoonotic disease that cannot be ignored.

Global productivity costs are estimated at USD 29.3 billion, particularly in Indonesia at USD 2.8 billion.⁸ In this study, assuming that the regional minimum wage for leptospirosis patients in Banyumas District in 2021 was USD 121.37 (IDR 1,970,000) per month or USD 1,456.54 (IDR 23,640,000) annually,²⁸ then that patients would incur substantial economic losses. The trend per year is that the minimum wage for each region has increased; consequently, the total costs due to

lost productivity would also increase over time.²⁹ This number indicates that leptospirosis can increase the poverty rate in a region. According to a study in India, leptospirosis causes patients to fall into poverty because hospitalization costs a median of USD 67.54 at a public hospital and USD 260.36 at a private hospital.³⁰

Leptospirosis is the world's most widespread zoonosis.^{31,32} It is challenging to diagnose leptospirosis in both clinic and laboratory. Consequently, this disease is frequently unrecognized in many countries, including Indonesia, and consequently, it is severely neglected.^{33,34} Leptospirosis has received particular attention in India because it causes death and has a significant economic impact on patients and the nation. There is a provision in the leptospirosis control program for using ambulance services and an annual unrestricted grant to refer suspected cases of leptospirosis to individuals in need. However, a previous study revealed that despite these efforts, patients still paid travel expenses during the referral process.³⁰

The Indonesian Ministry of Health, particularly the Directorate General of Infectious Disease Control and Management, district/city health offices, and primary health care (PHC) in Indonesia are responsible for leptospirosis prevention, in which the Ministry of Health and the Provincial Health Office play a role as facilitator and coordinator, and the District/City Health Office and PHC as technical action determiners. The leptospirosis control and management program consists of epidemiological investigations around the patient's residence, leptospirosis clinical lectures for PHC and hospital doctors, leptospirosis prevention meetings for Animal Source Disease Control officers and PHC surveillance officers, providing rapid detection tests and training for officers, health education on leptospirosis to the community, leptospirosis screening, and coordination meetings at the district/provincial level. Even though the above leptospirosis prevention activities have been implemented, leptospirosis cases still continue to run rampant, causing public disturbances and deaths. Besides, leptospirosis control is still being implemented in several districts and cities in Indonesia where there are indications of endemic leptospirosis.³⁵

Important policies for a leptospirosis control program include 1) passive and active surveillance, both at PHC and other public health services; 2) hospital or community-based methods for determining or finding cases of leptospirosis; 3) establishing a definition of a leptospirosis outbreak, including population, location, and duration; 4) establishing a diagnosis by determining suspect, probable and confirmed cases based on clinical manifestations and laboratory examination; 5) analyze the number of fatalities and fatality ratio; and 6) epidemic response includes a description of the type of outbreak investigation and identification of the causative agent.³⁶ Although the results of the leptospirosis cost of illness study revealed that the productivity loss rate due to leptospirosis was relatively high, the sample was limited to the healthcare facility perspective.

Further study is needed to overcome some of the limitations of this study, such as the fact that the average rate of productivity loss may only apply to leptospirosis patients who live modestly and have a certain level of education (low-middle economic level) and the majority of patients with leptospirosis nephritis disease. Another limitation of this study is that it only captures direct costs during hospital treatment. In contrast, indirect medical costs (travel costs, caregiver costs, and other costs related to treatment that are not captured in the billing information) are not shown in the billing information. However, this study provides billing information for leptospirosis patients. Thus, the costs are based on real patient data during treatment at health facilities (public hospitals).

Conclusion

Leptospirosis infects female and male patients in each age group without boundaries. In leptospirosis treatment, the cost of leptospirosis medicines is relatively high compared to other cost components, and patients eventually lose productivity. Leptospirosis is thought to cause poverty among the patients, especially workers, and burden the regional economy. Priority is given to the prevention and control of leptospirosis to prevent diagnosed complications, deaths, and economic burdens on society and local governments. Specifically, in the endemic areas where leptospirosis is frequently reported, appropriate strategies need to be created to reduce leptospirosis cases.

Abbreviations

DALYs: Disability-adjusted Life Years; CFR: case fatality rate; PR: prevalence rate; ALOS: Average Length of Stay; PHC: primary health care.

Ethics Approval and Consent to Participate

This study has obtained an ethical clearance approved by the Health Ethics Commission of the National Research and Innovation Agency, with Ethical Clearance Decree number 001/KE.03/SK/10/2022. The informants of this study were informed of the research objectives and purpose. All of the informants submitted verbal consent to participate in this study.

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Competing Interest

All authors declare that this study has no competing financial or personal interests.

Availability of Data and Materials

The authors stated that the secondary data was available to anyone interested in this study.

Authors' Contribution

All of the authors had equal contributions to this study. WPN, SDL, and WGP conceptualized this study. WPN, R, SDL, and WGP created the methodology, analyzed the data, wrote, reviewed, and edited the original draft and manuscript. IP, SN, LMP, DRF, AEN, and MAM wrote, reviewed, and edited the original draft and manuscript.

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Kesmas

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Article 10

7-31-2024

Exercise to Improve Asthma Control and Lung Function in Stable Asthma: An Evidence-based Case Report

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Exercise to Improve Asthma Control and Lung Function in Stable Asthma: An Evidence-based Case Report

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Abstract

Asthma is a heterogeneous disease with respiratory symptoms that vary over time and intensity. Exercise-induced asthma patients are advised to avoid strenuous physical activity, which can trigger bronchospasm. However, appropriate exercise can improve asthma control and lung function in stable asthma patients. A literature search was conducted on PubMed, COCHRANE, and EMBASE databases using Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines according to the specified eligibility criteria. Those studies were critically appraised using the Oxford Critical Appraisal Tool 4.0. Four articles were selected based on the PRISMA search strategy flowchart to assess their validity, importance, and applicability. There was a significant effect of aerobic exercise on lung function (p-value = 0.05) and asthma control (p-value = 0.004). There was a significant effect of breathing exercise on the quality-of-life outcome group (p-value <0.05) and Forced Expiratory Volume in 1 second (FEV₁)% predicted (p-value <0.001). Physical exercise for 30 minutes two to three times per week or yoga exercise for 60 minutes per day for 3-5 days improves lung function and asthma control in stable asthma patients.

Keywords: aerobic exercise, asthma, asthma control, breathing exercise, lung function

Introduction

Asthma is a heterogeneous disease characterized by chronic inflammation of the respiratory tract.¹ Asthma has respiratory tract symptoms, such as coughing, wheezing, shortness of breath, and chest tightness that vary over time and in intensity. Asthma can be accompanied by variable expiratory airflow limitations.¹ Asthma cannot be cured but can be controlled by administering the right medication to optimize the patient's quality of life.¹ The World Health Organization (WHO) states that 235–250 million people globally are affected by asthma, with at least 4.3% coming from the adult population.²

Patients with exercise-induced asthma (EIA) are advised to avoid strenuous physical activity because it can trigger bronchospasm.³ However, exercise such as aerobics can be beneficial for stable asthma, improve quality of life, and reduce the rate of asthma recurrence. Warm-up exercises are needed before doing exercises.^{4,5} The Global Initiative for Asthma (GINA) also recommends physical exercise as a non-pharmacologic add-on therapy, in addition to a healthy diet, weight reduction, allergen avoidance, and smoking cessation.¹ Therefore, this study aimed to analyze types of exercise that could improve asthma control and lung function so that it can be a recommendation for stable asthma patients.

Clinical Question

A 45-year-old woman came to the pulmonary clinic with a record of previous hospitalization for moderate asthma exacerbation. She had a record of asthma since childhood and started using the salbutamol inhaler for shortness of breath without a doctor's prescription in 1998. She had a family record of asthma from her father's side. The patient had no record of smoking or allergies. Her shortness of breath is triggered by fatigue, dry air, coughs, and air pollution. The patient had had several visits to the Emergency Room due to asthma attacks since the beginning of 2023 and had been hospitalized once. She complained of shortness of breath almost every day and sometimes woke up at night due to shortness of breath.

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Received: February 8, 2024 Accepted: July 15, 2024 Published: July 31, 2024 She was diagnosed with moderate persistent asthma. She received long-acting beta-agonists and medium-dose inhaled corticosteroids. She had used the medication regularly as recommended by the doctor but still complained of shortness of breath often. The patient temporarily did not want additional types of medication; thus, the doctor planned to provide add-on treatment in the form of exercise. Therefore, it is necessary to critically appraise the effect of exercise on improving asthma control and lung function. Can physical exercise improve asthma control and lung function in stable asthma patients?

Method

Search Strategy

A literature search was conducted on October 11, 2023, using PubMed, COCHRANE, and EMBASE databases, which offer access to either synthesized publication types or critically appraised and carefully selected references. The keywords used for the searching strategy were asthma, physical exercise, breathing exercise, asthma control, and lung function using boolean operators. All the articles in English were included. The search results were filtered to limit the literature to randomized control trials (RCTs) and systematic reviews published from 2018 to 2023.

The inclusion criteria for the literature search were systematic review and randomized control trial articles and asthma control and/or lung function test as the outcome. Meanwhile, for the exclusion criteria were exercise Induced Asthma (EIA), \leq 15 years old population, asthma with other comorbids, and acute asthma. The article search strategy can be seen in Table 1 and Figure 1 in the Results section.

The search literature obtained 224 studies to be screened based on abstract titles. The screening aimed to assess duplications and appropriate the study design according to this study's Population–Intervention–Comparison-Outcome (PICO) framework. Full-text literature was assessed according to the eligibility criteria, resulting in four studies to be analyzed for validity, importance, and applicability. Lung function and asthma control questionnaires were measured to assess the impact of exercise. Forced expiratory volume at 1 second (FEV₁) and peak expiratory flow (PEF) were parameters of lung function measuring the obstructive degree of the airway.

Asthma control is a condition of a subject that can fluctuate over time, varying from normal conditions to exacerbation or worsening of symptoms. Asthma patients with poor asthma control had more frequent exacerbations that might impact their quality of life. The questionnaires used to assess asthma control were the Asthma Control Questionnaire (ACQ), Asthma Control Test (ACT), or Asthma Quality of Life Questionnaire (AQLQ). *Critical Appraisal Methods*

Four studies were critically appraised. Critical appraisal used validity, importance, and applicability criteria based on the Oxford Critical Appraisal for three systematic review studies and one randomized control trial study. Those articles were critically appraised for assessment of the level of evidence on treatment benefits based on the 2011 Oxford Center for Evidence-Based Medicine (OCEBM) Level of Evidence.

Results

Four articles obtained from literature searching were: (1) A Systematic Review of the Effect of Physical Activity on Asthma Outcomes⁶, (2) Effect of Aerobic Exercise Training on Asthma in Adults: A Systematic Review and Meta-Analysis⁷, (3) Regular Exercise Improves Asthma Control in Adults: A Randomised Controlled Trial⁸, (4) Breathing Exercise for Adults with Asthma.⁹ The studies mentioned that physical exercise improves asthma control (using ACT, ACQ, AQLQ) and lung function tests (based on FEV₁). The physical exercises there were walking, running, jogging, spinning, treadmill running, muscle training, stretching, and breathing exercises such as yoga. They recommend that physical exercise be done in proper and gradual time, once to twice a week at minimum, with a 30-minute duration.

Kuder *et al.* (2021)⁶ revealed that 10 studies using treadmill, swimming, cycling, walking and aerobic training significantly improved the ACQ score between groups. Hansen *et al.* (2020)⁷ showed that 10 studies stated that using aerobic exercise reported significant improvement in FEV₁. Jaakkola *et al.* (2019)⁸ showed that aerobic exercise, muscle training, and stretching on 105 subjects gave improvement in PEF and ACT. Stantino *et al.* (2020)⁹ showed that breathing exercises included 22 studies that used yoga to improve ACT, ACQ, and FEV₁.

Table 2 shows the PICO characteristics and level of evidence from each study based on the 2011 OCEBM. Level 1 for RCT meta-analysis and level 2 for RCTs. Tables 3 to 5 show the critical appraisal results of three systematic review studies and one randomized control trial study using worksheets from the Oxford Critical Appraisal.

Table 1. Article Search Strategy

Database	Search Strategy				The Total of Article Used
PubMed	Terms (physi exerci exerci	ma[MeSH Terms]) OR (asthma[Title/Abstract])) AND (((((((aerobic exection)) AND (((((((aerobic exection)) OR (aerobic exercise[Title/Abstract])) OR (physical exercise[MeSH Terms])) OI (breathing exercises[MeSH Terms])) OI (ses[Title/Abstract])) OR (regular exercise[MeSH Terms])) OR (regular se[Title/Abstract])) AND ((y_5[Filter]) AND (randomizedcontrolledtrial[maticreview[Filter]))	rms])) OR R (breathing	87	3
COCHRANE	ID #1 #2 #3 #4 #5	Search MeSH descriptor: [Asthma] explode all trees MeSH descriptor: [Exercise] explode all trees MeSH descriptor: [Breathing Exercises] explode all trees #2 OR #3 #1 AND #4 with Cochrane Library publication date Between Oct 2018 and Oct 2023	Hits 15046 38609 1190 39596 59	59	1
EMBASE	'regula' exer':t	na'/exp AND ('exercise'/exp OR 'breathing exercise'/exp OR 'aerobic exer ar exercise'/exp OR 'physical exercise':ti,ab OR 'breathing exercise':ti, ab o ti,ab) AND ('lung function'/exp OR 'asthma control'/exp) AND ('systemat w'/exp OR 'randomized controlled trial'/exp) AND [2018-2023] /py	OR 'aerobic	78	0

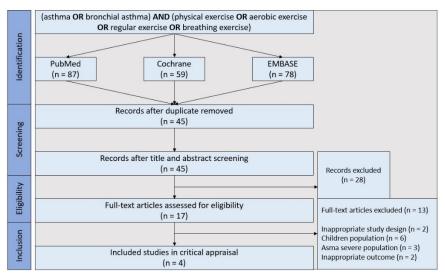


Figure 1. Search Strategy Flow According to PRISMA Guidelines

Table 4 shows the importance of each study. All studies found that exercise affected asthma control, which was measured by AQLQ, ACT, or ACQ. Three systematic review studies showed that exercise affected lung function, as measured by the FEV₁ parameter. The randomized control trial study by Jaakkola $et\ al.^8$ showed that exercise did not affect lung function as seen on PEF parameters. Jaakola $et\ al.^8$ measured the PEF of the control and intervention groups at three measurement points: baseline, three-month interval, and six-month interval. It did not show a significant mean difference (p-value = 0.35 in the morning and p-value = 1.47 in the afternoon).

Table 2. PICO Characteristics and Level of Evidence from the Literature

Authors	Study Design	P	I	С	0	Level of Evidence
Kuder <i>et al.</i> (2021) ⁶	Systematic Review	Asthma in the population aged ≥18 years	Walking/running, aerobics. Frequency: 1- 2x/week. Duration: 6 weeks-1 year	Control group (without exercise)	Physical exercise improves asthma control (ACQ), lung function (FEV ₁), quality of life (AQLQ)	1
Hansen <i>et al.</i> (2020) ⁷	Systematic Review	Asthma in the population aged 22-54 years with BMI 23.2-38.1 kg/m ²	Aerobic exercise (walking, jogging, spinning, treadmill running). Duration: 8-12 weeks	Control group (without exercise)	Exercise improved ACQ and FEV ₁	1
Jaakkola <i>et al.</i> (2019) ⁸	Randomized Control Trial	Mild/moderate asthma in the population aged 16-65 years	Aerobic exercise, muscle training, stretching at least 3x/week, for ≥30 minutes	Control group (without exercise)	ACT increased; lung function (PEF) did not significantly increase	2
Santino <i>et al.</i> (2020) ⁹	Systematic Reviews	Asthma in the population > 18 years	Breathing exercise	Control group (without exercise)	ACT, ACQ, and FEV ₁ improved	1

Notes: PICO = Population, Intervention, Comparison, and Outcomes, P = population, I = intervention, C = comparison, O = outcomes

Table 3. Critical Appraisal for Validity

			r		
Systematic Review	Clearly implied research question	Missed relevant studies	Appropriate inclusion criteria	Valid included	Similar results
Studies	research question	studies	inclusion criteria	studies	between studies
Kuder et al. (2021)6	+	+	+	+	?
Hansen et al. (2020)7	+	+	+	+/-	-
Santino et al. (2020)9	+	+	+	+	+
Randomized Control Trial Study	Randomized assignment of subjects	Similar baseline characteristics	Groups treated equally	All patients accounted for and analyzed	Blinding process
Jaakkola et al. (2019)8	+	+	+	+	-

Table 4. Critical Appraisal for Importance
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Table 4. Critical Appraisal for Importance				
Literature	Treatment Effect size	Treatment Effect Precision		
Kuder et al.	20 included studies on lung function outcomes:	The confidence interval is not clearly stated		
(2021)6	 5 studies had a significant effect 			
	 A study showed a positive but not significant effect 	Forest plots are not displayed		
	 14 studies had no significant effect 			
	12 included studies on asthma control outcomes:			
	 7 studies had a significant effect 			
	 5 studies had no significant effect 			
Hansen et al.	There is a significant effect of aerobic exercise on asthma	A forest plot with 3 outcome groups is displayed. Two		
(2020)7	control and lung function, but not significant on airway	outcome groups had significant effects on asthma		
	inflammation	control and lung function		
	 ACQ outcome group 	 Asthma control outcome group 		
	Mean difference -0.48 (-0.81 to -0.16) with P 0.004	CI -0.81 to -0.16 (narrow)		
	 FEV₁ outcome group 	 Pulmonary function outcome group 		
	Mean difference -0.36 (-0.72 to 0.00) with P 0.05	CI -0.72 to 0.00 (narrow)		
		 Airway inflammation outcome group 		
		CI -0.41 to 0.36 (narrow)		
		A narrow Confidence Interval shows precision		
Santino et al.	 There is a significant effect of breathing exercise on AQLQ 	A forest plot is displayed, showing the CI for each		
(2020)9	(up to 3 months)	outcome group		
	Mean difference 0.42 (CI 0.17 – 0.68)			
	 There is a significant effect of breathing exercise on 	The CI used is 95%, with a narrow CI range.		
	predicted FEV ₁ %			
	Mean difference 6.88 (5.03 – 8.73) with P < 0.0001			
Jaakkola <i>et al</i> .	- There is a significant effect of 6 months of exercise on ACT	The CI used is 95%, with a narrow CI range.		
(2019)8	Risk Difference (RD) 0.233 (CI 0.027 - 0.438) with P			
	0.032			
	 There is no significant effect of 6 months of exercise on 			
	PEF (morning and evening)			
	Mean difference 0.50 (-0.88 to 1.88) morning			
	Mean difference 1.26 (-0.53 to 3.05) evening			

Table 5. Critical Appraisal for Applicability

Studies	Different patient characteristics compared to the study		Feasible treatment
Kuder <i>et al.</i> (2021) ⁶	No. The research population in the study is in accordance with the age predilection of asthma patients in Indonesia, which starts in young adults. No comorbidities other than asthma.	-	Swimming 2x/week for 6 months Aerobic exercise (walking, running, stretching) at least 30 minutes per week for 8 weeks Cycling, treadmill, 3x/week for 12 weeks
Hansen <i>et al.</i> (2020) ⁷	No. The research population in the study is in accordance with the age predilection of asthma patients in Indonesia which starts in young adults. No comorbidities other than asthma	- -	Treadmill, breathing exercise 2x/week for 12 weeks Indoor cycling 3x/week for 8 weeks Aerobic exercise (walking, running, stretching) 2x/week for 3 months
Santino <i>et al</i> . (2020) ⁹	No. In this review study, the research samples in each included study are explained. Of the 14 included studies, 8 included Indian (Asian) populations so they could be adapted to Indonesian characteristics. Research sample in each study > 18 years (starting from young adults)	-	Yoga at least 60 minutes/day for 3-5 days
Jaakkola <i>et al</i> . (2019) ⁸	No. In this study, the sample age was stated to be 16-65 years. Diagnosed with asthma without other comorbidities. Do not do other physical activities at least 3x/week		Aerobic exercise (rapid walking, jogging, running, cycling) for at least 30 minutes 3x/week

Discussion

Four articles were obtained to conduct validity, importance, and applicability appraisal. The studies had lung function outcomes measured by FEV₁ and PEF. In contrast, asthma control was measured by the AQLQ, ACT, and ACQ questionnaires. The subjects had fulfilled the specified eligibility criteria. The intervention was physical exercise in the form of aerobic exercise (running, walking, cycling, swimming, treadmill) and breathing exercise (yoga).

The FEV $_1$ is the volume of air that can be exhaled from the lungs during maximum expiration in one second. The FEV $_1$ value is measured for one second from the start of maximal exhalation after maximal inhalation. PEF is the maximal measure of the airflow rate that can be exhaled from the lungs with maximum expiration. FEV $_1$ and PEF are not equivalent in determining the degree of airway obstruction, whether in COPD or asthma, so it is still necessary to measure those two parameters. This causes routine physical exercise in Jaakola *et al.* to have no significant effect on PEF. Another systematic review study stated that physical exercise affected FEV $_1$.

A systematic review by Wu $et~al.^{11}$ was excluded from this study because it involved a pediatric population (age \leq 15 years). The study showed a significant effect of aerobic exercise on PEF (p-value = 0.000). The study analyzed the pool effect of six studies, four involving the pediatric population and two involving the adult population. The study showed that PEF would have a significant and dominant effect on the child population compared to the adult population.

Based on the critical appraisal of the four studies, Kuder *et al.*⁶ did not show a pooled effect analysis in the forest plot. The importance of the study could not be measured due to the absence of a forest plot. The study by Jaakkola *et al.*⁸ was not excluded because it met the eligibility criteria and was not included in the three systematic reviews. The study showed that not all lung function parameters were affected by physical exercise. Hansen *et al.*⁷ and Santino TA *et al.*⁹ showed pooled effect analysis in forest plots for each outcome group so that the importance of these two studies could be measured significantly. Thus, three studies (Hansen *et al.*,⁷ Jaakkola *et al.*,⁸ and Santino *et al.*⁹) are recommended to be applied in clinical practice.

The recommendation is having physical exercise (by warming up first) in the form of aerobic exercise (running, walking, cycling, or swimming) for a minimum of 30 minutes two to three times per week 7.8 or yoga exercise for a minimum of 60 minutes per day for 3-5 days to improve lung function based on FEV₁ and asthma control based on ACT, ACQ, or AQLQ scores.

Conclusion

Physical exercise has a significant effect on lung function (FEV₁) and asthma control (ACQ, ACT, and AQLQ). The recommended physical exercise is aerobic exercise for at least 30 minutes two to three times a week or yoga exercise for at least 60 minutes per day for 3-5 days. The results of these three studies are feasible to apply in clinical practice scenarios.

Abbreviations

Embase: Excerpta Medica Database; OCEBM: Oxford Center for Evidence Based Medicine; EBCR: Evidence Based Case Report; RCT: Randomized Control Trial; EIR: Exercise Induced Asthma; ACQ: Asthma Control Questionnaire; AQLQ: Asthma Quality of Life Questionnaire; ACT: Asthma Control Test; FEV₁: Forced Expiratory Volume in 1 second; PEF: Peak Expiratory Flow

Ethics Approval and Consent to Participate

Not applicable

Competing Interest

The authors declare that they have no competing interests.

Availability of Data and Materials

The data supporting this study's findings are openly available in public repositories (PubMed, Cochrane, Embase) that issue datasets with DOIs (see the references).

Authors' Contribution

ARR and ATA conducted the data collection, wrote the manuscript, and reviewed each study for critical appraisal. TD commented on the manuscript, supervised the conducted data collection, and wrote the manuscript. All authors have read and approved the final version of the manuscript.

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Kesmas

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Article 11

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Multidrug-Resistant Organisms Infection on Mortality of Burn Patients at Public Hospital X in Jakarta: A Retrospective Study

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Abstract

Susceptibility to infection and increasing antibiotic resistance put burn patients at risk of developing infections caused by multidrug-resistant organisms (MDRO). This condition can progress to sepsis, increasing morbidity and mortality. This retrospective cohort study employed the medical record data of patients treated at Public Hospital X in Jakarta, Indonesia, from January 2020 to June 2022. Of 160 subjects, most were aged <60 years (82.5%) and had comorbidities (16.88%). The most common cause of burns was fire (86.25%). The use of medical devices was 90.63%, with a 14-day median length of stay. The most common gram-negative MDRO pathogens were *K. pneumoniae* (29.91%), *Enterobacter sp* (22.32%), and *Acinetobacter* (20.54%); 45% of patients infected with MDRO died. The bivariate analysis found an increased risk of death due to MDRO infection in burn patients (RR 1.103; 95%CI 1.004-1.211, p-value = 0.046). After adjusting for role variables (age, comorbidities, total body surface area, use of medical devices, length of stay) and from multivariate analysis, the confounding variables for MDRO infection and mortality were length of stay and age. MDRO infection increases the mortality rate in burn patients. Mortality in burn patients due to MDRO infection is greater than non-MDRO.

Keywords: burn, mortality, multidrug-resistant organisms

Introduction

Burn cases increase every year, especially in developing countries. This increase can be seen in high rates of morbidity and mortality, which have a significant physical, psychological, and economic impact.¹⁻⁵ The World Health Organization estimates 265,000 deaths by burn occur every year. In developing countries such as Bangladesh, Columbia, Egypt, and Pakistan, 17% of children with burns experience temporary disability, while another 18% have permanent disability.⁶ According to the 2013 Indonesian Basic Health Research, the prevalence of burns in Indonesia is 0.7%, with the highest incidence in Papua (2%) and Bangka Belitung Provinces (1.4%).⁷

Deaths from burns in Indonesia reach 195,000 cases annually. Public Hospital X in Jakarta receives more than 130 referral patients of burns from all over Indonesia each year, with the largest referrals coming from West Java Province and East Jakarta Municipality. Analysis of mortality data in adult patients of burns at the Public Hospital X in 2009-2010 showed a rate of 34% and 14.5% at a public hospital in East Java in 2007-2011. However, a 2017 study at the Public

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Email: merlindaveronica27101977@gmail.com Phone: +62 822-9898-9658

Received: May 1, 2024 Accepted: July 18, 2024 Published: July 31, 2024 Hospital X in Jakarta stated that the mortality rate for burn patients was 24%.8-10

The possibility of contracting an infection increases in burn patients due to damaged skin integrity and weakened immune system, thereby facilitating bacterial infiltration. Susceptibility to infections and increasing antibiotic resistance put burn patients at risk of developing infections caused by multidrug-resistant organisms (MDROs). These conditions can progress to sepsis, which can increase morbidity and mortality. Information and research regarding the clinical impact of MDRO infection in burns is still scarce. Therefore, this indicates the importance of conducting a study to analyze MDRO infections in burn patients, which could cause high treatment costs and the choice of antibiotics at an early stage to anticipate death. It is hoped that the results of this study will provide scientific data regarding the effect of MDRO infection on mortality in burn patients and assist the clinician in the rational selection of antibiotics (clinical pathway).

Method

This study was an observational study with a retrospective cohort design using medical record data. This study was conducted on the target population of burn patients treated at the Burn Unit of the Public Hospital X in Jakarta from January 2020 to June 2022. The accessible population concerned was burn patients treated at the Public Hospital X Burn Unit \geq 48 hours with culture examination results (tissue or blood) and pathogen growth. The sample was part of the population reached and met the criteria.

Data collected were age, sex, history of the use of medical devices, records of comorbidities, total body surface area (TBSA), length of stay, records of the use of empirical and definitive antibiotics, records of sepsis, skin and soft tissue infections, Urinary Tract Infection (UTI), type of culture, day of admission, last culture collection, last culture results, MDRO, type of antibiotic resistance, and type of pathogen in culture. Data were analyzed using SPSS Version 22.0 (free version). For univariate analysis, data were presented as percentages for categorical data and mean with standard deviation or median with minimum and maximum values for numerical data. Bivariate tests were carried out using the Chi-square test for categorical data and Mann-Whitney for numerical data. Multivariate tests were carried out using logistic regression tests.

Results

Of 160 patients, 100 (62.5%) were males and 60 (37.5%) were females; 28 (17.5%) were aged \geq 60 years, and 132 (82,5%) were aged \leq 60 years, with a median age of 46 years. There were 27 (16.88%) burn patients with comorbidities based on the Charlson index and 133 (83.13%) without comorbidities. There were 101 patients (63.13%) with TBSA \geq 30% and 59 patients (36.88%) with TBSA <30%. Major causes of burns were fire with 138 (86.25%), followed by electricity with 12 (7.5%), and hot oil/water with 10 patients (6.25%). Based on the source of transmission, 87 (54.4%) experienced skin and soft tissue infections, 64 experienced respiratory tract infections (40%), and 9 patients experienced UTI (5.6%). The use of medical devices in burn patients was 145 (90.63%), and 15 did not use medical devices (9.38%). The use of ventilators was 87 (54.38%), and the median length of stay was 14 days (in the range of 4 to 59 days).

Table 2 shows the MDRO pathogen based on the last culture of burn patients treated at the Public Hospital X Burn Unit, indicating that MDRO Gram-positive pathogens were found in 7 *Staphylococcus epidermidis* (3.13%) and *Staphylococcus aureus* (0.45%). Meanwhile, non-MDRO Gram-positive pathogens were found in 7 *Staphylococcus sp.* (26.92%), *Enterococcus faecalis* (15 .38%), *Staphylococcus saphrophyticus* (7.69%), and *Staphylococcus sp.* (3.85%). The most frequently encountered MDRO Gram-negative pathogens were *Klebsiella pneumoniae* (29.91%), *Enterobacter sp.* (22.32%), *Acinetobacter* (20.54%), *Pseudomonas aeruginosa* (16.52%), *Escherichia coli* (3.13%), *Enterobacter cloacea* (0.89%), *Enterobacter eurugenes* (0.89%), *Proteus vulgaris* (0.89%), *Serratia marcescens* (0.45%), *Burkholderia cloacea* (0.45%), and *Myroides* (0.45%). For non-MDRO Gram-negative pathogens, the most common were *Enterobacter sp.* (23.08%), *K. pneumoniae* (7.69%), *Acinetobacter sp.* (7.69%), *Proteus sp.* (3.85%), *Serratia sp.* (3.85 %).

Table 3 shows antibiotic resistance by pathogens from the last culture. Methicillin-resistant *Staphylococcus sp.* was found in 5 (2.65%), Methicillin-resistant *Staphylococcus aureus* was found in 1 (0.53%), Broad Spectrum *Beta Lactamase* in 54 (28.57%), Carbapenem-resistant *K. pneumoniae* was found in 47 (24.87%), Carbapenem-resistant *Acinetobacter* was found in 34 (17.99%), Carbapenem-resistant *P. aeruginosa* was found in 23 (12.17%), Carbapenem-resistant *Enterobacteriaceae* was found in 23 (12.17%), Carbapenem-resistant *E. coli* was found in 1 (0.53%), and Carbapenem-resistant *Myroides* was found in 1(0.53%).

Based on the results of bivariate analysis, the relative risk was 1.103 (95% CI 1.004-1.211) with a p-value of 0.046. Those results made the risk of patients exposed to MDRO infection dying during hospitalization 10% higher compared to non-MDRO patients dying during hospitalization (Table 4).

Table 1. Characteristics of Burn Patients at the Public Hospital X Burn Unit

Variable	n=160 (%)
Sex, n (%)	
Male	100 (62.5)
Female	60 (37.5)
Age (year), mean (SD)	45.6 (15.2)
Age group, n (%)	
≥60 years	28 (17.5)
<60 years	132 (82.5)
Comorbid according to the Charlson index, n (%)	
Yes	27 (16.88)
No	133 (83.13)
TBSA, n (%)	
10-≥30%	101 (63.13)
<30%	59 (36.88)
Medical device, n (%)	
Yes	145 (90.63)
No	15 (9.38)
Ventilator usage, n (%)	87 (54.38)
Cause of burn, n (%)	
Fire	138 (86.25)
Electricity	12 (7.5)
Hot oil/water	10 (6.25)
Length of stay (days), median (IQR)	14 (4-59)
Definitive antibiotic	129 (80.63)
MDRO, n (%)	
Yes	146 (91.25)
No	14 (8.75)
Lab parameter	
Leukocyte, mean (SD)	17179 (9192)
Thrombocyte, mean (SD)	32228 (14879)
PCT, median (IQR)	99 (1-22190)
Mortality, n (%)	
MDRO mortality	72 (45)
Non-MDRO mortality	3 (21.43)
Source of infection	
Skin and soft tissue	87 (54,4)
Airway	64 (40)
Urinary tract	9 (5.6)
Sepsis	96 (54.9)

Notes: TBSA = total body surface area, IQR = interquartile range, MDRO: multidrug-resistant organisms, SD = standard deviation, PCT = procalcitonin

Table 2. Multidrug-Resistant Organisms Pathogen Based on Last Culture

	MDRO n(%)	Non-MDRO n(%)
Gram Positive		
Staphylococcus sp.	7 (3.13)	7 (26.92)
Enterococcus faecalis	0 (0)	4 (15.38)
Staphylococcus saphrophyticus	0 (0)	2 (7.69)
Staphylococcus aureus	1 (0.45)	1 (3.85)
Gram Negative		
K. pneumoniae	67 (29.91)	2 (7.69)
Enterobacter sp.	50 (22.32)	6 (23.08)
Acinetobacter sp.	46 (20.54)	2 (7.69)
P. aeruginosa	37 (16.52)	0
E. coli	7 (3.13)	0
Enterobacter cloacea	2 (0.89)	0
Enterobacter eurugenes	2 (3.13)	0
Proteus sp.	2 (0.89)	1 (3.85)
Serratia sp.	1 (0.45)	1 (3.85)
Burkholderia sp.	1 (0.45)	0
Myroides	1 (0.45)	0
	Total MDRO isolate=224, n (%)	Total Non-MDRO isolate =27, n (%)

Notes: MDRO = multidrug-resistant organisms

Table 5 shows the relationship between confounding variables: age, comorbidities, TBSA, use of medical equipment, and length of stay, on the mortality of burn patients in the Public Hospital X Burn Unit. In the age category, there were 28 patients aged \geq 60 years, of which 17 subjects (60.71%) died during hospitalization. The Mann-Whitney test showed a significant relationship with p-value = 0.106. A significant relationship was found between comorbidities and death in burn patients. Of the 27 subjects with comorbidities, 17 (62.96%) died during the hospitalization period. The Chi-square test shows a significant relationship with p-value = 0.066.

Table 3. Antibiotic Resistance Based on Pathogen from Last Culture

Antibiotic resistance	Total (%)
Methicillin-resistant Staphylococcus sp.	5 (2.65)
Methicillin-resistant Staphylococcus aureus	1 (0.53)
Broad Spectrum Beta Lactamase	54 (28.57)
Carbapenem-resistant K. pneumoniae	47 (24.87)
Carbapenem-resistant Acinetobacter	34 (17.99)
Carbapenem-resistant P. aeruginosa	23 (12.17)
Carbapenem-resistant Enterobacteriaceae	23 (12.17)
Carbapenem-resistant E. coli	1 (0.53)
Carbapenem-resistant Myroides	1 (0.53)
	Total Isolate 189, n (%)

Table 4. Analysis of Multidrug-Resistant Organisms Infection Mortality in Burn Patients at the Public Hospital X Burn Unit

MDRO	Mortality n (%)		RR (95% CI)	p-value
	Yes	No		
Yes	72 (45.00)	74 (46.25)	1.103 (1.004-1.211)	0.046
No	3 (21.43)	11 (78.57)		

Notes: MDRO = multidrug-resistant organism, RR = relative risk *significance p-value < 0.05

The TBSA percentage showed a significant relationship with the mortality rate of burn patients. Of a total of 101 patients with TBSA \geq 30%, 67 people (66.34%) died during the treatment period. The Mann-Whitney test showed a significant relationship with p-value <0.001. Of the 145 subjects using medical devices while being treated at the hospital, 74 subjects (51.03%) died while being treated at the hospital, with the results of the Chi-square test showing a significant relationship with a p-value of 0.01. Length of stay also showed a significant relationship with p-value <0.001. The chi-square and Mann-Whitney tests proved a relationship between mortality in burn patients at the Public Hospital X Burn Unit with confounding variables such as age \geq 60 years, comorbidities, TBSA \geq 30%, use of medical devices, and length of stay.

Table 5. Relationship of Confounding Variables to Patient Mortality

Variable				
variable	Yes	No	p-value	
Age group, n (%)				
≥60 years	17 (60.71)	11 (39.29)	0.106	
<60 years	58 (43.94)	74 (56.06)		
Comorbidities, n (%)				
Yes	17 (62.96)	10 (37.04)	0.066	
No	58 (43.61)	75 (56.39)		
TBSA, n (%)				
≥30%	67 (66.34)	34 (33.66)	< 0.001	
10-<30%	8 (13.56)	51 (86.44)		
Medical device use, n (%)				
Yes	74 (51.03)	71 (48.97)	0.01	
No	1 (6.67)	14 (93.33)		
Length of stay (days), median (IRQ)	10 (4-41)	21 (6-59)	<0.001	

Notes: TBSA = total body surface area, IQR = interquartile range

Variables with a p-value of <0.25 in the bivariate analysis were included in the multivariate analysis: TBSA, length of stay, use of medical devices, comorbidities, and age. In the multivariate analysis with logistic regression, the fully customized Odds Ratio (OR) was obtained between the categories of MDRO infection and worsening after adding confounding variables in stages, starting from the smallest p-value in the bivariate (TBSA, length of stay, use of medical devices, and comorbidities), then changes in age in the Adjusted OR for the occurrence of worsening outcomes with each additional confounding variable (Table 6). Thus, Crude OR = 3.568 (0.956-13.317), p-value = 0.046, and Adjusted OR = 3.692 (0.815-16.716), p-value = 0.090 were obtained. Length of stay and age are confounding variables.

Table 6. Multivariate Analysis of Variables Influencing MDRO Infection Mortality in Burn Patients

	Variable	OR MDRO-Mortality (95% CI)	p-value	Coefficient B	Changes in Coef. B
Crude OR					
MDRO		3.568 (0.956-13.317)	0.046	1.272	
Adjusted (OR				
+	TBSA	3.515 (0.824-14.980)	0.089	1.256	1.26%
+	Length of stay	6.713 (1.230-36.628)	0.028	1.840	46.49%
+	Medical device use	3.546 (0.796-15.791)	0.097	1.266	0.79%
+	Comorbidities	3.692 (0.815-16.716)	0.090	1.306	3.15%
+	Aged >60 years	3.228 (0.711-14.658)	0.129	1.172	10.2%

Notes: OR = odds ratio, MDRO = multidrug-resistant organisms, CI = confidence interval, TBSA = total body surface area,

Length of stay and age are confounding variables because the change in coef B > 10 %

Crude OR 3.568 (0.956-13.317). p-value = 0.046

Adjusted OR 3.692 (0.815-16.716). p-value = 0.090

Discussion

The biggest cause of burns in this study was fire, with as many as 138 (86.25%), followed by electricity (7.5%) and oil/hot water (6.25%). A similar finding also went to a study by Hamzaoui $et\ al.^{13}$ reported that the most common causes were fire (52.38%), followed by hot water (28.57%), and electricity (7.93%). ALfadli $et\ al.^3$ also stated that fire was the most common cause of burns (62.69%), followed by hot water (27.86%). National Burn Respiratory 2017 reported that fire was the most common cause in burn patients (76% of the reported cases). Fire burn sufferers experience damage to the skin, loss of physical barriers, and impaired immune function that allows pathogens to enter the body. A total of 145 patients (90.63%) used medical devices, and more than 50% used ventilators. Similar results were also reported by Ellithy $et\ al.^{17}$ in which more than 60% of burn patients treated in the intensive care unit (ICU) used a ventilator. Ressner $et\ al.^{18}$ in Iraq reported that 92% of bacteremia patients use ventilators and only 23% of non-bacteremia use ventilators. Meanwhile, Chen $et\ al.^{19}$ reported that 62.2% of burn patients use ventilators. The use of medical devices is thought to be a source of infection. This is often found in inpatients, such as the use of peripheral and central venous catheters, urinary catheters, nasogastric tubes, and mechanical ventilators because medical devices can cause trauma to the skin or mucosa and allow bacteria to enter the blood.

In this study, the first most common source of infection was the skin and soft tissue (54.4%), followed by the respiratory tract (40%) and the urinary tract (5.6%). Similar results were found in a study conducted by Chukamei *et al.*, stating that skin and soft tissue infections are caused by various microorganisms such as bacteria and fungi, viruses, mycobacteria, and protozoa.²⁰ Sepsis was found in 96 patients (54.9%), which was confirmed by Lin's study as having pathogenic bacterial infections (31%) and MDRO (18.2%), more often occurring in third-degree TBSA and caused by inhalation injury. It also reported that bacteremia patients had longer hospitalization (p-value <0.001), long-term use of mechanical ventilation (p-value <0.001), and sepsis (p-value <0.001).²¹

Samsarga $et\ al.^1$ found a relationship between MDRO infection and duration of antibiotic administration, sepsis, pneumonia, and death. They also found MDRO infection associated with sepsis OR 36.53 (95%Cl 2.05-652.45) and an increased risk of death with OR 57.09 (95%Cl 1.41-2318.87) and TBSA. Chen $et\ al.^{19}$ reported that the most common sources of hospital-associated infections (HAI) found in burn patients are bacteremia (bloodstream infection), UTI, pneumonia, tracheobronchitis, skin and soft tissue infections, and surgical site infections (SSI). This is related to the length of hospital stay, the number of surgical procedures performed, and some surgical procedures, which can increase the risk of death and the high cost of treatment.

This study revealed that the length of stay for patients in the burn unit was 4 to 59 days, and empirical antibiotics were given 160 (100%). Chen $et~al.^{19}$ reported that the average length of stay of burn patients was 18 days. Samsarga $et~al.^{1}$ reported that the median duration of antibiotics with MDRO infection was seven days, and the duration of antibiotics was not associated with length of stay and acute kidney infection (AKI). Almost similar results were also reported by Santos et~al. that MDRO infection was not associated with length of stay and administration of antibiotics. This shows the type of bacteria and duration of antibiotic administration is influenced by the patient's clinical response and surgical interventions, such as tangential excision and skin grafting.

In this study, various types of MDRO and non-MDRO bacteria were found to cause infections in burn patients. The majority of pathogens obtained from culture results were Gram-negative bacteria. From the results of the latest tissue or blood culture examination, the most common pathogens causing MDRO infections were *K. pneumoniae* (29.91%), *Enterobacter* (22.32%), *Acinetobacter* (20.54%), *P. aeruginosa* (16.52%), and *E. coli* (3.13%). In contrast, the most

common non-MDRO pathogen infections were *Enterobacter* (23.08%), *K. pneumoniae* (7.69%), and *Acinetobacter* (7.69%). The Gram-positive pathogens causing the MDRO infections in the tissue or blood culture are *Staphylococcus epidermidis* (3.13%), *Staphylococcus aureus* (0.45%), while for the non-MDRO Gram-positive pathogen is *Staphylococcus epidermidis* (26.92%). Chen *et al.*²³ reported that the most common Gram-negative bacteria in burn patients were *P. aeruginosa, Acinetobacter baumannii, Klebsiella spp., Stenotrophomonas spp., <i>E. coli,* and *Enterobacter cloaceae*. It also reported that 30% were caused by MDRO infection, and most frequently encountered were Carbapenem-resistant *Acinetobacter baumannii* (14.6%) and Carbapenem-resistant *Klebsiella* (2.4%).²³

The most common pathogens encountered during treatment days 8 to 28 were *A. baumannii, Chyseobacterium spp., and S. maltophilia*, but the most common pathogen in tissues was *P. aeruginosa* usually found on days of hospitalization <14 days and the MDRO infection by a Gram-positive pathogen was Methicillin-resistant *Staphylococcus aureus* (11.3%). Burn patients in the ICU have more predisposing factors for infection: wider and deeper TBSA, longer wound healing, impaired immune function, multi-organ dysfunction, and longer hospitalization. The ICU environment can increase the risk of pathogen transmission through equipment, bacterial colonization on equipment surfaces, medical waste and invasive procedures such as central veins, catheters, tracheotomy, bronchoscopy, and mechanical ventilation. An increased risk of MDR in injured patients may occur due to prolonged antibiotic use, repeated invasive procedures, and prolonged hospitalization.²⁴

In this study, the mortality of burn patients with MDRO infection reached 45% (p-value = 0.046), with a relative risk of 1.103 (95%CI 1.004-1.211), making the risk of patients exposed to MDRO dying during hospitalization 10% higher when compared with patients without MDRO exposure to die during hospitalization. The Chi-square test results also showed a strong relationship between MDRO mortality and infection in burn patients. Santos *et al.* reported that the mortality of burn patients with MDRO infection (10.6%) was higher than the mortality of patients without MDRO infection (6.3%).²² A study by Samsarga *et al.* found a significant relationship between mortality and MDRO infection in burn patients (OR = 9.75; 95%CI = 2.00-47.50) and that burn patients with MDRO were in the same condition of a much higher risk of death during hospitalization.¹ Similar results were found in the study by Tanuwijaya *et al.*,² which compared *bacteremia* due to MDRO with burn patients, in which higher mortality was found (RR = 18.6; 95%CI = 11.1-31.1; p-value <0.01).

In this study, after adjusting for confounding variables: TBSA (p-value <0.001), length of stay (p-value <0.001), use of medical devices (p-value <0.01), comorbidities (p-value <0.066), and age (p-value = 0.106). In multivariate analysis, the length of stay and age were confounding variables; non-confounding variables for mortality in burn patients with MDRO infection were TBSA, medical devices, and comorbidities. In this study, the OR (95%CI) after adjusting for TBSA was 3.515 (0.824-14.980), adding medical devices to 3.546 (0.796-15.791), and comorbidities to 3.692 (0.815-16.716).

After multivariate analysis, age was a confounding variable influencing the mortality of MDRO infection in burn patients with OR (95%CI) = 3.228 (0.711-14.658) and a change in Coef B of 10.2%. Old age (age group \geq 60 years) was a risk factor for increased mortality in burn patients. This is consistent with the study by Galeiras *et al.*,²⁵ which reported that age and mortality are linearly proportional if the population of children under 18 years is not included. Moreau *et al.*²⁶ created AGESCORE, a score that has been validated in predicting mortality after experiencing thermal injury based on age. In this scoring, the risk of mortality in burn patients increases with age. This condition is caused by old age, and there is a decrease in the function of the respiratory and cardiovascular systems. Thus, the mortality of elderly patients when they experience injuries also increases due to the failure of compensation from the cardio-respiratory function.²⁷ Besides, old age is associated with the physiological decline of the skin. Therefore, the immune function in elderly patients tends to be lower than in adult patients.²³

The median length of stay in this study was 14 days (4-59), and after multivariate analysis, length of stay was found to be a confounding variable also affecting MDRO infection mortality in burn patients with OR (95%CI = 6.713 (1.23-36.628) and changes in Coef. B 46.49%. A study by Van Yperen *et al.*²⁴ in the Netherlands reported that the length of stay of burn patients in the burn unit was an average of 13 to 16 days, and the patients treated came from referral health facilities. From an administrative perspective, long length of stay is associated with morbidity due to injury cost and quality of care. Chukamei *et al.*²⁰ reported that length of stay was influenced by antibiotic use, previous medical records, type of insurance, degree of burn, organ affected, and lower socioeconomic status associated with poor health status, more susceptibility to injury, and increased risk of hospitalization. Salehi *et al.*²⁷ reported the prevalence of comorbidities in burn patients (18.5%) and comorbidities with old age increased to 57%; diabetes and heart failure were the most frequent comorbidities.

This study examined the effect of MDRO infection on mortality in burn patients and used a cohort design in which the cohort design could explain the relationship between subjects and risk factors and their impact was the strength of this study. The independent and dependent variable data included in the analysis were complete and could be analyzed. This study also considered several confounding variables so that the relationship between MDRO infection and acquired mortality was independent. Meanwhile, the weakness is retrospective with data taken from medical records, and the authors could not control the condition, quality, and standardization of measurement of variables in previous studies, especially variables susceptible to recall bias.

Conclusion

The mortality of injured patients is influenced by MDRO infection, length of stay, and age. Therefore, an optimal treatment and management of such a condition is needed. Infections must be treated with a holistic approach, especially in managing infections, identifying pathogens, antimicrobial therapy, and preventing the spread of nosocomial infections.

Abbreviations

MDRO: multidrug-resistant organisms; TBSA: total body surface area; UTI: Urinary Tract Infection; IQR: interquartile range; SD: standard deviation; OR: odds ratio; ICU: intensive care unit.

Ethics Approval and Consent to Participate

This study has been approved by the Faculty of Medicine Universitas Indonesia No: KET-1023/UN2.F1/ETIK/PPM 00.02/2022, dated September 26, 2022.

Competing Interest

The authors declared no competing interest in this study.

Availability of Data and Materials

The data is available upon request.

Authors' Contribution

RMV, JK, CMR, LN, MS, HS, EY, AW, and EJN conceived and designed the study and led the data collection and statistical analysis. MR proofread the Indonesian and English languages and revised the manuscript. All authors have read and approved the manuscript. All author contributed to the final manuscript.

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Data Mining Analysis with Orange in the Development of Tuberculosis Among Diabetes Mellitus Patients

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Abstract

Prevention and treatment of diabetes will have a positive influence on tuberculosis (TB) since people may get TB because they have diabetes mellitus (DM). Recording and reporting through the TB Information System are not run optimally because of many factors. The information system must be strengthened to be used by private health facilities. This study used secondary data from the 2013 and 2018 Indonesian Basic Health Research (IBHR). The data was analyzed univariately and analyzed further using Orange Data Mining Tools to test the screening tool model used to predict TB in diabetic individuals. The total sample in this study from each data was 38,136 people. The 2013 IBHR stated that 749 people (2%) were diagnosed with pulmonary TB, while the 2018 IBHR stated that 97 people (0.3%) were diagnosed in the previous six months. The results of the Orange analysis showed that precision and recall calculations in this study were quite good, at 0.9. Therefore, the model would likely predict the occurrence of TB in diabetic individuals. According to Orange, the TB-DM electronic screening tool model tends to estimate the incidence of TB in diabetic individuals.

Keywords: diabetes mellitus, Orange analysis, screening, screening tool, tuberculosis

Introduction

Tuberculosis (TB) is the leading cause of death worldwide. In 2022, the largest number of new TB cases was in Southeast Asia (46%), followed by Africa (23%) and the Western Pacific Region (18%). In 2021, 10 countries accounted for two-thirds of new TB cases worldwide: India, Indonesia, China, the Philippines, Pakistan, Nigeria, Bangladesh, the Democratic Republic of Congo, South Africa, and Myanmar. In 2022, the TB case notification rate (CNR) in Indonesia reached 724,309 cases, indicating that 75% of TB patients have been confirmed, identified, detected, or reported. Also, the treatment coverage (TC) for TB reached 74.7%. This figure represents a notable improvement in TB treatment coverage compared to the preceding years but is still lower than a target of 90%. In 2022, Indonesia's TC for TB is projected to reach 48%, significantly below the government's target of 80%.

In 2021, the total number of TB cases identified in Jakarta was 26,854, with East Jakarta registering the highest incidence of TB cases, followed by Central and West Jakarta.³ The CNR in 2022 was 426 per 100,000 people. The TB TC was 100% in 2022, successfully exceeding the national target of 90%.⁴ In contrast, the success rate in 2022 was 81%, slightly under the national target of 90%.⁵ According to Indonesia's national TB control strategy for 2020-2024, the main efforts to improve TB case finding and treatment include mandatory TB case-finding reporting in all health facilities, active case finding in people with TB risk factors, improving the quality of recording and reporting (notification) in all health facilities, expanding and strengthening TB diagnosis and treatment services, treatment monitoring, and optimizing TB-related promotion and education in the community.⁶

Since 2016, the Regulation of the Indonesian Minister of Health No. 67 of 2016 Concerning TB Control has controlled the policy of reporting TB discoveries (notice). According to the policy, TB is an infectious disease that must be reported by each health establishment providing TB services. The TB notification policy has been modified in Presidential Regulation No. 67 of 2021 Concerning TB Control, requiring case reporting within six months or at specific intervals if necessary.

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Received : February 10, 2024 Accepted : July 24, 2024 Published: July 31, 2024 Each region carries out the outcomes and reports at the district/city level to the province until they reach the applicable ministry or agency.8 However, private health facilities continue to play a small role in TB case detection and treatment in Indonesia. The intricacy of the form for reporting TB patients is the cause of low notification among private practitioners. Another determinant is staff reporting TB cases; 50% of the personnel submitting TB notifications have not attended training or workshops for WiFi TB applications, an Android-based application to report the suspect or new TB cases.9

According to Ronacher *et al.*, more people across Africa suffer from TB because they have diabetes mellitus (DM) than because they contract HIV. Diabetes prevention and treatment will have a positive impact on TB prevention. The TB Prevention Therapy Program is critical not only for children and people living with HIV/AIDS but also for family members living in the same house as TB patients, especially if they have DM.¹⁰ TB screening is an endeavor to discover TB patients in a specific community, such as the diabetic population. Based on the Indonesian consensus in the management of TB-DM, TB screening procedures for diabetic individuals can be carried out at First Level Health Facilities/*Fasilitas Kesehatan Tingkat Pertama* (FKTP) and advanced referral health facilities by conducting interviews to observe TB symptoms or risk factors in the diabetics and chest x-ray examinations to examine abnormalities in the lungs. If the FKTP examination is not accessible, the patient is directed to an advanced referral health facility or network radiology laboratory.¹¹

In the age of digital transformation, the Indonesian Ministry of Health (MoH) developed an Android-based application called WiFi TB in 2017 to streamline the notification reporting procedure. This application is designed to allow private health facilities to record case findings and link them to primary health care (PHC). It includes tools for uploading data on TB suspects, TB cases, patient treatment monitoring, and patient treatment monitoring results reporting. Another application, called SOBAT TB, is used to share information regarding TB control among the general public, patients, communities, patient organizations, and medical personnel. This application has a self-filtering feature and is intended to provide accurate information about TB to the general public and facilitate access to TB health service facilities. Last, the EMPATI TB application is designed to help with TB therapy, especially for those who are drug-resistant. However, these applications are not used optimally. There are still problems with the WiFi TB application launched since its implementation because of the lack of human resource capability in entering data into the application, problems with network disruption, quota availability, and a lack of outreach of WiFi TB to private health facilities. Because the SOBAT TB and EMPATI TB applications are relatively new, they are currently still in the evaluation stage and require community outreach in their implementation and use. 14

TB Information System, the main software of the TB case recording and reporting system in Indonesia used by all stakeholders from primary to secondary health facilities (primary health care, hospitals, private practitioners, clinics, laboratories, and pharmacies), health offices, and the MoH, has not been optimally utilized. This condition is caused by insufficient human resources, less funding for recording and reporting programs in health institutions, inadequate integrated information systems, and poor internal networking.¹⁵ As a result, the TB Information System must be strengthened so that health facilities, particularly FKTP, can use this existing application effectively.

This study analyzed the 2013 and 2018 Indonesian Basic Health Research (IBHR) data with a target population of patients with DM records to identify determinants of TB disease, which was used as a screening guideline and as reinforcement in creating information systems and digital transformation in the form of e-screening. This e-screening tool increases tuberculosis notification, particularly in private health facilities. The Orange Data Mining Tool application was used to test the screening tool model to predict TB in people with DM. Data mining is the process of collecting valuable or relevant information from large amounts of data to uncover certain patterns in the data and use it to predict or make judgments.

This program can also be utilized for machine learning for candidates in the fields of biology, biomedicine, and informatics. The data mining in the Orange software uses a widget system, where each widget has its function, which can receive input or produce output. Orange has data entry and filtering capabilities, categorization, evaluation with cross-validation and sampling-based processes, regression, and data visualization. The final result of a series of model testing processes is accuracy, describing how accurately the e-model of the TB-DM screening tool classifies correctly, precision describing the accuracy between the requested data and the prediction results provided by the model, and recall or sensitivity describing the success of the model in retrieving information. This study provided benefits to TB-DM control programs by increasing the implementation of the TB Information System in private health facilities and improving

information on TB suspects or new cases.

Method

A quantitative method was used in this study. The predictors of TB in diabetic individuals were studied using secondary data from the 2013 and 2018 IBHR. This study used Lemeshow's (1991) two-proportion difference hypothesis test formula to select the sample. To find out the description of each variable, univariate data analysis was used in which the findings were reported in a distribution table. Data from the 2013 and 2018 IBHR were examined to determine the availability of data required, specifically data on TB risk factors in diabetic individuals (host and environmental factors) and the totals of TB and DM cases. The data were entered into the SPSS Version 26.0 (Licensed under IBM, New York, USA) data analysis tool, and data cleaning was performed to identify missing data or outliers prior to data analysis.

Furthermore, an analysis was performed using the Orange software Version 3.0 (general public license/free version) in March-April 2023 to test the screening tool model used to predict TB in diabetic individuals. In this study, regression analysis of predictor factors was performed using Orange. The first step was converting data entry into a dataset the file widget could read. The previous input dataset would be taken to the data table widget, where the input dataset was displayed in spreadsheet form to retrieve the data or filter the required data with the select row widget feature, producing suitable data. This data would be entered into a logistic regression model to determine the logistic regression coefficient and model regularization.

The model was evaluated using the test widget and scored through supervised machine learning, testing the learning algorithm on the data and displaying evaluation results that could be used to analyze the performance of the classifier using the confusion matrix widget, displaying the number/proportion of occurrences between predicted classes (predicted values) and actual class (actual value). The final results of this model testing process were "accuracy," describing how accurately the model was in classifying accurately; "precision," describing the accuracy between the requested data and the anticipated results provided by the model; and "recall," or "sensitivity," describing the success of the model in retrieving information.

The data consisted of several variables, each with a certain category. For pulmonary TB, categories included individuals diagnosed within the past year, more than a year ago, and those not diagnosed at all, with some missing data. The DM was categorized based on individuals diagnosed with diabetes, those undiagnosed, and missing data. Age was divided into seven groups: 12-17, 17-25, 25-35, 35-45, 45-55, 55-65, and over 65 years. Sex was categorized as male or female, with some missing data. Education level included individuals who were uneducated, not completing elementary school, attained elementary school, junior high school, senior high school, diploma (DI/DII/DIII), and higher education, with some missing data. Employment status was categorized into unemployed, students, civil servants/police/armed forces, private employees, self-employed, farmers, fishermen, laborers, other occupations, fresh graduates, and missing data. The weight and height measures variables indicated whether these measures were taken, with some missing data. The variables kidney failure diagnosis, cancer diagnosis, and rheumatic/joint disease diagnosis indicate whether a person was diagnosed with the condition, with some missing data.

Smoking records included regular and occasional smokers, former regular and occasional smokers, non-smokers, and missing data. The alcohol intake record was categorized by those consuming alcohol, not consuming alcohol, and missing data. Fasting blood sugar and temporary blood sugar variables were divided into controlled and uncontrolled categories. Ventilation variables for the bedroom, kitchen, and living room indicated whether the ventilation area was adequate (>10% of the floor area), inadequate (<10% of the floor area), or nonexistent, with some missing data. The availability of health facilities, such as public and private hospitals, primary health care, clinics/physician practices, midwife/maternity homes, integrated health care, village health posts, and village maternity clinics, was indicated, with some respondents unsure or missing data.

In addition to univariate analysis, this study also used the Orange analysis to obtain the results of accuracy, precision, and recall calculations by using tests and scores which could be obtained through logistic regression, random forest, Support Vector Machine (SVM), and Naïve Bayes. Logistic regression is employed when the predicted variables are categorical in nature. Therefore, it is necessary to perform numeric encoding of the variables. Random Forest is a multiple decision tree algorithm created in a randomized manner to ensure greater stability in the developed method. The SVM can generate the input-output mapping function from labeled training data in the form of a classification function.

This function exhibits high simplification performance, thus deemed an effective classifier due to its independence from prior knowledge.²⁰

Naïve Bayes comprises a collection of simple probabilistic algorithms based on Bayes' theorem, rendering it one of the most frequently utilized classification algorithms.²¹ This model has good precision and recall at 0.9 due to imbalanced data, which shows that most do not have TB diagnoses, so the model will tend to predict it. Furthermore, the confusion matrix, which is a table containing predicted and actual values, is used for evaluation. The confusion matrix is useful for assessing the performance of classification models with two or more classes as output.²² A Receiver Operating Characteristic Curve is constructed from this conflation matrix, which can be used to measure the overall diagnostic performance of a test and compare two or more diagnostic tests.²³

Results

Table 1. Frequency Distribution Table

013 Indonesian Basic Health Research			2018 Indonesian Basic Health Research		
Variable	n	%	Variable	n	%
Pulmonary Tuberculosis			Pulmonary Tuberculosis		
Yes, within the last ≤1 year	185	0.5	Yes, within the last ≤1 year	97	0.3
Yes, >1 year	749	2	Yes, >1 year	150	0.4
No	37,202	97.6	No	37,213	97.6
	07,202	37.0	Missing data	676	1.8
Diabetes Mellitus			Diabetes Mellitus	070	1.0
/es	795	2.1	Yes	1,061	2.8
No		97.4	No	35,399	2.0 95.4
NO	37,341	97.4		,	
_			Missing data	1,676	1.8
Age			Age		
2–17 years	1,364	3.6	12–17 years	1,287	3.4
17–25 years	4,331	11.4	17-25 years	4,417	11.6
25–35 years	6,781	17.8	25–35 years	6,354	16.7
5-45 years	9,042	23.7	35-45 years	8,527	22.4
5–55 years	7,875	20.6	45–55 years	8,067	21.2
5–65 years	5,280	13.8	55-65 years	5,778	15.2
·65 years	3,481	9.1	>65 years	3,706	9.7
Sex			Sex		
Male	16,100	42.2	Male	15,386	40.3
'emale	22,036	57.8	Female	22,074	57.9
			Missing data	676	1.8
ducation Level			Education Level		
Ineducated	2,940	7.7	Uneducated	2,769	7.3
lot completing elementary school	5,532	14.5	Not completing elementary school	5,505	14.4
Elementary school	12,825	33.6	Elementary school	11,085	29.1
unior high school	7,055	18.5	Junior high school	7,369	19.3
enior high school	7,873	20.6	Senior high school	8,450	22.2
Diploma I/II/III	779	2	Diploma I/II/III	845	2.2
Higher education	1,132	3	Higher education	1,439	3.8
0	-,		Missing data	674	1.8
Employment Status			Employment Status	0, 1	1.0
Jnemployed	13,326	34.9	Unemployed	12,955	34
tudents	2,050	5.4	Students	2,098	5.5
Civil Servants/Police/Armed Forces	1,090	2.9	Civil servants/Police/Armed Forces	618	1.6
Private Employees	2,487	6.5	Private Employees	2,734	7.2
self-employed	4,761	12.5	Self-employed	5,350	14
Farmers	8,134	21.3	Farmers	7,865	20.6
Fishermen	6,134 267	0.7	Fishermen	163	0.4
					9.5
aborers	4,127	10.8	Laborers	3,640	
Other occupations	1,429	3.7	Other occupations	2,037	5.3
Fresh Graduates	465	1.2	Fresh Graduates	-	
			Missing data	676	1.8
Veight Measurement			Weight Measurement		
'es	38,004	99.7	Yes	37,318	97.9
No	132	0.3	No	142	0.4
			Missing data	676	1.8
leight Measurement			Height Measurement		
'es	37,928	99.5	Yes	-	
No.	208	0.5	No	-	
Cancer Diagnosis			Cancer Diagnosis		
'es	90	0.2	Yes	107	0.3
No	38,046	99.8	No	37,353	97.9
			Missing data	676	1.8

013 Indonesian Basic Health Research			2018 Indonesian Basic Health Research		
Variable	n	%	Variable	n	%
Kidney Failure Diagnosis			Kidney Failure Diagnosis		
Yes	114	0.3	Yes	163	0.4
No	38,022	99.7	No	37,297	97.8
			Missing data	676	1.8
Rheumatic/Joint Disease Diagnosis	E (07	147	Rheumatic/Joint Disease Diagnosis	2.624	0.5
Yes	5,607	14.7	Yes	3,634	9.5
No	32,529	85.3	No Missing data	33,826 676	88.7 1.8
Smoking Record			Smoking Record	070	1.0
Yes, every day (regular)	9,371	24.6	Yes, every day (regular)	9,524	25
Yes, sometimes (occasional)	1,962	5.1	Yes, sometimes (occasional)	2,998	7.9
No, but previously smoking every day	1,052	2.8	No, but previously smoking every day	-	- 7.5
No, but previously smoking sometimes	917	2.4	No, but previously smoking sometimes	_	_
Never at all	24,834	65.1	Never at all	24,938	65.4
	,		Missing data	676	1.8
Alcohol Intake Record			Alcohol Intake Record		
Yes	-	-	Yes	738	1.9
No	-	-	No	36,722	96.3
			Missing data	676	1.8
Fasting Blood Sugar			Fasting Blood Sugar		
Controlled	25,441	66.7	Controlled	29,060	76.2
Uncontrolled	12,695	33.3	Uncontrolled	9,076	23.8
Temporary Blood Sugar			Temporary Blood Sugar		
Controlled	37,864	99.3	Controlled	37,864	99.3
Uncontrolled	272	0.7	Uncontrolled	272	0.7
Bedroom Ventilation			Bedroom Ventilation		
Adequate, the area is $\geq 10\%$ of the floor area	16,462	43.2	Adequate, the area is $\geq 10\%$ of the floor area	16,515	43.3
Inadequate, the area is < 10% of the floor area	16,700	43.8	Inadequate, the area is <10% of the floor area	15,071	39.5
Nonexistent	4,974	13	Nonexistent	5,473	14.4
			Missing data	1,077	2.8
Kitchen Ventilation			Kitchen Ventilation		
Adequate, the area is ≥10% of the floor area	15,715	41.2	Adequate, the area is ≥10% of the floor area	14,611	38.3
Inadequate, the area is <10% of the floor area	16,088	42.2	Inadequate, the area is <10% of the floor area	14,131	37.1
Nonexistent	6,333	16.6	Nonexistent	7,838	20.6
Living Doom Vontilation			Missing data	1,556	4.1
Living Room Ventilation	10 505	48.5	Living Room Ventilation	10.010	52
Adequate, the area is $\geq 10\%$ of the floor area Inadequate, the area is $< 10\%$ of the floor area	18,505 15,398	48.5 40.4	Adequate, the area is ≥10% of the floor area Inadequate, the area is <10% of the floor area	19,819 12,489	32.7
Nonexistent	4,233	40.4 11.1	Nonexistent	3,482	9.1
Nonexistent	4,233	11.1	Missing data	2,346	6.2
Public Hospital			Public Hospital	2,540	0.2
Available	26.664	69.9	Available within the district/city	30,754	80.6
Unavailable	11,472	30.1	Available in the nearest district/city	3,636	9.5
onavanable	11,172	50.1	Unavailable	531	1.4
			Do not know	2,539	6.7
			Missing data	676	1.8
Private Hospital			Private Hospital		
Available	20,568	53.9	Available within the district/city	30,754	80.6
Unavailable	17,568	46.1	Available in the nearest district/city	3,636	9.5
	,		Unavailable	531	1.4
			Do not know	2,539	6.7
			Missing data	676	1.8
Public Primary Health Care			Primary Health Care		
Available	34,628	90.8	Available within the district/city	34,316	90
Unavailable	3,508	9.2	Available in the nearest district/city	2,363	6.2
			Unavailable	64	0.2
			Do not know	717	1.9
			Missing data	676	1.8
Clinic/Physician Practice			Clinic/Physician Practice		
Available	20,987	55	Available within the district/city	30,437	79.8
Unavailable	17,149	45	Available in the nearest district/city	1,852	4.9
			Unavailable	1,405	3.7
			Do not know	3,766	9.9
			Missing data	676	1.8
Midwife/Maternity Home			Midwife/Maternity Home		
	25 (55	67.3	Available	-	-
	25,655				
Available Unavailable	12,481	37.3	Unavailable	-	-
Unavailable Integrated Health Care	12,481	37.3	Unavailable Integrated Health Care	-	-
Unavailable			Unavailable	-	-

2013 Indonesian Basic Health Research			2018 Indonesian Basic Health Research		
Variable	n	%	Variable	n	%
Village Health Post			Village Health Post		
Available	4,811	12.6	Available	-	-
Unavailable	33,325	87.4	Unavailable	-	-
Village Maternity Clinic			Village Maternity Clinic		
Available	5,677	14.9	Available	-	-
Unavailable	32,459	85.1	Unavailable	-	-

The selected respondents in this study were 38,136 people from each of the 2013 and 2018 IBHR data. Table 1 depicts the frequency distribution of TB risk factors according to the 2013 and 2018 IBHR. The 2013 IBHR revealed that 749 out of 38,136 participants (2%) had been diagnosed with pulmonary TB in the previous year, while, in the 2018 data, 97 out of 38,136 participants (0.3%) had been diagnosed with pulmonary TB in the previous year. DM affected 795 people (2.1%) in 2013 and 1,061 (2.8%) in 2018. More than half of respondents in the 2013 and 2018 IBHR were in the age group of 35-45 years at 23.7% and 22.4%, respectively. Furthermore, most respondents in this study, according to the 2013 and 2018 IBHR, were mostly females (at 57.8% and 57.9%, respectively), graduated from elementary school (33.6% in 2013 and 29.1% in 2018), and worked as farmers (at 21.3% and 20.6%, respectively).

Of 38,136 respondents, 99.7% were weighed in 2013, and 97.9% were weighed in 2018. In addition to weight, height was recorded in 2013, with 37,004 respondents (99.5%) having their height measured. In 2018, there was no data on height measurement. For cancer diagnosis, 90 respondents (0.2%) had the diagnosis in 2013 and 107 respondents (0.3%) in 2018. A total of 114 respondents (0.3%) in 2013 and 163 respondents (0.4%) in 2018 had been diagnosed with kidney failure for three months or longer. Then, 5,607 respondents (14.7%) in 2013 and 3,634 people (9.5%) in 2018 had rheumatic/joint disease.

Most respondents in 2013 and 2018 (65.1% and 65.4%, respectively) were non-smokers. There was no data on alcohol intake records in 2013; however, most respondents (96.3%) did not consume alcohol in the previous month in 2018. A total of 25,441 respondents (66.7%) in 2013 and 29,060 respondents (76.2%) in 2018 had control of their fasting blood sugar. In terms of temporary blood sugar, 99.3% of respondents in 2013 and 0.7% of respondents in 2018 had control of it.

In 2013, respondents had ventilation in their bedroom (43.2%), kitchen (41.2%), and living room (48.5%), with an area of 10% of floor area for each. While in 2018, respondents had an area of 10% of the floor area for bedroom ventilation at 43.3%, 38.3% for kitchen ventilation, and 52% for the living room. In terms of the availability of health facilities, 69.9% of respondents confirmed a public hospital available in their area in 2013, while 80.6% said there was a hospital in their district/city in 2018. In addition to public hospitals, the presence of private hospitals was explored, and 53.9% of respondents in 2013 and 80.6% in 2018 confirmed the availability of private hospitals in their area.

Most respondents (90.8%) claimed primary health care was available in their neighborhood in 2013; also, 90% (34,316) respondents confirmed the same in their district/city in 2018. In 2013, 20,987 individuals (55%) said there was a doctor's clinic in their neighborhood; in 2018, 30,437 people (79.8%) said there was a doctor's clinic in their district/city. In 2013, 25,655 people (67.3%) said there were midwife practices/maternity homes in their area, but there was no data on midwife practices/maternity homes in 2018. There were 25,407 respondents (66.6%) reporting that they found integrated health care in their neighborhood unit in 2013, but there was no data on the existence of integrated health care in 2018. In 2013, 33,325 people (87.4%) said there were no village health posts in their area, but there was no data on the existence of village health posts in 2018. In 2013, 85.1% of respondents said there were no village maternity clinics in their area, but there was no data on the existence of them in 2018.

Discussion

DM has been highlighted as a significant risk factor for pulmonary TB by the World Health Organization (WHO). Previous systematic review and meta-analysis studies have found that the incidence and prevalence of TB cases in patients with diabetes are quite high.²⁴ A previous study indicated that the risk of TB increased by 2-4 times in diabetic patients compared to non-diabetic individuals.²⁵ Diabetic individuals are at a higher risk of acquiring pulmonary TB due to weakened immunity, which increases the chance of infection in the lungs.²⁶ Another study found that TB is more likely to occur in diabetic individuals due to their reduced immune systems.²⁷ Early detection is critical in preventing TB infection in diabetic individuals; however, early detection of TB-DM is still uncommon, particularly in developing

countries.²⁷ In Indonesia, there is no strategy for screening for TB-DM, even though diabetic individuals are three times more likely to get TB than people with HIV/AIDS.²⁸

Patients with diabetes, cancer, and/or three of the five primary symptoms of TB are the objectives of e-screening. The same symptoms of pulmonary TB and lung cancer make identification and early detection difficult.²⁹ Diabetic individuals should be checked for TB, according to the WHO. Before developing a TB-DM screening tool, the model must be tested, which may be done using the Orange software to predict TB in diabetic individuals. This model aims to predict whether or not someone has TB. The TB variable in this study was divided into three categories: those diagnosed within the past year, more than a year ago, and those not diagnosed at all. The diagnosed and never-diagnosed categories have been combined into the "TB" category. In addition to Orange, other software such as WEKA, KNIME, and SPSS Modeler can be utilized, each with advantages and downsides. Orange has the advantage of displaying more interactive data analysis and data visualization.³⁰

Orange software can be utilized to diagnose diseases. In a previous study, Orange was employed to determine the diagnosis of liver disease in individuals using methods such as Decision Tree, Random Forest, SVM, Neural Network, Naïve Bayes, K-Nearest Neighbors, and Logistic Regression. Through the confusion matrix, accuracy rate, precision rate, training time, and testing time were evaluated, yielding results indicating relatively brief testing and training times. Additionally, it was identified that the four best-performing methods based on accuracy rates are Logistic Regression, Neural Network, Random Forest, and Naïve Bayes. A previous study has used Orange to analyze models to predict the quality-of-life domain of DM patients in a population using sensitivity, precision, and accuracy. The neural network model based on the Area Under Control (AUC), precision, accuracy, and ROC analysis values is the best model for predicting the utility of the quality-of-life domain of DM patients.

In addition to evaluating models, Orange can be used to compare the classification algorithms of several models. A study by Mohi revealed that Orange was used to compare the classification algorithms of the decision tree, Naïve Bayes, and K-Nearest Neighbors models to classify two types of medical data to be tested based on previously conducted health tests.³³ Another study showed that Orange can be used to predict and classify benign and malignant breast cancer by using three classification models: Random Forest, Naïve Bayes, and AdaBoost. The prediction accuracy was 100%, 80%, and 80%, respectively.³⁴ Random Forest produced the best categorization results of the three models. In contrast, Orange can diagnose disease, predict outcomes, and evaluate models with high accuracy and efficient testing times. However, Orange also has some limitations. It offers fewer variants of data mining methods compared to other tools, and it does not support workflow modularity. Orange is effective for certain practical applications, but it may not be as efficient as other tools in terms of the variety of methods offered and the ability to manage complex workflows.³⁵

Conclusion

This study's contribution will benefit the TB-DM control program. The developed e-screening tool has the potential to significantly enhance TB notification and control efforts, especially within private health facilities. Integrating this tool into existing health information systems makes it possible to improve the early detection and management of TB in diabetic individuals, thereby contributing to better health outcomes. The TB-DM e-screening tool will improve the implementation of the TB Information System, increasing TB notification at private health facilities. Future studies should focus on refining the model and expanding its application to other regions and populations to validate its effectiveness and scalability.

Abbreviations

TB: tuberculosis; CNR: case notification rate; TC: treatment coverage; DM: diabetes mellitus; FKTP: Fasilitas Kesehatan Tingkat Pertama/First Level Health Facilities; MoH: Ministry of Health; IBHR: Indonesian Basic Health Research; WHO: World Health Organization.

Ethics Approval and Consent to Participate

This study was approved by the Community Health Research and Ethics Commission, Faculty of Public Health, Universitas Indonesia (Reference 46/UN2.F10.D11/PPM.00.02/2023 dated March 03, 2023).

Competing Interest

The author declared no significant competing financial, professional or personal interests that might have affected the performance or presentation of the work described in this manuscript.

Availability of Data and Materials

The data used in this study were not publicly available. A reasonable request for the dataset can be sent to the National Institute of Health Research and Development/Badan Penelitian dan Pengembangan Kesehatan of the Indonesian Ministry of Health.

Authors' Contribution

MRB was responsible for the entire process, including the conceptualization, design, analysis, writing, and revision of the manuscript. AB was responsible for supervising the findings of this work. CC was involved in the analysis of the findings. All authors discussed and approved the final manuscript.

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Smoking Habit at Home and Upper Respiratory Infection in Infants Aged 6-12 Months

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Smoking Habit at Home and Upper Respiratory Infection in Infants Aged 6-12 Months

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Abstract

Upper Respiratory Tract Infection (URI) is an acute infection caused by viruses, fungi, and bacteria. Smoking habit at home is a risk factor for URI in infants. This study aimed to determine a relationship between smoking at home and the incidence of URI in infants. This study was conducted the fourth week of February 2010 until the third week of April 2010 in Kampar District, Indonesia. This analytical study used a case-control design and cluster random sampling. The samples comprised 162 cases and 162 controls, infants aged 6-12 months. The cases were 162 infants aged 6-12 months suffering from URI within the last month. The controls included mothers visiting primary health care with infants aged 6-12 months and not suffering from URI within the last month. Data analysis took a logistic regression. This study showed that smoking habit at home had an Odds Ratio of 2.68 times (95%CI: 1.51-4.81) for experiencing URI compared to infants whose families did not have such habit. Health promotion of the dangers of smoking at home through a family approach and anti-smoking campaigns must be more intensively carried out among all Indonesian families to control URI.

Keywords: habit, smoking, home, upper respiratory infection

Introduction

Upper respiratory infection (URI) is an acute disease attacking one or more parts of the respiratory tract from the nose to alveoli, including adnexal tissue such as the sinuses, middle ear cavity, and pleura.¹ URI is the main cause of morbidity and mortality for infants aged under one year in developing countries where the 2016 URI incidence in the age group under one year was 169,163 cases,² while the number of URI incidence in infants is around 6-10 times each year.³,⁴ Currently, URI still remains a major public health problem in Indonesia. According to the 2013 Indonesian Basic Health Research, the prevalence of URI based on diagnosis in Riau Province was 10.9%, while the prevalence of URI based on diagnosis and symptoms reached 17.1%. However, the prevalence of URI in this province is still lower than the national prevalence at 13.8% based on diagnosis and 25% based on diagnosis and symptoms.⁵-7 The 2023 Indonesian Health Survey results found that Indonesia's prevalence of URI in infants aged less than one year with a diagnosis was 4.4%. Moreover, the prevalence of ARI in babies less than one-year-old with diagnosis and symptoms was 26.6%.³

The high rates of morbidity and mortality due to URI in developing countries relate to a risk factor of smoking at home.^{7,9-13} A report estimates smoking prevalence at 9% in 2020–2025, contributing to deaths worldwide, and half of smokers die from smoking-related illnesses and diseases.¹⁴ Cigarette smoke at home can cause health problems for the family compared to a healthy home without cigarette smoke around.¹ Several studies have found many risk factors for the incidence of URI in infants and toddlers, including smoking habit at home, poor nutrition in infants, low birth weight, insufficient breastfeeding, homes with high population density, incomplete immunization, sex, lack of vitamin A, iron deficiency, vitamin D or calcium deficiency, age of the baby, health services, low socioeconomic status, and cigarette smoke.^{1,15,16}

The high incidence of URI and the high smoking behavior of the population aged 15 years and older have shown an increase to 36.3% in 2013 from 34.2% in 2007.7 Other studies found a relationship between people closest to the family

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Received: April 29, 2024 Accepted: July 22, 2024 Published: July 31, 2024 smoking at home and the URI incidence in toddlers.^{17,18} Therefore, this study aimed to determine a relationship between smoking habits at home and URI in infants aged 6-12 months. This study is pivotal in strengthening policies against smoking at home in Indonesia.

Method

This quantitative study used a case-control design to determine the relationship between smoking habits at home and the incidence of URI in infants aged 6-12 months. Data collection was carried out through structured interviews with respondents using questionnaires, including an initial survey. This study started by collecting initial data, writing a proposal, collecting primary data, and writing the results. The sampling method was cluster sampling, in which the sampling unit was the primary health care (PHC), which would take samples of 162 cases and 162 controls. Of the 27 PHCs in the Kampar District of Riau Province, Indonesia, 15 PHCs with the highest incidence of URI were selected.

This study was carried out in the fourth week of February 2010 until the third week of April 2010 using primary data, including data on the characteristics of mothers and their infants aged 6-12 months comprising (1) infant characteristic factors (records of infants exposed to immunization for measles and diphtheria, pertussis, and tetanus (DPT)); (2) maternal sociodemographic factors (education, knowledge, and maternal occupation); (3) those visiting the selected PHCs for treatment and were diagnosed with URI; (4) having controlled for non-URI by a doctor at the PHC and recorded in the URI register book who met the sample criteria and then followed up for interviews using a questionnaire. The data used in this study was taken in 2010 and had no data updates.

Measurements and observations were taken to obtain data on infants' body weight, records of measles and DPT immunizations, and the presence of burning smoke at home. Besides, this study validated whether any subject information was true, such as the infant's birth date in the Road-to-Health Card/Kartu Menuju Sehat they had. Stata 11 software with Serial Number 3101506243955 was then employed for the data analysis, including a univariate analysis to determine the distribution of each variable, bivariate analysis to determine the relationship of the independent variable (smoking habit at home) with the dependent variable (URI), and multivariate analysis with multiple logistic regression.

Results

The final parsimonious model described the association between smoking at home and the incidence of URI. Therefore, the final multivariate analysis model obtained is shown in Table 1. Based on the results, the habit of smoking at home has an OR of 2.68 times (95% CI: 1.51-4.81) for experiencing URI compared to not smoking after being controlled for the variable of not being exclusively breastfed. The results of this study proved the hypothesis that the habit of smoking at home increases the incidence of URI in infants aged 6-12 months compared to not having such a habit. The final model equation obtained from this study is as follows:

Logit P (URI in infants) = β 0 + β (presence of smoking habit at home) + β (exclusively breastfed). Logit P (URI in infants) = -3.96 + 3.36 (any smoking habit at home) + 2.19 (not being exclusively breastfed)

Table 1. Final Model of Multivariate Analysis of the Relationship between Smoking Habit at Home and Upper Respiratory Infections

Variable	В	S.E	p-value	OR	95% CI
Smoking habit at home	3.36	0.79	0.001	2.68	1.51-4.81
Not being exclusively breastfed	2.19	1.23	0.025	3.68	1.91-7.09
Constant	-3.96	0.09	0.00	-	-

Notes: S.E = Standard Error, OR = odds ratio; CI = confidence interval.

The presence of a smoking habit at home is an indicator affecting health, especially in infants under one year of age. From the results of the final model of multivariate analysis, the presence of the habit had an OR of 2.68 times (95%CI: 1.51-4.81) for experiencing URI compared to infants who did not have a smoking family at home. This is statistically significant with p-value = 0.001 after controlling for the variable of not being exclusively breastfed. Those infants whose families were known to have smoking habits at home were more likely to be found in the case group (URI) than in the control group (non-URI). The results showed that smoking habit at home was a variable influencing the URI incidence.

Discussion

Increasing interventions implemented to strengthen healthy families without anyone smoking in the house can be done through a family approach program.² A family approach is crucial for all family members to always maintain the health of their infant in the first year of life. The results are fundamentally confirmed by a study by Nuriman stating that the presence of smoker family members is a risk factor for URI in infants.¹⁹ The consistency of this study can also be seen in previous studies, which found that the habit increases the likelihood of URI by 2.05 times compared to not having the habit in the family.^{12,17-19} Zulaikhah *et al.* found that family members who smoke at home increase the risk of respiratory tract infections by 1.35 times greater than family members who do not.¹⁰

Smoking is a public health problem and has economic and environmental impacts.²⁰ Smoking can reduce levels of antibacterial molecules.¹⁴ Smoking habits can cause air pollution in the house and disrupt the defense mechanism of the respiratory tract, resulting in acute respiratory tract infections in toddlers.^{9,12,16,21} In a study by Purba *et al.* in 2023, 34 parents (44.2%) have a smoking intensity of 11-20 cigarettes per day.¹³ This is also in line with other studies' findings that a smoker at home has a higher risk of developing the common cold compared to the non-smoker in their family.^{3,12}

The URI control program is immediately accelerated through advocacy and community outreach regarding the nosmoking movement and overcoming smoking risk factors.³ This advocacy and outreach is a pivotal activity to obtain political commitment from regional and central governments and raise public awareness. All smokers are prohibited from smoking indoors, especially those infants aged less than one year.^{9,10,19,22} Cross-sector collaboration should be made involving the police, religious leaders, social services, education services, subdistricts, and community leaders to reduce the prevalence of smoking in society.^{10,23}

This study showed that the smoking habit at home increased the incidence of URI in infants aged 6-12 months. Handling the URI is not only done through a treatment (curative) but also by increasing promotive and preventive efforts. A "Health Family"-based health promotion in the form of counseling inside and outside the building is suggested to enforce smoking cessation at the PHCs, integrated health care, and other health facilities. 5,10,22

Modifying risk factors in a stop-smoking at home needs to be implemented in a family approach through a healthy lifestyle. 9,11,24,25 A healthy lifestyle through anti-smoking campaigns and a family approach through health promotion to family members not to smoke inside and outside the home must be encouraged through communication, information, and education at home or in the infant's room. Community outreach activities encouraging clean and healthy behavior through smoking prohibitions can create a healthy environment. 5,10

URI control can be carried out by increasing human resource capabilities through short training, medicine supplies, facilities and infrastructure, required health equipment, and validation of routine recording and reporting. Regular supervision by the personnel in charge of the program should be implemented by carrying out active supervision and monitoring program evaluation. Inhalation of cigarette smoke by infants impairs local lung resistance as well as mucociliary clearance ability.^{11,18}

Cigarette consumption by fathers has been proven to increase the likelihood that children under five will experience respiratory problems.^{9,11,12,18,19} A longitudinal study by Qamarya *et al.* presented that smoker mothers impacted their infants in which the cotinine entered into the breast milk and could be detected in the infant's urine.²³ Infants breastfed using a bottle by smoker mothers at home were found ten times more likely to have a higher level of urinary cotinine.²³ Cotinine is a chemical produced when the body breaks down nicotine from inhaled smoke.²³ This study, however, has a limitation. The limitation is that the data obtained was more than ten years ago. However, it is still considered very effective in creating a sustainable "healthy home without cigarette smoke"-based health promotions.

Conclusion

This study highlights that smoking habit has a significant relationship with URI in infants. For this study's finding, health promotion of the dangers of smoking at home through a family approach, as well as anti-smoking campaigns, must be carried out more intensively in all Indonesian families to control URI.

Abbreviations

URI: upper respiratory infection; PHC: primary health care; DPT: diphtheria, pertussis, and tetanus.

Ethics Approval and Consent to Participate

This study was granted permission from the Dean of the Faculty of Public Health Universitas Indonesia No. 889/PT.02.H5.FKMUI/I/2010 dated on February 22, 2010.

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Competing Interest

The authors declare no competing interest in this study.

Availability of Data and Materials

The data is available upon request.

Authors' Contribution

MR, NPS, and TE conceived and designed the study, proofread Indonesian and English languages, led the data collection and statistical analysis, and revised the manuscript. All authors have read and approved the manuscript.

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Passive Smoking and Its Correlation with Stunting in Children: A Systematic Review

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Abstract

Passive smoking is a significant risk factor for stunting in children, highlighting the urgent need for effective public health measures. This study aimed to investigate the association between passive smoking and stunting in children aged 0 months-7 years. Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, a comprehensive literature search was conducted across multiple online databases, including PubMed, ProQuest, Science Direct, Willey Online Library, Sage Journal, Cambridge University Press, and Oxford Academic. The quality of included articles reporting observational studies was assessed using the Critical Appraisal Skill Programme (CASP) checklist, presenting data through narrative synthesis. Findings suggested that passive smoking significantly contributed to the risk of stunting in children. Most reviewed articles were from low-income countries and reported studies with various age groups, demographic characteristics, and self-reported measures. Establishing a causal relationship remains challenging, with 99% of these studies using a cross-sectional design. Based on these findings, further study into this relationship using more comprehensive study designs is necessary. Interventions for mothers and children experiencing stunting should also be prioritized to reduce risk factors and strengthen protective factors.

Keywords: child stunting, passive smoking, public health, systematic review

Introduction

Child growth is an important metric for assessing nutritional health. However, child growth is vulnerable to a variety of influences, including chronic malnutrition, which can lead to stunting, a condition in which children are significantly shorter than their age. This condition not only marks a gap in human development but also significantly increases the risk of death, which limits the children's ability to reach their full intellectual and physical potential. As recognized by the World Health Organization (WHO) as an important nutrition target, stunting reflects broader dietary, health, and socioeconomic challenges that interfere with healthy growth. 1-4

The WHO Global Nutrition Targets 2025 identifies stunting as impaired growth resulting from inadequate nutrition and repeated infections in the first 1,000 days of life, affecting between 171 and 314 million children under the age of five worldwide. 5,6 Indonesia, in particular, shows a high prevalence of stunting, second only to Southeast Asia, with a very high figure of 43.8% among the under-five, according to the 2018 Indonesian Basic Health Research data. Stunting occurs due to complex factors, including fetal growth retardation, maternal and child nutrition and infections, and environmental influences, such as exposure to cigarette smoke. Stunted growth in early childhood has serious impacts on mental health, intellectual intelligence (IQ), cognitive, psychomotor, and motor development, and increases susceptibility to fatal infections.8

Although the causes of stunting are diverse, a significant gap is found in awareness among Indonesian mothers regarding its determinants, leading to misunderstandings and maladaptive behaviors. A previous study shows that exposure to cigarette smoke can cause an increased risk of stunting.8 Most studies have focused on nutritional aspects, but the potential role of environmental factors, especially exposure to passive smoke, remains to be explored.9-11 This analysis aimed to investigate the correlation between exposure to passive smoke and the incidence of stunting in

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Received: May 7, 2024 Accepted: July 29, 2024 Published: July 31, 2024 children, using a systematic review to answer the question: "Is exposure to passive smoke correlated with increased incidence of stunting in children?" According to this study, passive smoking significantly contributes to the risk of stunting in children in terms of diverse age groups and demographic characteristics.

Method

Search strategy

Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 10 guidelines, this systematic review refined its search strategy by leveraging the Population, Intervention, Comparison, and Outcome (PICO) framework to optimize the study plan. 12,13 This study was conducted through a comprehensive search of several electronic databases, including PubMed, ProQuest, Science Direct, Willey Online Library, Sage Journal, Cambridge University Press, and Oxford Academic, from September 1-December 13, 2023. The search terms were refined through initial searches and testing of truncations "*" and wildcards "?," ultimately focusing on "passive smoking" AND "stunting" OR passive smoking AND stunting.

Inclusion and exclusion criteria

This study included open-access and full-text articles published between 2018-2023, which reported the association between passive smoking and child stunting. The last five years of research were selected because the study used the most recent primary research articles. Exclusions applied to studies that did not focus on stunting involved non-child samples, did not have full-text accessibility, were ongoing studies, or were not written in Indonesian or English. However, studies with abstracts in both languages were accepted without imposing language restrictions on the full text.

Screening procedures

To ensure the integrity of reviews, duplicate articles were removed, and independent article selection was performed based on title and abstract by a third primary reviewer. The discrepancies were resolved through discussion and thorough full-text review based on criteria applied in this study.

Data analysis and quality assessment

Data extraction included study identification, objectives, location (world), participant demographics, methodology (PICO and PRISMA Flow Diagram), and anticipated outcomes. Article quality assessment used the Critical Appraisal Skill Programme (CASP) Checklist for Observational Studies without using global quality ratings. A narrative synthesis approach for data analysis was adopted as recommended by systematic review guidelines.

Results

The search yielded 1,375 articles, with 25 duplicates subsequently excluded. Of the remaining 1,350 articles, title and abstract screening led to the exclusion of 845 articles. A total of 505 articles were comprehensively reviewed, with 12 meeting the inclusion criteria. These studies, conducted in Indonesia, China, Japan, and India between 2018 and 2023, were predominantly cross-sectional observational designs with one case-control study. The total number of participants in these studies was 257,590, with sample sizes ranging from 57 to 206,898. The stunting assessment included measurements of height-for-age, weight-for-height, and body mass index (BMI), supplemented with WHO Z-scores and questionnaires to assess the sociodemographic factors and the impact of passive smoke on stunting. The PRISMA flowchart reflects the selection, as shown in Figure 1.

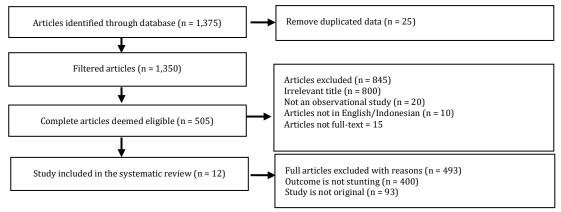


Figure 1. Review Process PRISMA Flow Diagram

Table 1. Characteristics of Included Articles

Author (Year)	Country	Design	Sample Characteristic	Sample Size	Finding
Hasnita <i>et al.</i> (2022) ⁴	Indonesia	Cross- Sectional	The regional data sample from the 1-PPGBM application selected is Padang Pariaman District.	574 respondents were selected as samples, and 316 people experienced stunting.	Correlation of the stunting incidence with cigarette exposure (26.6%). There is a significant relationship between the stunting incidence and cigarette smoke (p-value = 0.001).
Widyawati et al. (2021) ⁸	Indonesia	Cross- Sectional	Children in the age group of under 5.	The number of samples was 128 respondents. Data collection used questionnaires and anthropometric measurements (weight, body length, and baby head circumference).	Analysis of factors related to stunting obtained p-values for the last education factor of parents (0.161), exclusive breastfeeding record (0.794), LBW (1.000), exposure to cigarette smoke during pregnancy (0.303), and after birth (1.000). The test results showed no relationship between record of cigarette exposure during pregnancy and stunting, but the group exposed during pregnancy was more likely to have stunted children compared to those not exposed.
Astuti <i>et al.</i> (2020) ¹¹	Indonesia	Cross- Sectional	Children in the age group of 25–59 months old.	months. Cigarette exposure was assessed based on duration using a cigarette smoke exposure scale questionnaire.	Bivariate statistical tests using Chi-square and Fisher's exact test showed a correlation between stunting and the length of exposure to cigarettes (p-value <0.001; or 10.316).
Shinsugi <i>et al.</i> (2022) ¹⁵	Japan	Cross- Sectional	Children in the age group of 12-59 months.	900 of 3,000 survey areas were randomly selected, and 900 children aged two years and older prior to elementary school were selected.	Smoker fathers or mothers during pregnancy and childbirth can increase the incidence of stunting (aOR: 5.78, 95%CI: [3.48–9.60], p-value <0.001) and wasted (aOR: 7.02, 95%CI: [3.30–15.0], p-value <0.001).
Li et al. (2022) ¹⁶	China	Cross- Sectional	The physical growth indexes of children are height-for-age, weight-for-height, and BMI-for-age. BMI is generally measured by the comparison of a child's weight (kg) and height (kg/m2): BMI = weight (kg)/height (m2). The physical growth of children is assessed by the WHO z-score (Z-score = (analyzed index - median of reference standard)).	5,529 children aged 0 to 71 months and their caregivers were randomly selected using multistage stratified cluster sampling from 72 villages in rural Hunan, spread across 24 cities in 12 countries.	There is no correlation between passive smoking and stunted child growth (p-value = 0.953).
Saeni <i>et al.</i> (2020) ¹⁷	Indonesia	Case Control	57 people	All mothers with stunted children, while controls were mothers with children with normal height. Inclusion criteria include: 1. Willing to be involved in the study; and 2. Having a KMS card.	Exposure to cigarette smoke was not statistically associated with stunting (p-value = 0.090; OR = 0.31).
Qamarya et al. (2022) ¹⁸	Indonesia	Cross- Sectional	Mothers who have children	100 mothers	Children exposed to cigarette smoke and stunting were 13.3%, and those not at 0%. The Chi-square test showed a p-value of 0.007, meaning that there is a relationship between cigarette smoke exposure and stunting, with OR 95%CI = 0.867. This shows that the children exposed have a 0.867 times greater likelihood of experiencing stunting compared to those not exposed.
Islam <i>et al.</i> (2020) ¹⁹	India	Cross- Sectional	Children under the age of five and have child stunting status from the latest national family.	206,898 children aged >5 from the most recent national families.	Not being exposed to cigarette smoke can reduce the prevalence of stunting by 4%, 1%, and 1% of the current prevalence at 38%.
Chao <i>et al.</i> (2022) ²⁰	China	Cross- Sectional	Children in the age group 6- 17 years old.	41,439 children aged 6– 17 included from 30 provinces in mainland China.	Exposure to passive smoke in households inhibits children's growth, and it is recommended to support smoke-free homes.
Kadir <i>et al</i> . (2021) ²¹	Indonesia	Cross- Sectional	57 people	66 parents with children aged >5 in the Kintamani I Primary Health Care working	The study showed a p-value = 0.011 (<0.05); hence, there is a relationship between parental smoking behavior and stunting in children aged 2-5 years, with a correlation strength value of 0.33 so that the variable of

				area.	parental smoking behavior with stunting in children
					aged 2-5 years has a low correlation relationship. In
					conclusion, parental smoking behavior has direct and
					indirect effects on child growth and development.
Muchlis <i>et al</i> . (2023) ²²	Indonesia	Cross- Sectional	221 children	Children aged 0 to 59 months from poor areas in Indonesia.	Predictors of stunting in children aged >5 years are smoker fathers (a0R 1.8; 95%CI=1.281-4.641), smoker parents increase the risk of stunting (COR 3.591; 95%CI = 1.67-3.77), longer exposure to cigarette smoke. Exposure to cigarette smoke for three hours a day increases the risk of stunting in children (COR 2.05; 95%CI 1.214-3.629), and the use of conventional cigarettes increases the risk (a0R 3.19; 95%CI 1.139-67.785). This study indicates the negative impact of smoker parents on their child growth. It is pivotal to reduce the prevalence of smokers by implementing a smoke-free home policy to prevent stunting.

Notes: aOR = adjusted odd ratio, OR = odd ratio, COR = crude odd ratio; CI = confidence interval, LBW = low birth weight, BMI = body mass index, KMS = Health Card/Kartu Menuju Sehat, PPGBM = Community-based Nutrition Reporting Recording/Pencatatan Pelaporan Gizi Berbasis Masyarakat.

After adjusting for confounding factors, multiple logistic regression analysis showed that boys with low birth weight (LBW) for gestational age tended to experience stunting (aOR: 5.78, 95%CI: [3.48-9.60], p-value <0.001), while those with high birth weight for gestational age had a lower probability (aOR: 0.26, 95%CI: [0.11-0.60], p-value <0.01). In contrast, girls with LBW for gestational age tended to experience stunting (aOR: 4.04, 95%CI: [2.43–6.73], p-value <0.001) compared to others. Exposure to passive smoke for more than three hours a day increases the risk of stunted growth in children.

This study revealed that boys were more at risk of stunting with parents who had positive smoking status compared to girls. A significant correlation was found between stunting and cigarette smoke (p-value = 0.001). This is because nicotine has the potential to interfere with oxygen delivery by 30-40%, as well as the absorption of calcium, minerals, and vitamin C, which are very important for growth. This study found a relationship between stunting and the duration of exposure to cigarette smoke (p-value <0.001; OR 10.316). The exposure to cigarette smoke increased the risk of stunting by up to 10 times.

Passive smoking and stunting occurred because environment and nutrition played an essential important role in stunting prevention efforts. Short mothers with a good environment and nutrition were less likely to have stunted children. Therefore, the first 1000 days of life are a crucial variable that requires great attention. The Chi-square test produced a p-value of 0.007, indicating a correlation between cigarette smoke exposure and stunting with OR 95%CI = 0.867. Based on the results of this study, children exposed to cigarette smoke had a 0.867 times greater likelihood of experiencing stunting compared to those not exposed.

In addition, this study also revealed that passive smoking raised the condition risk [OR =1.520, 95%CI: 1.318, 1.753]. A similar relationship was reported between the variables, particularly among children aged two to five years (p-value = 0.011), with a correlation strength value of 0.33. This indicated that parental smoking behavior with stunting had a low relationship. In conclusion, parental smoking behavior has direct and indirect effects on child growth.

The prevalence of stunting was 145 people, or 65.6% of the population. In addition, children living with smoker parents were 157 people (71%), and the most exposure could be attributed to fathers among 147 participants (67.4%). Predictors of stunting in children aged more than five years were fathers who smoke (AOR = 1.8; 95%CI = 1.281-4.641), and both parents who smoke further increase the risk (COR = 3.591; 95%CI = 1.67-3.77). Other influential factors were exposure to cigarette smoke for more than three hours daily (COR = 2.05; 95%CI = 1.214-3.629) and using conventional cigarettes (AOR = 3.19; 95%CI = 1.139-67.785). High smoking prevalence can increase stunting because cigarettes contribute to household expenses in low-income families.

There was no relationship between passive smoking and stunting for several reasons. First, economic conditions, culture, religion, life, and living habits differ between ethnic groups. Second, the samples, index definitions, and report data vary. The association test did not show any relationship between records of exposure to cigarette smoke during pregnancy and stunting. However, there was a possibility of stunting in the group exposed to cigarette smoke during pregnancy compared to the group not exposed (p-value = 0.100).

Discussion

This study highlighted a significant association between passive smoke and stunting in children, corroborating findings from several studies. Most studies emphasized an association between passive smoke and stunting, with maternal sociodemographic and psychological factors also playing an important role. Passive smoke emerges as an important risk factor for stunting, highlighting the detrimental impact of passive smoke exposure on child development. Passive smoking is one of the known risk factors for stunting in children, and most studies have shown a significant association. This analysis is not only limited to passive smoking habits but also includes maternal sociodemographic and psychological factors, in line with previous reports that collectively affect the incidence of stunting.

There were twelve articles analyzing the association of passive smoking with stunting.^{4,8,11,15-22} Mixed results were described, with eleven articles^{4,11,15-22} reporting that cigarette smoke exposure contributed to stunting disease, while one article⁸ reported the absence of a relationship. Bivariate analysis showed that children, the passive smokers, have a higher risk of stunting in adolescence. In this context, participants have fathers, mothers, and/or other family members in the same household who actively smoke.³ This is consistent with previous reports in Indonesia showing that paternal smoking is associated with severe malnutrition.³ Handriani *et al.* revealed that exposure to cigarette smoke increased weight gain risk in LBW infants by 2.19 times more than others.²³

An increase in tobacco expenditure proportions from 3.6% in 1993 to 5.6% in 2014, accompanied by a decrease in important expenditures, such as carbohydrates and protein, had created long-run impacts on stunted children. Children with smoker parents had a weight growth of 1.5 kg and a height growth of 0.34 cm, which was lower compared to others with non-smoker parents. In addition, children with smoker parents had a probability of experiencing stunting 5.5% (percentage point from average) higher compared to those with non-smoker parents. This had been controlled with genetic, environmental, and nutrition variables. In terms of household welfare, higher smoking expenditure increased the probability of households being continuously poor.^{24,25}

High smoking contributed to a rise in stunting prevalence.²² A previous study of children aged 16-24 months stated there is an association between smoker parents and child stunting, with a p-value = 0.601 and OR = 1.15. This indicated that smoker parents were 1.15 times more at risk of having stunted children compared to non-smoker parents. Parental smoking could affect stunted children by two methods.^{22,26,27} Children exposed to passive smoke potentially experience the same effects as active smokers. A 2018 report was carried out by the Universitas Indonesia Center for Social Security Studies according to data exploration of the Indonesian Family Life Survey. The results showed that the likelihood of having stunted children for the smoker parents was >5.5% compared to the non-smoker parents.²⁸ Tobacco smoke affects the absorption of nutrients in children, affecting their growth and development. The use of Javanese conventional cigarettes, well-known as *Kretek*, increased the risk of stunted growth.^{22,29} The exposure to smoke for three hours more a day increased the risk of stunting, which applies to the use of *Kretek* as well.²²

A safe environment is usually free from pollution caused by the smoker members of the family. Some reports show that cigarettes contain around 4,000 types of dangerous compounds. Lead toxins in cigarettes include nicotine, carbon monoxide, and tar. The content of cigarette smoke affects gene mutations. Smoking exposes children to dangerous chemicals that inhibit their growth. The cost of cigarettes also reduces the cost of meeting household needs so that nutritional intake is reduced.^{21,30,31} Exposure to cigarette smoke, both during pregnancy and during child development, is correlated with the risk of stunting. In low- and middle-income countries, cadmium in cigarette smoke disrupts the balance of calcium, zinc, and cadmium in the body, causing impaired bone formation and slow growth.³⁰

A study found that those exposed to cigarette smoke were shorter than those not exposed [β = -2.897, 95%CI): -3.090, -2.703] and had a greater likelihood of stunting [OR = 1.520, 95%CI: 1.318, 1.753]. The impact of cigarette smoke exposure was the same for all sexes but correlated with age, especially at the age of six to eight years (OR = 3.708, 95%CI: 2.572, 5.346). The risk of stunting increased with the duration of smoke exposure, with risk levels of 1.246 (CI: 1.053,1.474), 1.904 (CI: 1.572–2.305), and 3.263 (CI: 2.203,4.833) for those exposed for 1–10, 11–55, and 56 minutes/day, respectively, which recommends a dose-response correlation.²⁰ This analysis shows that exposure to smoke inhibits the growth of school-age children. A previous study in China showed that the prevalence of girls (43%) was higher than that of boys (40%), and a positive correlation with age was observed. Based on region, the prevalence of children in South and Southwest China was higher, at 47%, while 33% was obtained in Northeast China.²⁰

Exposure to passive smoke is common in low-income families, especially those with low education levels. Children with smoker parents had higher serum thyroglobulin and thiocyanate concentrations at birth and aged one year than others. These results suggest that the passive transfer effect of smoking (thiocyanate) stimulates thyroglobulin secretion.

Some reports have also revealed that smoking during pregnancy causes neonatal thyroid dilatation.^{20,22} Cigarette smoke could cause clogged blood vessels, leading to substance inhibition needed by the body. Therefore, the body's vulnerability could happen because of an imbalance, causing the development of various diseases. The same impact was also felt by children exposed to cigarette smoke. This exposure caused people in the environment to be passive smokers, thereby increasing the risk of stunting.^{17,32,33} Apart from the direct effect of stunting, smoking also had the potential to cause health problems indirectly. This occurred because family income was predominantly spent on cigarettes rather than nutritional needs, particularly children.³⁴

Based on previous reports, three toxic compounds are carcinogenic (benzo(a)pyrene, 4-aminobutylene, and acrylonitrile) and can poison mothers and babies. In addition, cigarette smoke contains 400 chemicals, and 200 of them are reported to be very toxic. CO is a toxic substance that can cause blood vessels to cramp, increase blood pressure, and tear blood vessel walls. CO gas can cause hemoglobin desaturation, reducing oxygen circulation to tissues and causing myocardium. This gas is reported to have the potential to replace O_2 bound to hemoglobin. Exposure duration to cigarette smoke was significantly correlated with stunting in children aged 25-59 months. Exposure for three hours more a day raised the risk by 10.316 times. Most stunted children had fathers with a record of smoking for more than three years and three times more a day. Previous analysis in Indonesia has shown that paternal smoking is strongly associated with stunting due to the chronic effects of low-quality diets in households where fathers are smokers. A correlation might also occur with a decrease in the proportion of weekly household expenditure on quality food (eggs, fish, fruits, and vegetables).

According to some studies, there was no correlation between passive smoking and stunting.^{27,16} Bella *et al.* revealed that children whose fathers had moderate/high smoking intensity tended to be skinnier and stunted by 2.93 and 3.47 percentage points.²⁸ While the intensity of the father's smoking did not have a significant effect on overweight. This analysis observed the effect of the father's smoking status on child malnutrition, which was insignificant because the amount of nicotine smoked by parents was not measured; thus, the threshold value that could trigger inflammation was unknown. In this report, this was not proven, possibly because the levels of TNF, interleukin 1, and interleukin 6 were not measured. This condition could also be caused by low levels of these mediators due to various factors. Therefore, the hypothesis in this study was not proven, possibly because low levels of mediators were not enough to trigger an increase in leptin hormone production. This study's results indicated that the statistical significance of cigarette consumption may be reduced by the influence of external variables, such as maternal height, which has the potential to have a stronger effect. An alternative interpretation may indicate that varying nicotine content in each type of cigarette makes direct comparisons unreliable.²⁶

This systematic review has carefully examined the association between passive smoke and stunting in children, revealing a strong correlation. Evidence suggests that children exposed to passive smoke, especially from parents, are at higher risk of stunting. This finding is consistent across studies, highlighting the detrimental impact of environmental tobacco smoke on child growth and development.

The complexity of stunting, influenced by multiple elements, including socioeconomic status, nutritional intake, and environmental factors, underscores the challenges in addressing this public health problem. However, the consistent association between passive smoke and stunting highlights the need for targeted interventions to protect children from exposure to passive smoke. Efforts to reduce the impact of passive smoke should include public health campaigns aimed at reducing smoking in the presence of children, implementing smoke-free home policies, and educating parents about the risks associated with tobacco smoke exposure. Furthermore, broader strategies to combat stunting should address malnutrition, improve maternal health, and improve living conditions to promote optimal child growth.

The findings suggest an influence of passive smoke on stunting, suggesting increased awareness among policymakers and mothers. Despite the inability to establish causality due to the largely cross-sectional study design, evidence suggests a significant impact of passive smoke on child growth. Future studies should expand the scope to include other potential stunting factors and use longitudinal designs to better understand causal pathways.

Strengths and Limitations

All included articles were of strong/moderate quality. In addition, the sample population consisted of children aged 0 months-7 years. During the selection process, there was no age limit on the samples made, thus increasing the breadth and sensitivity of the review. The articles included were carried out in various countries, with various educational institutions and households, so the review is representative. However, the majority was conducted in middle- to low-

income countries (77.7%), which might increase the risk of applying the results only to low-income countries. The articles did not use the same measurement tools and questionnaires, and standards for instruments were not established in several articles. All articles in this review relied on self-reported data, which could be affected by individual dishonesty, social desirability, self-evaluative capacity, and interpretation, thus introducing self-reported bias.

Furthermore, as 99% had a cross-sectional design, it is inconclusive. Although eight databases were often used to search for eligible articles, there might be articles in other databases that were not previously considered. The reasons are that the study does not focus on stunting, involves non-child samples, lacks accessibility of full text, is ongoing research, or is not written in Indonesian or English. Given the limitations of predominantly cross-sectional studies in this review, there is an urgent need for longitudinal studies to establish causality between passive smoke and stunting. Such studies will provide a deeper understanding of temporal relationships and potential mechanisms underlying these associations, informing more effective prevention and intervention strategies.

Conclusion

This review shows the significant relationship between passive smoking and stunting in children, calling for concerted efforts from policymakers, healthcare providers, and communities to reduce children's exposure to tobacco smoke and address the broader determinants of stunting.

Abbreviations

WHO: World Health Organization; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analysis; PICO: Population, Intervention, Comparison, Outcome; BMI: body mass index; aOR: adjusted odd ratio; OR: odd ratio; COR: crude odd ratio; CI: confident interval; LBW: low birth weight.

Ethics Approval and Consent to Participate

Not applicable.

Competing Interest

The authors declare no substantial competing financial, professional, or personal interests that could have influenced how the work described in this publication was performed or presented.

Availability of Data and Materials

The data is publicly available from PubMed, ProQuest, Science Direct, Willey Online Library, Sage Journal, Cambridge University Press, and Oxford Academic databases published from 2018-2023. For more information, the reader can contact the corresponding author.

Authors' Contribution

AR contributed to the manuscript's conceptualization, data screening, supervision, and writing. The manuscript was conceived and written with the help of K, HH, and F.

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New Approach to Mapping Regional Vulnerability in Controlling Tuberculosis Disease in Indonesia

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New Approach to Mapping Regional Vulnerability in Controlling Tuberculosis Disease in Indonesia

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New Approach to Mapping Regional Vulnerability in Controlling Tuberculosis in Indonesia

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Abstract

Tuberculosis (TB) is still a health problem in Indonesia because its prevalence ranks second in the world after India in 2023. Regional factors, inadequate health facilities, and limited resources (financial, human, and infrastructure) are challenges requiring innovation to help the government control TB. TB eradication efforts need to be made with a comprehensive and effective approach. One method used is to look at the vast territory of Indonesia; therefore, mapping the vulnerability of TB is highly recommended. Using a Geographic Information System is expected to help map the TB vulnerability areas in Indonesia. Given several epidemiological, socio-geographic, and environmental factors influencing TB, the question arises of how to map TB vulnerability areas in Indonesia. This study used a cross-sectional design, secondary data was collected from several sources, and a vulnerability analysis was performed by considering several socio-environmental epidemiological variables. Furthermore, after the analysis, the TB area vulnerability category would be obtained along with a map of TB vulnerability areas in Indonesia according to regional and district analysis units. This study produces a TB susceptibility index and map for Sumatra, Java-Bali, and other regions in Indonesia.

Keywords: Geographic Information System, Indonesia, tuberculosis vulnerability

Introduction

The problem of tuberculosis (TB) in Indonesia from year to year has not shown any decrease in morbidity and mortality rates. According to the 2023 Global TB report, Indonesia was ranked second with the highest prevalence in the world.¹ The Indonesian Ministry of Health has made various control efforts in this matter.² However, the problem of TB is not only a problem between diseases or agents in humans, but TB is a complex problem like other infectious diseases, where apart from the epidemiological elements considered, other elements are no less important. Health development cannot be separated from the health system, where all elements must be considered, including system components and several other influencing factors.³

Indonesia has a very large area of 5,193,250 km², starting from Sabang City at 95°E and Merauke District at 141°E (6°N-11°S and 95°E-141°E) and Weh Island (6°N) to Rote Island (11°S), with regional topography covering land and sea. Indonesia has a land area of 1,919,440 km² and 17,580 islands spread throughout the country, both from geographical locations located on two large continents (Asia and Australia) and two oceans (Pacific and Indian). Geomorphology, which includes various surface forms (lowlands, highlands, and mountains), will affect temperature, plant types, and mineral content, affecting population density and infrastructure development.⁴ The TB eradication efforts in this regard need to be made with a comprehensive and effective approach. One method to use is to look at the vast territory of Indonesia; therefore, mapping TB vulnerability is a highly recommended method.^{2,5} Mapping TB vulnerability aims to identify areas which are vulnerable to increased morbidity and mortality due to TB, so that prevention and control efforts for the disease

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can be carried out appropriately and efficiently.

Remote sensing-based TB vulnerability analysis uses data and information from satellite imagery and remote sensing technology. 6-8 It should be emphasized that remote sensing is one of the input and process variables in this study and does not stand alone. Other variables used in this study are epidemiology, social, environment, health services, and TB programs. Host epidemiological data are utilized to identify TB carriers or individuals, including characteristics of age, sex, occupation, diabetes mellitus, HIV/AIDS, exposure to cigarette smoke or smoking habit, household contact with TB patients, and other variables used in the study, as described in the method section. If available, several variables can utilize spatial information, such as population density, access to health services, and the environment. 9-15 After all input variables are obtained, either with remote sensing or other data support, a TB vulnerability modeling analysis will be carried out with district analysis units throughout Indonesia.

The benefits of remote sensing-based TB vulnerability analysis in Indonesia are (1) identifying areas at high risk of spreading TB; this can help the government through the Ministry of Health in efforts to control the disease effectively; (2) planning interventions and monitoring and evaluation programs for controlling TB, then making comparisons after intervention; (3) Geographic Information System (GIS) makes it possible to integrate data from various sources, including environmental and social health data, demographics, and geography. This allows for comprehensive and accurate analysis of influential factors to the spread of TB; (4) combining data and conducting TB control vulnerability modeling analysis, then visualizing the data in the form of maps, which makes it easier to understand and communicate information to stakeholders. The existing TB vulnerability mapping can help identify areas with high TB incidence so that control efforts will be targeted, effective, and focused on these areas.

Method

This study applied a cross-sectional approach. Secondary data analyzed were data coming from the 2023 TB Information System, 2023 Indonesia Health Survey, 2018 Indonesian Basic Health Research, 2019 Health Facility Research, 2019 Facilities and Infrastructure, 2023 Statistics Indonesia, and 2023 Meteorological, Climatological, and Geophysical Agency, with city/district analysis units in Indonesia. Apart from host variables already mentioned in the previous section, there were also agent variables, including TB-causing bacteria: drug-resistant TB bacteria and drug-sensitive TB bacteria.

Environmental data was utilized to examine risk factors for TB, such as physical and social environments (temperature, humidity, sunlight, or air particulates), income level, poverty, slum housing, families living in healthy homes covering the housing density, sanitation, and air quality around the house, ownership of social security, and ownership of health insurance. Health services included the availability and readiness of health services, as well as population access to TB health services in the area. Intermediate and output indicators of the TB program in the Ministry of Health (in this study referred to as the Micro TB program) were financing (2023 TB Information System), TB governance/leadership (2023 TB Information System), logistics (2023 TB Information System), information systems (2023 TB Information System), screening of suspected TB patients, detection of Acid-Fast Bacilli (AFB) + TB patients, treated TB patients, TB patients who failed treatment (default), success rate (cure rate), and re-treated TB cases, drugresistant TB cases starting second-line treatment, TB-HIV patients receiving antiretroviral (ARV) during TB treatment, the number of TB cases found in prisons or detention centers, number of children under five years of age receiving INH preventive treatment, TB cases found and reported by the community or community organizations, case notification rate (CNR) treated, coverage of treatment of all cases, coverage of detection of resistance cases, and success rate of treatment of drug-resistant TB patients, percentage of TB patients who knew their HIV status, financing (2023 TB Information System), TB Management/Leadership (2023 TB Information System), case detection rate (CDR), CNR, and Cure Rate.

Univariate analysis was performed on each variable to determine the distribution of the variables studied. Bivariate analysis was performed to determine the relationship between two variables and calculate OR using a 2 x 2 table at a confidence level of 0.05 and a confidence level of 95%. (α = 0.05). Furthermore, risk or vulnerability analysis was conducted on each group or latent variable to create a map with a district analysis unit.

Results and Discussion

Since studies on TB vulnerability have not been found as a weakness of this study, a vulnerability determination method was used by following the steps applied to several vulnerability analyses conducted by the Regional Agency for

Disaster Management. It turns out that, for some remote sensing data, there was no support for this study; therefore, a mapping with the help of GIS was made so that later this data would be used as initial data for geospatial field monitoring. The results of this study are expected to obtain several values, which include host vulnerability to TB, vulnerability to TB, environmental vulnerability to TB, vulnerability to TB health services in Indonesia, and vulnerability to TB programs in Indonesia.

In host vulnerability, several studies mentioned people of productive age, men, people with TB contact, people with diabetes mellitus, people living with HIV or AIDS, and people with cigarette exposure. 12-15 While the vulnerability of the population to agents in Indonesia is a group of drug-sensitive and drug-resistant, it could be one or even several drug types. 13 Environmental vulnerability could be physical environment, such as exposure to air pollution. This could be caused by fuel used for cooking or outdoor environments continuously polluted, socioeconomic groups vulnerable to TB, for example, living in unhealthy houses, slums, or densely-populated settlements, poor population groups, and residents receiving assistance or social security. There are still differences in several indicators from several agencies, so when mapping input, a version will be created according to the indicators created by each agency. 13-15 Due to the vulnerability of health services to limited data completeness, the data processing results are health services and health centers. In the TB program, some TB successes will be influenced by logistics, finances, and several other constraints, which will be very interesting to discuss in more depth. Furthermore, a vulnerability map is made, which is expected to be considered in policy-making for TB control in Indonesia.

Conclusion

Vulnerability analysis using sensing, which is one of the input variables, is it not the only one? This is an important step in TB eradication in Indonesia and allows to identify areas with high levels of vulnerability and estimated factors for possible interventions applied to reduce vulnerability. The TB eradication program in Indonesia is expected to be successful and become a possible alternative to be implemented in Indonesia with proper implementation.

Abbreviations

TB: tuberculosis; GIS: Geographic Information System; CNR: case notification rate.

Ethics Approval and Consent to Participate

Ethics Approval on Health Research No. 128/KE.03/SK/07/2024.

Competing Interest

The authors declare that there is no conflict of interest.

Availability of Data and Materials

Not applicable.

Authors' Contribution

MHH is the researcher and idea originator/initiator; AH checks variables; D seeks references; HS for the writing completion; AA searches publications and references; MRK and MH observe far sensing and create a map; R, K, NEP, and DB making operational definition; CTP and MNFS analyzing service availability and readiness assessment for health services; YB, NEWS, DL analyzing the host and agent data.

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