

Kesmas

Jurnal Kesehatan Masyarakat Nasional

(National Public Health Journal)

Quarterly Journal

**Special Issue: Responses to Post-Pandemic COVID-19
Sustainable Healthcare Disaster and Management**

Handling by: Prof. Dewi Susanna, MS

Measuring the Success of *PeduliLindungi* Application Use for Supporting COVID-19 Prevention: A Case Study among College Students in Jakarta, Indonesia (pp. 11-16)

Does It Still Show a Deficit? Arguing Post-COVID-19 Health Financing System in Bogor, Indonesia (pp. 17-21)

The Effect of COVID-19 Pandemic-Induced Stress on Reproductive-Age Women's Menstrual Cycle Regularity (pp. 39-43)

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Dear Editorial Team, Authors, Viewers, Subscribers, and Readers.

This has been a third Special Issue of Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal). From the two previous editions, Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal) have curated good quality articles regarding the COVID-19 pandemic. Nowadays, there is an issue of the pandemic becoming the endemic. I hope there will be articles discussing about this issue in this edition, so that the society will have good insight to facing the endemic. (Kelvin, Jakarta)

INFORMATION

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Grech ED. ABC of interventional cardiology. 2nd ed. Chichester: Wiley blackwell; 2011. Available from: <https://ebookcentral.proquest.com/lib/imperial/detail.action?docID=822522>
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Pullen LC. Antibiotic resistance continues to be a problem in children. *Medscape*; 2017. Available from: <https://www.medscape.com/viewarticle/860801>
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Editorial

Dear respectful colleagues,

Welcome to the third Special Issue, a peer-reviewed open access journal examining articles in types of reviews, case reports, case studies, opinions, commentaries, policy briefs, mini-research, and any non-research articles.

After two full years of the pandemic, many issues related to post-COVID-19 life arose. In several countries, it seems that the virus has been considered endemic. Although the number of cases decreased almost worldwide compared to a year before, new cases are still being recorded. Some countries like Indonesia are uncertain whether to shift the COVID-19 from pandemic to endemic. Indonesia is still experiencing rising cases until mid-2022, especially in major provinces like Special Capital Region of Jakarta, West Java, Banten, East Java, and Bali (covid19.go.id, July 28, 2022).¹ Therefore, health protocols should be continued, vaccination should be completed, and diagnostic tests should be carried out. Most importantly, implementing the five strategies to build community health resilience to anticipate any circumstances in the future should be prioritized. The shift from pandemic to epidemic remains a question. Post-pandemic evaluation is critical for understanding the policy's effectiveness and the impact on the financing mechanism during the pandemic (pp. 4-10).

PeduliLindungi apps which certifies users to access public facilities and displays the COVID-19 vaccination certificates, supports the Indonesian Government's mobility restrictions during the COVID-19 pandemic. Most college students use the apps. The study shows that user's satisfaction was influenced by perceived benefit, self-efficacy, system quality, and information quality. The apps can evaluate the user's compliance with the vaccination program. In addition, it can be converted into a personal health record, one of the main goals proposed by the Ministry of Health (pp. 11-16).

A study evaluating the hospital's role in dealing with the COVID-19 was very important which includes the financial scheme in taking care of the patients. Hospitals have become important centers in combating the COVID-19 cases, particularly at the district level, which accommodates many cases. The case of Bogor City, West Java Province, Indonesia showed the necessity of evaluating health financing at the hospital level by analyzing the

reimbursement system and looking closely at the hospital claims calculations from reimbursement fees set by the Indonesian-Case Based Groups (INA CBGs) managed by the Social Security Administrative Body or *Badan Penyelenggara Jaminan Sosial (BPJS) Kesehatan* (pp. 17-21). The study claimed that almost one-quarter of medical care episodes in the hospitals in Bogor City of Indonesia demonstrated a deficit financial system. It is essential to evaluate hospital claims calculations from reimbursement fees set by the INA CBGs. Further studies are encouraged to calculate the mean differences between the pre- and post-COVID-19 situations once the Indonesian government has proclaimed the COVID-19 pandemic to have passed.

The industrial sector's activities have been crucial in dealing with the pandemic. The pandemic threatening the continuity of human activity also means impeding the industry's productivity. A study on the prevention and control of the spread of the the COVID-19 in the mining industry focused on the managerial and operational scopes of prevention and control according to the International Labour Organization guidelines. The evaluation shows that the total average score for all factors' completion is 89.41%. The results shows that nine important critical factors could be maintained and that planning, resources, and management systems in the concentrating division have been implemented well. Workers' active participation and awareness also support the implementation of policies and programs. The implementation of prevention and control in the industry was adequate as indicated by declining of peak numbers as soon as the policies and programs are implemented (pp. 22-29).

Vaccination is a critical method for preventing the spread of COVID-19 in every country. However, addressing people's knowledge and beliefs is vital to getting optimum immunization coverage for the COVID-19. Misperception among people is always a possibility. A systematic review of misperceptions of the vaccine in Indonesia finds that the average response of people who receive the vaccine believe that it is an antibody that fights the virus. There is also a desire to seek accurate information on vaccines using social media. The acceptance of vaccination increases among those believing in immunization's benefits, safety, and effectiveness. The government can affect people's perception and acceptance of vaccines, especially those with a negative response to the

vaccination, because they concerned on their side effects, safety, and effectiveness, in which the problem emerges due to insufficient information and certainty. One main reason raised is about the halal issue of vaccine. While, others believe that the COVID-19 means a world conspiracy that could affect their future, so they rejected the vaccine (pp. 30-38).

The pandemic also induced stress for all communities, especially for people living in areas with relatively high numbers of cases. This stress may have affected women's menstrual cycles. One study shows the effect of the COVID-19 pandemic on menstrual cycle regularity in reproductive-age women (pp. 39-43). This study presents that the high stress induced by the pandemic is associated with an irregular menstrual cycle in reproductive-age women. There is an association between high stress and dysmenorrhea, hypomenorrhea, and menorrhagia. Health care personnel in constant contact with the COVID-19 cases also manifested menstrual irregularity.

The COVID-19 management mostly involved avoiding infection, treatment, preparation for funeral of the death, and contact tracing. Some pregnant women patients of COVID-19 follow with the urinary tract infections (UTIs) (pp. 44-48). During the pandemic, pregnant women, one of the vulnerable groups, need to be noticed. They should have had access to health provisions, but it is not easy. They have to confirm that they are tested negative to avail of the needed services, such as routine medical checkups, to ensure their fetal's health. A study on the significance of trimester-specific thyroid hormone reference intervals among Iraqi pregnant women found that pregnant women infected with COVID-19 had *Escherichia coli* as the most frequent pathogenic bacteria in their urinary system, which is also the most prevalent cause of urinary tract infection (pp. 81-88). The isolated uropathogens showed high resistance to Gentamicin, Cefuroxime and Ceftriaxone and were sensitive to Ampicillin and Nitrofurantoin. It is suggested to monitor the most efficient bacteriostatic medications against pathogenic UTIs, such as Ampicillin, Amikacin, Erythromycin, and Nitrofurantoin.

Another important issue was the difficulty of accessing medical attention during the pandemic. Therefore, it is necessary to discuss the way to handle specific health problems. Some health program promotes in managing individual health could be addressed at home. Applying a self-management approach to health issues is essential. The study aimed at understanding patients' experiences while using diabetes self-management applications (apps) (pp. 67-73). The patients in this study have positive and negative perceptions of diabetes self-management apps. Their perceptions are influenced by sociocultural factors, such as the patient's location, age, education, and motivation for getting better condition. The

study also suggests to explore other stakeholders' perceptions, such as health professionals and local or national authorities, in implementing diabetes self-management. (pp. 49-53)

Parents whose children living with cancer are at risk of psychological distress. Psychological distress negatively impacts the health of patients and their families, especially during the pandemic. Several studies have mentioned that parents have experienced insomnia symptoms, such as difficulty sleeping, waking up at night, getting up early, and having trouble going back to sleep. Some have suicidal tendencies which affect their health and that of their families. Health practitioners must prioritize early cancer detection and provide efficient interventions to support parents experiencing psychological distress. Increasing information, creating peer-support groups, and promoting mental health, especially among at-risk groups like families of cancer patients, are ways to increase resilience. The study on systematic review of psychological distress among parents of children with cancer raises the issue that might be important to follow up (pp. 56-42).

The study evaluating vitamin D and anti-mullerian hormone levels in infertile Iraqi women discusses a significant correlation between anti-müllerian hormone (AMH) and vitamin D levels in both fertile and infertile women (pp. 63-66). The infertile group had a high percentage of vitamin D deficiency. Therefore, routine vitamin D testing and therapy among deficient individuals to avoid ovarian reserve depletion appear ineffective. Nonetheless, vitamin D may play an important role in human reproduction, and ongoing prospective and translational research initiatives are desperately needed to investigate the possible impact of vitamin D.

There is a systematic review of coping strategies among mothers with premature babies (pp. 74-80). This review aims to identify coping factors, techniques, and interventions to enhance the maternal coping. The results stated that the influential factors to the coping by mothers with premature babies are the delivery method, availability of proper information support, and maternal self-efficacy. The strategies implemented by mothers to cope with the situation are belief in God, gratefulness, a closer bond with premature babies, support-seeking, and focusing on the baby's condition progress.

The present special issue paper will open the discussion on the pandemic and post-pandemic conditions. Evaluating the success and effect of the policy should be continuously raised to inspire more appropriate action in the future.

Finally, I am so very grateful for the invitation to express an editorial for this special issue 'Responses to post-pandemic COVID-19, sustainable healthcare disaster and management'.

Thank you for all of the contributors and reviewers so that the article could be published on time. I would also like to express my sincere thanks and appreciation to Dewi Susanna, who does an outstanding job as the Editor in Chief.

Tris Eryando,
The Editorial Board Member

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COVID-19 in Indonesia: Is There a Shift from Pandemic to Endemic?

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Abstract

The world is still facing the Coronavirus Disease 2019 (COVID-19) pandemic, and the current challenge is the epidemic, which was thought to have become endemic, but it seems far from that. This article describe the recent progress of the COVID-19 globally, including in Indonesia, and what should be done towards building community health resilience. Each day, more than 500,000 new cases are being detected worldwide. This condition shows that the present pandemic is not over and still requires global vigilance. The challenge faced by the world, and Indonesia, is to develop resilient communities as a prerequisite to controlling any future epidemic. This can be achieved by adopting five strategies: strengthen and promote access to public health and social services, promote health and wellness and disaster preparedness, expand communication and collaboration, engage at-risk individuals and activate programs to protect their health, and build social connectedness.

Keywords: community health resilience, COVID-19, endemic, policy response

Introduction

Since the detection of the first cases in Wuhan City, Hubei Province, China, in December 2019, the world has been facing a pandemic caused by the Coronavirus Disease 2019 (COVID-19). After first classifying COVID-19 under Public Health Emergencies of International Concern (PHEIC), the World Health Organization (WHO) finally declared it a global pandemic on March 11, 2020, to ensure that the worldwide community and governments work together to fight the disease.¹

The WHO COVID-19 dashboard data, as of June 10, 2022, shows that the virus already exists in 228 countries, affecting 532,201,219 people and causing 6,305,358 deaths.² Based on WHO data, the highest number of cases is in Europe (222,417,177), followed by the United States of America (158,983,746), the Western Pacific (61,735,224), Southeast Asia (58,217,287), the Middle East, and Africa. Globally, the daily number of cases fluctuates and seems to be declining lately. However, the numbers are still relatively high, as shown in Figure 1, which illustrates daily new cases of COVID-19 around the world from January 2020 to June 20, 2022; as seen, the cases peaked at almost 4 million in January

2022.³

In Indonesia, as of June 12, 2022, there have been 6,059,937 cases and 156,641 deaths since March 2, 2020.⁴ In response to the pandemic, the Indonesian Government formed the COVID-19 Mitigation Task Force to support high-level coordination and also declared large-scale social restrictions (LSSR) to prevent the spread of the virus.^{5,6} Indonesia faces enormous challenges in dealing with the pandemic, such as the unpreparedness of primary health facilities, hospitals, laboratories, infrastructure, and equipment. However, Indonesia has been considered successful, with an adequate public health approach without abandoning the economically disadvantaged.

The number of cases has started to decline compared to the first year of the pandemic. Those circumstances created a polemic as to whether it has shifted to endemic. However, the different meanings of endemic, pandemic, and epidemic should be rechecked. The Center for Disease Control and Prevention defines each of these three levels of disease strictly. Endemic is the constant presence of an infectious disease in a population within a certain area. Epidemic refers to an increase, often sudden, in the number of cases of a disease, above what is

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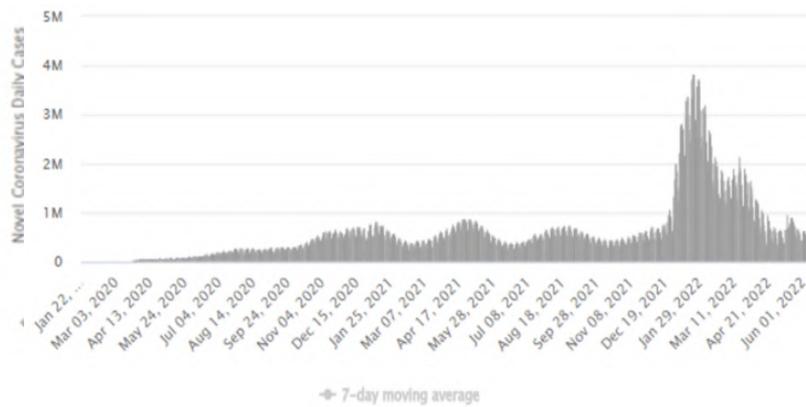


Figure 1. Daily New Cases of COVID-19 from January 2020 to June 2022 in Million⁵

normally expected in the population in an area. A pandemic is an epidemic that has spread to several countries and continents with massive infections.⁷

More than a decade ago, epidemiologists identified applicable factors for pandemics as new, infectious, fast-spreading, severe diseases with high attack rates, a wide geographic extension, and low herd immunity.⁸ These were all recognizable in the early COVID-19 cases around the world. The current challenge is that the epidemic, thought to have become endemic, seems far from being so. This article describes the recent progress of COVID-19 globally, including in Indonesia, and the polemic of shifting status from pandemic to endemic.

Method

This is a commentary article developed from observing the recent progress of COVID-19 cases globally and the response from the Indonesian Government. This article relies on global data on COVID-19 from open-access sources, which are the WHO dashboard, worldometers.info/coronavirus, National Agency for Disaster Management/*Badan Nasional Penanggulangan Bencana* (BNPB), and Databoks (databoks.katadata.co.id). Data observed consisted of daily new cases of COVID-19 globally and in Indonesia, from January 2020 to June 2022. The total number of COVID-19 cases in Indonesia crossed 6 million, and the latest positivity rate of COVID-19 cases in the Special Capital Region of Jakarta was from May to June 2022. The data were descriptively analyzed to determine the possible causes for the increase in COVID-19 cases and resultant government policy changes throughout the pandemic. The data are presented to answer the polemic of the shifting status to endemic.

Results and Discussion

After a brief decline during the last few days, the pos-

itive confirmed cases of COVID-19 in Indonesia have increased slightly, with an average of 500 cases per day. The Special Capital Region of Jakarta has shown an increasing trend of daily cases since June 7, 2022. The COVID-19 cases reported in Jakarta were 260 on June 7, 288 on June 8, 276 on June 9, and 333 cases on June 10, 2022.⁹

On June 10, 2022, the Minister of Health of the Republic of Indonesia explained that the Omicron subvariant BA4 and BA5 had entered Indonesia with four confirmed cases.¹⁰ This variant can avoid the immunity formed by the vaccine and spreads faster than other COVID-19 variants. Throughout the pandemic, the increase in cases has always been caused by new variants; similar trends were seen in Europe, Asia, and the United States. The Omicron subvariant is known to be more infectious than the previous severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variant.¹⁰

The COVID-19 pandemic has not only destroyed the health sector but all aspects of life, including the social and economic aspects. During the last two years, the whole world has been working relentlessly to prevent the increase in COVID-19 cases. Still, due to low awareness and discipline among the public, there are difficulties regarding the importance of implementing strict health protocols.

Various efforts and policies were implemented. However, not all achieved the expected results. Even though the number of cases has started to decrease compared to the first year of the pandemic, and there is a polemic as to whether it has shifted to endemic, new cases are still being discovered. In the last 24 hours (June 10, 2020), 574,365 new cases were found worldwide.³ This ensures that the pandemic is not over yet and still requires vigilance from all countries.

In Figure 2, since the early detection of COVID-19 in Indonesia, there has been a sharp increase in cases from

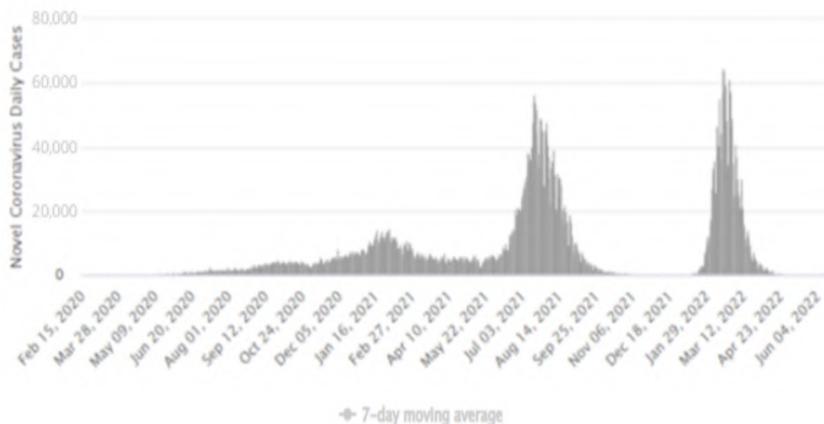


Figure 2. Daily New COVID-19 Cases in Indonesia from March 2020 to June 2022⁵

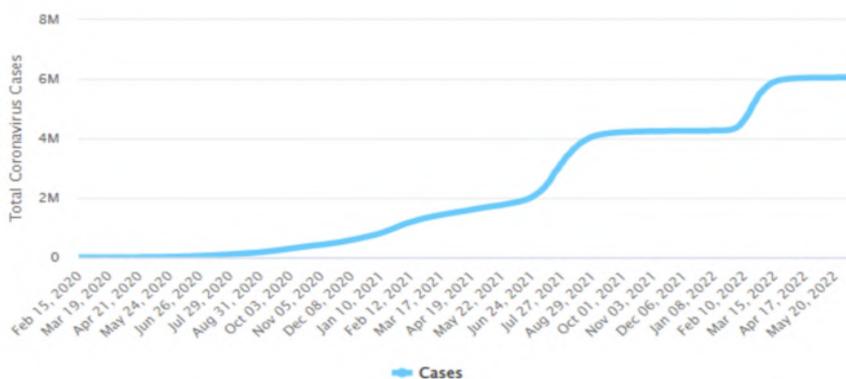


Figure 3. Total COVID-19 Cases in Indonesia⁵

June to September 2021 due to the Delta variant. It was then followed by a slow decline for some months. Later on, another increase happened in February 2022 due to the Omicron variant.³ Figure 3 illustrates the cumulative number of COVID-19 cases in Indonesia from February 2020 to May 20, 2022, reaching more than 6 million.³

Figure 4 shows the increase in the positivity rate of COVID-19 cases in the Special Capital Region of Jakarta from May to June 2022. The positivity rate is the proportion of positively-infected people to the total number of people tested.¹¹ In response to the increase in the spread of COVID-19, the Indonesian Government, through the Ministry of Home Affairs, has extended the implementation of restrictions on community activities/*Pemberlakuan Pembatasan Kegiatan Masyarakat* (PPKM) from June 7 to July 4, 2022.¹² The PPKM rules are contained in the Instruction of Minister of Home Affairs No. 29 of 2022 concerning PPKM Level 1 in the Java and Bali Regions; then, the Instruction of Minister of Home

Affairs No. 30 of 2022 concerning PPKM outside Java-Bali, with only Teluk Bintuni District has PPKM Level 2. The President of the Republic of Indonesia emphasized that the PPKM will continue until COVID-19 is under control.

The COVID-19 will not automatically disappear or be over simultaneously in all countries, proven by almost 500,000 new cases daily worldwide.² Uncertainties regarding the COVID-19 pandemic include the mutations of the virus, as well as the effectiveness of the vaccines to protect from new variants. The mutation abilities of COVID-19 remain its greatest danger, whereby local and national variants appeared within a few months of the global outbreak.¹⁵

There are pros and cons to the transition from pandemic to endemic.¹⁴ While variants remain a key feature of COVID-19, there is a more structured transition, wherein the coronavirus is shifting from its existence as a pandemic to an endemic virus. The supporters argue

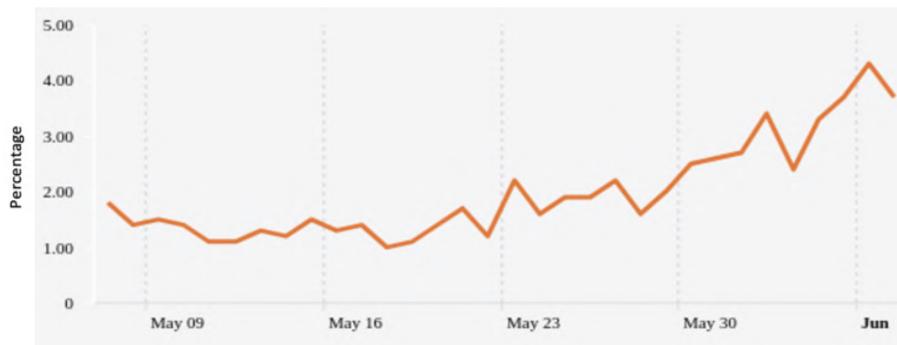


Figure 4. Positivity Rate of COVID-19 Cases in Special Capital Region of Jakarta (May-June 2022)¹¹

that it will happen if public policy demands double and booster vaccinations for adults, combined with social distancing and wearing masks.¹⁴ The opposers argued that if no community declares victory on the outbreak, societies should demonstrate clear attitudes, practices, and policies, permitting the long-term management of COVID-19. In other words, they are managing COVID-19, not as a pandemic but progressively as an endemic, where the cases are persistent and low-level, but only in those areas with high vaccination rates. Low-vaccination rate areas will not see a shift to endemic. The pandemic may end when almost everyone has immunity, preferably because they were vaccinated or infected and survived.¹⁵ In Indonesia, the coverage of the vaccinated population has attained almost 97% for the first vaccine dose, 81% for the second, and 26% for the third (booster).¹⁶ The effectiveness of boosters in preventing mortality due to COVID-19 has been documented. Analysis of 1,792,360 COVID-19 cases in Indonesia from January 1 to June 30, 2022, shows that persons who did not receive the COVID-19 vaccine were 28 times more likely to die compared to those who received a booster. While those who got the first vaccine dose were 15 times more likely to die compared to those who received a booster.¹⁷ Another study found that participants who received a booster had 90% lower mortality due to COVID-19 than participants who did not receive a booster.¹⁸

The world has made significant progress immunizing almost 70% of people worldwide with at least one dose against COVID-19, although this rate is only 14.8% in low-income countries.¹⁹ At the same time, health experts have raised concerns about the declining effectiveness of certain vaccines, including those developed in China. The risk of prematurely believing that the pandemic is shifting towards endemic status is that the world will be unprepared to face a more dangerous variant of the virus against which existing vaccines may be ineffective.²⁰

A current publication in the *New England Journal of*

Medicine explained that omicron subvariants BA.2.12.1, BA.4, and BA.5 were more likely to escape neutralizing antibodies induced by both previous infection and vaccination than prior omicron subvariants BA.1 and BA.2.²¹ The BA.2 variant now makes up around 86% of all sequenced cases globally and is known to be more transmissible than the BA.1 and BA.1.1.^{19,21} Omicron may develop mutations to escape the immunity elicited by BA.1 infection, suggesting that BA.1-derived vaccine boosters may not achieve broad-spectrum protection against new Omicron variants.²² Other researchers also said that Omicron BA.4 and BA.5 variants show reduced neutralization by serum triple AstraZeneca or Pfizer vaccines compared to BA.1 and BA.2. Hence, a significant reduction in the neutralization of BA.4 and BA.5 raises the possibility of Omicron reinfections. However, scientists continue to emphasize the importance of vaccines to avoid the devastating effect of the virus.²³

Since the vaccination does not cover all populations worldwide, at this time, it cannot be claimed that COVID-19 is endemic. The R_0 , the basic number for reproduction, the number of increasing cases without any intervention can be referred to determine whether it is reaching an endemic stage.²⁴ If $R_0 < 1$, it will be considered endemic, and this condition will prove that COVID-19 will not spread in the future. Hence, vaccination continues to be a powerful strategy to reduce community transmission. Diagnostic tests still need to be carried out, health protocols must still be implemented, and antiviral treatment is still required. The point is that people cannot be complacent but need to remain cautious and realistically monitor active cases because COVID-19 is still mutating.

At the same time, testing rates are reducing globally, which hinders monitoring the evolution of the virus, and almost one billion people in lower-income countries remain unvaccinated.²⁵ Vaccine supply has indeed improved, but issues related to political commitment, oper-

ational capacity, and finance, combined with vaccine hesitancy driven by misinformation. Regarding this, the WHO delivers four requests to all countries: first, call for policy commitments to boost vaccination, testing, and treatment; second, is the demand for local investment; third, a need for financial commitments to fully fund the WHO's Strategic Preparedness, Readiness, and Response Plan; and fourth, call for political commitment to support the Financial Intermediary Fund and a new architecture for global health security.²⁵

The Lancet COVID-19 Commission Task Force for Public Health Measures to Suppress the Pandemic was instituted to identify critical points for government consideration on public health interventions to control COVID-19.²⁶ The Task Force reviewed two public health interventions: institutional measures and behavioral-change measures. Among institutional measures, the successful strategies toward COVID-19 control are the government measures to minimize interpersonal contact; ensure early and widespread community testing, promote contact tracing, provide quarantine of contacts and isolation of cases and vaccination; strengthen health systems, including those for testing and vaccination, as well as services addressing other health needs; provide consistent public communications and reliable political leadership. The behavioral-change measure found that changes in public behaviors characterize the primary defense mechanism against COVID-19. The highly-effective vaccines are ineffective at the population level unless huge numbers of people agree to be vaccinated. Human behavior in terms of performing health protocols is the key to managing the COVID-19 pandemic; protective behaviors will still be essential, assuming only partial protection by vaccination and the emergence of new strains of the virus.

The statement above is in line with the WHO's five priorities for the next five years, consisting of: first, promoting health by addressing the root causes of disease and creating the conditions for good health and well-being; second, providing health services by reorienting health systems towards primary health care as the foundation of universal health coverage; third, protecting health by strengthening the global architecture for health emergency preparedness, response, and resilience; fourth, powering progress by harnessing science, research, innovation, data, and digital technologies; and fifth, performing by building a stronger WHO that delivers results, and is reinforced to play its leading role in global health.²⁷ The challenge faced by the world and Indonesia in the future is the need for resilience as a prerequisite to be able to control any epidemic in the future. The US Department of Health and Human Services, Community Health Resilience (CHR) stated that "the ability of a community to use its assets is to strengthen public health and healthcare systems and to improve the

community's physical, behavioral, and social health to withstand, adapt to, and recover from adversity."²⁸

Five strategies can be adopted from the National Preparedness and Response Science Board's Community Health Resilience to build resilient communities.²⁸ The first strategy is strengthening and promoting access to public health, healthcare, and social services. It is needed to support health resilience during disasters and emergencies, whereby people know how to access care and are not limited by actual or perceived barriers to services. The second is promoting health and wellness alongside disaster preparedness. To enable people to face daily life as well as disaster-related challenges, information and education on public health, emergency preparedness, and community health resilience interventions should be delivered. The third is expanding communications and collaboration. There is a need to build networks that include social services, behavioral health, community organizations, businesses, academics, at-risk individuals, and faith-based stakeholders, in addition to traditional public health, healthcare, and emergency management partners. The fourth is engaging at-risk individuals and the programs that serve them, and taking an active part in protecting their health and aiding their community's resilience, strengthening the community as a whole. The fifth is building social connectedness. People are more empowered to help one another after a significant disturbance in communities, then building social connectedness can be an important emergency preparedness action. Beyond COVID-19, health systems must be able to provide quick responses while continuing to deliver essential health interventions and public health functions where financing arrangements will be a crucial element of this resilience.²⁹

Learning lessons from the Northeast and Southeast Asian countries, South Korea and Vietnam have been very successful in managing the COVID-19 crisis. Their death rates per 100,000 population were well below those of many Western countries, implying more effective crisis management than in many other parts of the world.³⁰ While their populations undoubtedly suffered and their economies contracted, the damage was not nearly as severe as elsewhere. Both South Korea and Vietnam demonstrated state effectiveness in their planning and management of the pandemic. Hopefully, the COVID-19 pandemic would likewise help strengthen public health and healthcare systems and improve the community's health resilience in the future, in Indonesia and globally.

Conclusion

COVID-19 cases have started showing a decline as compared to the first year of the pandemic. However, new cases are still being discovered; therefore, there is

no apparent shifting from the pandemic to the endemic stage. Thus, the health protocols should be continued, vaccination should be completed, diagnostic tests need to be carried out, and the most important step to be taken is to implement five strategies to build community health resilience for anticipating and successfully managing any such situation in the future.

Abbreviations

COVID-19: Coronavirus Disease 2019; PHEIC: Public Health Emergencies of International Concern; WHO: World Health Organization; LSSR: Large-Scale Social Restrictions; BNPB: *Badan Nasional Penanggulangan Bencana*; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus-2; PPKM: *Pemberlakuan Pembatasan Kegiatan Masyarakat*; CHR: Community Health Resilience.

Ethics Approval and Consent to Participate

Not applicable.

Competing Interest

The authors have no conflict of interest.

Availability of Data and Materials

The data and materials are available publicly in the mass media quoted in this article.

Authors' Contribution

LH conceptualized, drafted, and revised the manuscript, as well as provided the final approval of the version to be published. KNS provided valuable input and data to be used in this article.

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Measuring the Success of *PeduliLindungi* Application Use for Supporting COVID-19 Prevention: A Case Study among College Students in Jakarta, Indonesia

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Abstract

The Indonesian Government has launched *PeduliLindungi* (PL) mobile apps as a COVID-19 preventive tool. This study aimed to describe the PL utilization and determine the factors influencing its successful use among college students. This study used a cross-sectional design and a total population sampling at a university in the Special Capital Region of Jakarta, Indonesia. The Delone and Mclean Information System Success Model was adopted to measure the use of the apps. The Spearman's rank correlation test was performed to determine the relationship between two variables. Furthermore, 354 respondents participated in this study. The respondents used the apps mostly to display the vaccination certificate and check in/out from public facilities. The overall user satisfaction value towards the application was 3.83 ± 0.76 . The system quality ($\rho = 0.621$, p -value < 0.001) and information quality ($\rho = 0.626$, p -value < 0.001) were associated with the user satisfaction while the user satisfaction ($\rho = 0.471$, p -value < 0.001), was correlated to the perceived benefit. In brief, perceived benefit was positively correlated with the user's satisfaction, whereas user satisfaction was positively correlated with self-efficacy, system quality, and information quality.

Keywords: adolescent, COVID-19, evaluation study, health information system, mobile health

Introduction

The World Health Organization (WHO) has not revoked the status of the Coronavirus Disease 2019 (COVID-19) pandemic since it was officially declared in early 2020.¹ Despite adopting different preventative initiatives, evidence reveals that COVID-19 occurrences are still present, albeit at a much lower rate.^{2,3} However, while it is hard to tell when the pandemic will end, several experts believe that the COVID-19 will continue but that the end of the pandemic is imminent.^{4,5} The COVID-19 is also expected to be another recurring disease that health systems and communities will have to cope with.⁵ Therefore, even after the COVID-19 vaccine discovery, other non-pharmaceutical-based preventive activities at the community level must be intensified.⁶

Digital technology might help track the spread of disease and promote health to understand the preventive actions needed to stop COVID-19 from spreading better.⁷ According to Kalgotra, *et al.*, information systems might play various roles during the pandemic, including information support to raise awareness, provide preventive care, facilitate community movement, establish trust, and provide an evaluation.⁸ The Indonesian Government

has developed a mobile apps called *PeduliLindungi* (PL). With its multiple capabilities in tracking, warning, and fencing, the PL is meant to enhance the government's health monitoring efforts in countering the COVID-19 pandemic.⁹ Surveillance, downloading vaccination certificates, information on the COVID-19 test results, telemedicine information, vaccine registration, and evidence for accessing public services are the PL features.¹⁰

Although the PL has several features to aid in the COVID-19 transmission prevention, it is only beneficial if the community uses it properly. The desire to use the PL was positively associated with actual use in a prior study (t count: $2.73 > 1.7$).¹¹ The previous study also stated that the apps had been well received by users.¹¹ According to a study by Primahadhiputra,¹² the acceptance of the PL was influenced by perceived usefulness, perceived ease of use, and subjective norm. On a scale of 1 to 5, the acceptance score of the PL in that study was 3.88 in the user group, 3.69 in the non-user group, and 3.78 for the overall model. Another study found that using the PL had a substantial impact on people's perceptions and attitudes to the benefit of the apps.¹³

Although several studies on the acceptability of the

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PL apps have been undertaken, to the best knowledge, no publications evaluate the use of the PL application using the Delone & McLean Information System Success Model (D&M IS Success Model). The D&M IS Success Model was one of most popular and well-validated methods for determining the success of an information system.¹⁴ It is a model published in 1992 based on theoretical and empirical studies undertaken by several researchers in the 1970s and 1980s.¹⁵

In contrast to the Technology Acceptance Model, which examines acceptance of information system, measurement of information systems using the D&M IS Success Model is intended to measure the success or effectiveness associated with using information systems. Several studies have used the D&M IS Success Model for evaluating information systems. The previous studies showed that the model had been used for examining the determinants of the success of various information systems, such as online learning systems (OLS), virtual education systems, and electronic health records.¹⁶⁻¹⁸

Therefore, a study needs to be carried out to measure the success of PL utilization using the D&M IS Success Model framework. The study is expected to provide beneficial information to the stakeholders to improve the efficacy of implementing information technology applications at the moment and in the future to strengthen the government's and community's resilience during pandemics. Therefore, this study aimed to describe the utilization of the PL and determine influential factors to the successful use of the apps among university students in the Special Capital Region of Jakarta.

Method

This cross-sectional study was conducted at one university in the Special Capital Region of Jakarta. Jakarta was selected as the study site since the region was the epicenter of the virus in Indonesia, with the highest number of COVID-19 cases among all Indonesian provinces by January 2022.³ The university was also selected as a study site because, according to a report by Statistics Indonesia/*Badan Pusat Statistik* (BPS) published in July 2021, the age group under 30 was not more compliant in implementing health protocols during the pandemic than other age groups.¹⁹ Furthermore, during the pandemic, young individuals have a high level of mobility, putting them at risk of contracting the COVID-19. A study stated that even though there is a policy of learning from home, teenagers still visit restaurants or malls as they usually did before the pandemic, or look for facilities during online learning.^{20,21} Data collection was carried out from December 26, 2021, to January 2, 2022.

The population of this study was 409 active students from the first to eighth semester of health study programs at one university in Jakarta, Indonesia. The minimum

sample size was calculated using the WHO sample size software with the hypothesis test for two population proportion formula, with a value of 5% level of significance and 80% power, with a minimum of 257 samples. The sample was chosen using the total sampling method, which involves an examination of the whole population.²² Since this study was intended to quantify the success of the PL utilization, only students using the apps in the previous month were included in the study sample.

Data was collected by filling out online questionnaires through the Microsoft Form application and the study assistants helped distribute the questionnaires to all the samples. The purpose and scope of the study were conveyed to the prospective respondents in the study explanation text before they filled out the questionnaire. Only those accepting the informed consent section were allowed to continue with the questionnaire. No penalty was applied for potential respondents who refused to participate in the study. Throughout the study, anonymity and confidentiality were preserved.

The questionnaire was divided into several sections. The first section contained a question on the respondents' characteristics, such as sex, age, semester, and area of residence. The following part included questions to assess the effectiveness of implementing information systems based on a prior study utilizing the D&M IS Success Model Framework.²³ The D&M IS Success Model identified and described the relationships among the seven critical dimensions of IS success: information quality, system quality, service quality, system use/usage intentions, user's satisfaction, and system benefits.^{15,24} Questions related to the success of information systems consisted of subsections: training related to system usage (whether or not the respondent had received sufficient information related to the apps through the website, poster, campaign, etc. or not) (1 question), system quality (3 questions), information quality (3 questions), user's satisfaction (1 question), system benefits (11 questions), the apps utilization (1 question), and system features (10 questions). A Likert scale was applied, ranging from rarely (less than once a week) to always (every day) for the apps use questions and from strongly disagree (1) to strongly agree (5) for other questions.

The data analysis was conducted using RStudio ver. 2021.09.1. Kolmogorov-Smirnov test was performed to determine the normality distribution of the data. The respondent characteristics and seven dimensions of the D&M IS Success Model were analyzed descriptively to show the frequency, mean, and standard deviation (SD). The Spearman's Rank correlation test was performed to determine the relationship between the two variables.

Result

Initially, 423 students responded to the questionnaire.

Later, 69 respondents were excluded from this study because they had not used the apps in the last 30 days. Finally, 354 respondents were included in this study. Most respondents (71.8%) were above the age of 20 and lived in the in the greater Jakarta, well known as *Jabodetabek* which stands for Jakarta, Bogor, Depok, Tangerang, and Bekasi (83.6%). Most respondents rarely used the apps (46.9%), and less than 2% used it regularly. The top five reasons by the respondents for using the apps were to display the COVID-19 vaccination certificate (83.3%), as proof of access to public services (77.4%), get an update on the COVID-19 case statistics (20.3%), to display the COVID-19 test result (20.1%), and to register for COVID-19 vaccination (11.3%) (Table 1).

Table 2 shows the average and standard deviation (SD) values for the seven dimensions of the modified D&M IS Success Model. In terms of perceived net benefit, the respondents agreed that the PL helped them access public services and showed the COVID-19 vaccination certificate with an average score of 4.32±0.69 and 4.29±0.70, respectively. The overall user’s satisfaction among the respondents ranged between neutral and satisfied (3.83±0.76). The respondents agreed that system quality-wise, the PL is beneficial, easy to use and easy to learn. Information such as vaccine certificates, COVID-19 diagnosis and so on was accessible on the PL (4.18±0.71). All questions on the self-efficacy and training items were assessed between neutral and satisfied.

The result of the one-sample Kolmogorov-Smirnov

test is presented in Table 3 which shows that all the dependent and independent variables are not normally distributed (p-value<0.05). Therefore, this study performed the Spearman rank correlation test to analyze the correlation between the variables.

Table 4 shows the result of Spearman's Rank correlation analysis between factors according to the D&M IS Success Model for the PL use among the respondents. Training is positively correlated with respondents' self-efficacy ($\rho = 0.360$, p-value<0.001). The respondent’s self-efficacy is attributed to the PL use ($\rho = 0.138$, p-value = 0.009) and user’s satisfaction ($\rho = 0.528$, p-value<0.001). The system quality ($\rho = 0.621$, p-value<0.001) and information quality ($\rho = 0.626$, p-value<0.001) is associated with the user’s satisfaction. The user’s satisfaction ($\rho = 0.471$, p-value <0.001), but not the use of PL ($\rho = 0.042$, p-value = 0.427), is linked to the perceived net benefit.

Discussion

Of the 423 students responding to the questionnaire, 354 (83.69%) utilized the PL in the past month. According to the BPS report, 78.7% of people used the apps.²⁵ This figure is greater than the COVID-19 contact-tracing apps in Japan (21.3%) but lower than the NHS COVID-19 mobile apps in the United Kingdom (84.1%).^{26,27} According to study in Germany, offering incentives improved the adoption of a COVID-19 contact-tracing apps.²⁸

This study showed that most respondents used the PL

Table 1. Characteristics of the Respondents (n = 354)

Characteristic	Category	n (%)
Age (years)	20 years	254 (71.8%)
	>20 years	100 (28.2%)
Semester	1	85 (24.0%)
	3	91 (25.7%)
	5	83 (23.4%)
	7	95 (26.8%)
Residence location	Jabodetabek	296 (83.6%)
	Non-Jabodetabek	58 (16.4%)
Frequency of use/access to the PL in the past month	Very rarely (less than once a week)	166 (46.9%)
	Rarely (once a week)	96 (27.1%)
	Often (several times a week)	86 (24.3%)
	Always (every day)	6 (1.7%)
Features of the function used in the PL	To display the COVID-19 vaccination certificate	295 (83.3%)
	Proof of access to public services	274 (77.4%)
	To obtain an update on the COVID-19 case statistics	72 (20.3%)
	To display the COVID-19 test result	71 (20.1%)
	To register for the COVID-19 vaccination	40 (11.3%)
	To seek information on the current travel regulations	37 (10.5%)
	To seek information on health care services for the COVID-19	27 (7.6%)
	To seek information on the COVID-19 testing (antigen/PCR) facilities	25 (7.1%)
	To create an electronic health alert card (e-HAC)	24 (6.8%)
To seek information on telemedicine	22 (6.2%)	

Notes: Jabodetabek = the greater Jakarta including Jakarta, Bogor, Depok, Tangerang and Bekasi, PL = *PeduliLindungi*, COVID-19 = Coronavirus Disease 2019, PCR = Polymerase Chain Reaction, e-HAC = Electronic-Health Alert Card.

Table 2. Dimension of the The Delone & McLean Information System Success Model

Variable	Statement	Mean	SD
Perceived net benefit	PL gives me a notification when I am entering the red zone	3.74	0.80
	PL helps me provide current COVID-19 case statistics	3.79	0.74
	PL helps me provide information on the updated travel regulation	3.66	0.76
	PL gives me a notification when I am in a crowded place	3.55	0.81
	PL helps me show the COVID-19 vaccination certificate	4.29	0.70
	PL helps me show the COVID-19 test result	3.95	0.77
	PL helps me access public services	4.32	0.69
	PL helps me register for the COVID-19 vaccination	3.57	0.88
	PL helps me provide information on Telemedicine	3.49	0.73
	PL helps me provide information on antigen/PCR test	3.57	0.74
Use	PL informs me about health care for COVID-19 treatments	3.58	0.74
	How often did I open/access the PL in the past month	2.81	0.86
User's satisfaction	Overall, I am satisfied with the PL	3.83	0.76
System quality	PL is easy to use	4.12	0.67
	PL is a beneficial apps	4.23	0.64
	PL is easy to learn	4.05	0.71
Information quality	Information on the PL is highly relevant for preventing COVID-19	3.88	0.76
	Information on the PL is highly accurate	3.61	0.79
	Information provided by the PL is easily understood	3.97	0.66
	I can easily access information (such as vaccine certificate, COVID-19 diagnosis, etc.) on the PL	4.18	0.71
Self-efficacy	I have sufficient knowledge of the PL features	3.66	0.82
	I have enough ability to use PL	3.93	0.67
	I am comfortable using PL	3.79	0.72
Training	I have received sufficient information on the PL features and use (from website, poster, campaign, and so on)	3.28	0.91

Notes: PL = *PeduliLindungi*, COVID-19 = Coronavirus Disease 2019, PCR = Polymerase Chain Reaction, SD = Standard Deviation.

Table 3. Result of One Sample Kolmogorov Smirnov Test

Variable	D	p-value
Training	0.949	<0.001
Self-efficacy	0.989	<0.001
System quality	0.987	<0.001
Information quality	0.989	<0.001
Use	0.977	<0.001
User's satisfaction	0.972	<0.001
Net perceived benefit	0.989	<0.001

Note: D = Reference value from the Kolmogorov-Smirnov Table

Table 4. Result of the Spearman's Rank Correlation Test

Independent Variable	Dependent Variable	ρ	p-value
Training	Self-efficacy	0.360	0.000
Self-efficacy	Use	0.138	0.009
System quality	Use	0.033	0.541
Information quality	Use	-0.016	0.764
Self-efficacy	User's satisfaction	0.528	0.000
System quality	User's satisfaction	0.621	0.000
Information quality	User's satisfaction	0.626	0.000
Use	User's satisfaction	0.023	0.664
Use	Net perceived benefit	0.042	0.427
User satisfaction	Net perceived benefit	0.471	<0.001

to show their vaccination certificates (83.3%) and evidence of access to public facilities (77.4%). According to the BPS report, the apps is most commonly used to access the COVID-19 vaccination certificates (65.6%), check-in/check-out public facilities (42.1%), and verify the COVID-19 test results (17.1%).²⁵ One of influential factors on the frequency of the apps by respondents while visiting public facilities is strict monitoring by officers on duty.²⁹

The findings revealed that respondents did not obtain enough information to operate the PL. Indeed, these attributes affect respondents' capability to use the apps. However, insufficient knowledge of the apps's functionality and privacy concerns may influence their decision not to use it.²⁷

Respondents also considered that the information generated by the apps was unreliable. According to one study, the zone information status displays different information if used on two separate devices in the same region.³⁰ Furthermore, the study suggests that there are still concerns with system satisfaction.³⁰ User's satisfaction with information systems was influenced by information security and privacy.³¹ There is an issue that the PL has been afflicted with security and privacy issues over user information.³² As a result, these factors can undoubtedly influence user's satisfaction with the PL apps.

This study found that by only approximately 20% of respondents used the PL to update the current circum-

stances of COVID-19 in Indonesia. This feature might be improved by including more information on COVID-19 transmission and prevention. It is critical as knowledge about the prevention and transmission of the COVID-19 as a newly emerging infectious disease still grows. Therefore, people should continue to update their knowledge to act appropriately in preventing the COVID-19 transmission.^{33,34} Furthermore, the existence of the *infodemic* (the rapid spread of information—both accurate and inaccurate—in the age of the internet and social media) phenomenon emphasizes the need for this effort.³⁵

Specifically, this study found that self-efficacy positively influenced actual use and user's satisfaction. This finding was in line with the results of previous studies.^{23,36,37} This study also found that self-efficacy was related to the perceived training regarding the apps use. It implied that training activities on the PL utilization should be intensified through campaigns, educational posters, and educational video. Moreover, the results of this study found that system quality significantly influenced user's satisfaction, which was in line with findings from previous reports.^{14,38} It highlighted that improving system quality was crucial to increasing the PL user's satisfaction. However, there were still complaints from the PL users that the system was slow in operating, especially in terms of scanning barcodes while entering public facilities, finding the user's location, or showing the results of the COVID-19 test.

The Ministry of Health of the Republic of Indonesia has developed the the 2024 Blueprint of Digital Health Transformation Strategy, stating that the development of a health technology ecosystem with the development of service applications and health data management will be continuously implemented.³⁸ Moreover, there is a discourse on expanding the utilization of the PL in the future, not only for the COVID-19 prevention, but also in other fields such as maternal and child health. Therefore, it is necessary to constantly improve the system and information quality of the PL as an apps. It is also critical to disseminate information on the PL to the public, hence they can use it correctly.

Because this study exclusively used health students as the study sample, individuals who were educated and living in urban area were more likely to be the participants. As a result, the study findings might not be applicable to all people under this age range with various scientific backgrounds. Furthermore, additional study is required to determine the performance of the PL apps in a larger population.

Conclusion

Most of the college students in this study use the PL for various purposes, including accessing public facilities

and displaying the COVID-19 vaccination certificates. The study shows that user's satisfaction was influenced by perceived benefit, in which the user's satisfaction was influenced by self-efficacy, system quality, and information quality. Various efforts may be considered to lift the success of the apps use, such as increasing knowledge of its features, providing incentives to use the apps, reinforcing discipline in using the apps, particularly while utilizing public facilities, and improving the quality of systems and the apps information.

Abbreviations

PL: *PeduliLindungi*; COVID-19: Coronavirus Disease 2019; WHO: World Health Organization; D&M IS Success Model: the Delone & McLean Information System Success Model; OLS: Online Learning Systems; BPS: *Badan Pusat Statistik* (Statistics Indonesia); Jabodetabek: the greater Jakarta which includes Jakarta, Bogor, Depok, Tangerang and Bekasi; SD: Standard Deviation; PCR: Polymerase Chain Reaction; e-HAC: Electronic-Health Alert Card.

Ethics Approval and Consent to Participate

Ethical approval and consent to participate have been obtained prior to data collection from the Ethical Commission of the Faculty of Health Sciences, Universitas Islam Negeri Syarif Hidayatullah Jakarta, with Ethical Clearance Number: Un.01/F.10/KP.01.1/KE.SP/06.08.038/2022.

Competing Interest

The authors declare that there are 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 that support the findings of this study are available upon reasonable request.

Authors' Contribution

MIN and CR developed the study design. MIN and CR participated in the data collection. MIN and Y participated in the data analysis. MIN, CR, Y, and NMN helped to draft the manuscript. All authors revised the manuscript critically and approved the final version of the manuscript.

Authors' Contribution

The authors would like to thank all respondents and research assistants who involved in this study.

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Does It Still Show a Deficit? Arguing Post-COVID-19 Health Financing System in Bogor, Indonesia

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Abstract

Before the COVID-19 pandemic, the Bogor City Government regulated to cover the health financing claim during the Indonesian National Health Insurance (NHI) integration period due to the lower amount of health care claim per episode in regional hospitals compared to ones that NHI paid. This study aimed to address post-COVID-19 health financing at two hospitals in Bogor City, West Java Province, Indonesia. Descriptive analysis using the aggregate statistical summaries was taken to explore the medical care episodes of the data series at two hospitals for the last two years. Of the 890 checked medical records data, the deficit occurred in 197 (22.1%) medical care episodes, while five (0.6%) exceeded the hospitals' tariffs. The remaining 688 (77.3%) medical care episodes had suits with the Indonesian-Case Based Groups. Almost a quarter of medical care episodes in aggregate experienced a deficit in the two years before the pandemic. This study is the first to provide new insight into the discussion on medical care financing in a developing country's post-pandemic era in a newly-implemented NHI system.

Keywords: health financing, health insurance, medical care financing, post-COVID-19

Introduction

The Indonesian Government has confirmed to fully cover the health financing for Coronavirus Disease 2019 (COVID-19) medical care in all health care facilities during the COVID-19 pandemic.^{1,2} The pandemic began in early 2020, and there remains uncertain indication when COVID-19 ends in Indonesia. In the end, the Indonesian Government enters the end of the present pandemic situation along with the revocation of COVID-19 health protocols, including permitting the Eid al-Fitr holiday exodus (*mudik*) and allowing people to take off their face masks in open spaces.

Before the pandemic, most of low- and middle-income countries were still facing the national issue of health financing, including Indonesia.^{3,4} The previous situation of Indonesian health insurance system has led the government, coordinated by the Social Security Administrative Body/*Badan Penyelenggara Jaminan Sosial Kesehatan (BPJS Kesehatan)*, to define the consecutive fare for each medical care that health facilities deliver.^{5,6} A tariff was set by the 10th International Code of Diagnosis (ICD-X), which includes all medical care into Indonesian-Case Based Groups (INA-CBG) payment sys-

tem.⁷

On the other hand, the Indonesian Government has forced all citizens to enroll in the National Health Insurance (NHI), either as a premium-aid or as an independent insurance policy-handed participant.^{8,9} It means that all health facilities, including hospitals, must obey the insurance system under the Indonesian Government.^{7,9} In addition, the Indonesian Act No. 44 of 2009 concerning hospitals also stipulates the practice of health information system mechanism, including its application toward the INA-CBG in these health care facilities.

The Indonesian Government, through *BPJS Kesehatan*, acknowledged that the establishment of INA-CBG aimed at covering each hospital's expenditure for a medical care delivery to the insurance policy-handed patients of *BPJS Kesehatan*.^{10,11} However, the hospitals insisted that the INA-CBG is not applicable in all cases by ICD-10, which caused the requested claim, in particular medical care, to be less than the hospital's expenditure. Hospitals suffered a deficit in the last two years of the *BPJS Kesehatan* insurance implementation, which made several hospitals choose to refuse specific patients for their benefit. This study aimed to address post-COVID-

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19 health financing in hospitals by analyzing the reimbursement system that the local government of Bogor City, West Java Province, proposed to cover health financing costs before the pandemic situation.

Method

This study employed a secondary data analysis on the deviant of payment claims for two years at two hospitals in Bogor City. Descriptive analysis was taken to describe the summary statistics of the deviation claim per episode of medical care. As a pilot study, this type of study was meant to present rough calculations regarding these phenomena in aggregate.

This study was focused on two hospitals: one private hospital and one public hospital. While the private hospital is managed by the consortium, the state hospital is under the management of the Bogor City Government. Both hospitals are located in Bogor City, West Java Province, Indonesia. The dataset was derived from the hospitals' patient records from the last two years. There were 890 medical care episodes in this study. All patient records confirmed that the patients were Bogor City locals. There was no discrepancy within the demographics or related therapy calculation per medical claim.

Each medical care episode claim was calculated; it was either matched or mismatched with the INA-CBG system (Figure 1). All the mismatches were classified as deviation claims and analyzed with two statistical evaluations. The descriptive statistics identified the mean first and evaluated the standard deviation. Most disease records with a total claim had been distributed using deviant approved graphics.

Since the study was done in aggregate, the parameters of this study could not be applied to the whole population of Bogor City (internal validity). This study bias also had implications for the non-adjustment calculations on specific issues, including the effectiveness and efficiency of health financing in the study setting. However, these pilot

findings could be the way to examine the calculation results before the COVID-19 phase, which can be more generally estimated for the post-COVID-19 era.

This study applied general descriptive statistics, such as frequency distributions. The two years of two different hospitals' insurance claims were identified by their distribution percentages according to the INA-CBG diagnoses. Additionally, the deviance between the hospitals' insurance fares on the INA-CBG claims was inspected and summarized by its rate per medical care episode.

Result

In Table 1, the highest 12 medical care cases are briefly described. Although other medical care cases had a higher percentage than these 12, the group's tariffs reflected the magnitude of the rest of the organizations' problems (Table 1).

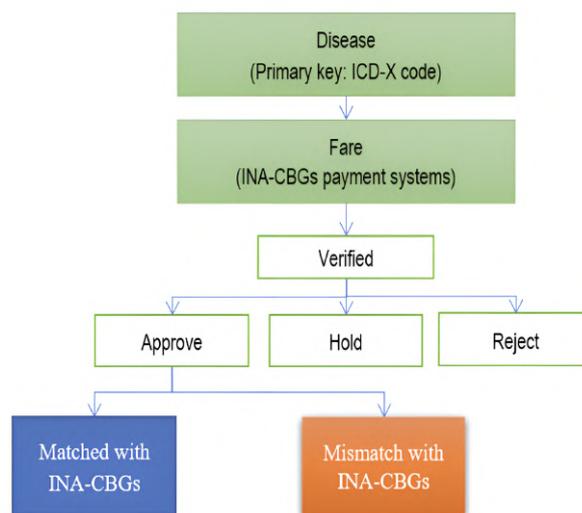


Figure 1. The Framework of Medical Care Financing in Bogor City

Table 1. The Highest 12 Medical Care Cases at Two Hospitals in Bogor City

INA-CBG Code	Description of INA-CBG Code	INA-CBG Tariffs Paid (IDR)	% (n = 890)
A-413-I	Light, nonbacterial infections	2,517,800	7.1
K-417-I	Abdominal pain & other gastroenteritis (light)	2,771,255	3.9
K-417-II	Abdominal pain & other gastroenteritis (medium)	3,561,900	3.0
L-140-III	Procedure on the skin, under the skin tissue, or on the breast	14,733,629	2.8
J-120-III	Procedure on the heavy, non-complex breathing system	24,301,700	2.5
A-413-II	Moderate nonbacterial infection	2,989,100	2.1
J-416-II	Simple pneumonia & medium whooping cough	5,371,700	1.5
K-111-III	Weight peritoneal adhesiolysis procedure	20,272,900	1.3
M-150-I	Lightweight tissue procedure	5,358,400	1.2
A-414-I	Bacterial and other parasites infectious disease	3,051,914	1.1
L-411-II	Moderate breast tumor	4,184,205	1.1
O-610-I	Lightweight cesarian surgery operating procedure	4,424,300	1.1
Others	-	5,177,321,242	71.3

Note: INA-CBG = Indonesian-Case Based Groups

Table 2 shows that 688 (77.3%) medical care episodes suit the INA-CBG system correctly, while five (0.6%) have a lower fare than the INA-CBG system. It found that 793 medical care episodes (89.1%) taken by the hospitals were accorded properly. However, the remaining 197 (22.1%) medical care episodes had a higher fare than the INA-CBG systems. Of the 197 medical care episodes of deviant, univariate analysis was carried out on the deviant amount of IDR 1.00 to 32,898,060.00.

Table 3 shows hospital claims which are higher than how much *BPJS Kesehatan* can fulfill. This table shows the difference between rates per episode of medical services determined by *BPJS Kesehatan* through the INA-CBG system and rates per episode of medical services in hospitals, where the average (mean) difference is IDR 6,068,355.99. However, the standard deviation of IDR 6,483,870.71 informed the probability of error as the range falls too far.

Discussion

Although the Indonesian Government has provided the COVID-19 financing due to the National Economic Recovery Plan/*Pemulihan Ekonomi Nasional* (PEN),¹² this does not change the fact that medical care episodes during the pandemic were considered huge expensive. During the COVID-19 situation, it is undoubtedly the case that this country is not only losing its economic advantage, but also changing in sociocultural aspects,¹³ and people's lives have been in danger during this period of disruption. This study argued that the level of health care in the upcoming post-COVID-19 era could offer the same potent deprivation if the stakeholders at all levels, including people, central and local governments, and health care facilities, assume it to be business as usual.

Statistically, this study showed that the deviance in the values of INA-CBG in the hospitals' fares varied in each medical episode. This deficit indicated that most of the deviance might be dynamically estimated. This situation raised the issue of how much the hospitals could lose and how to present a viable platform for the local government to provide a maximum subsidy for the citizens. Statistical analysis had been generally performed to measure the gap in health financing in the developing countries health care setting over time.¹⁴ As a demographically large country, Indonesia has also initiated the evidence-based approach to solving this issue, particularly in vulnerable communities, such as the poor in Bogor City.¹⁵ Initially, Bogor City implemented prior regional health insurance called Regional Health Insurance/*Jaminan Kesehatan Daerah* (*Jamkesda*). At the same time, in several regions of Indonesia, it has been integrated with *BPJS Kesehatan* insurance gradually, which started in 2014.^{16,17} On the other hand, *Jamkesda* in Bogor City runs differently from the others, which influenced

Table 2. Deviant per Episode of Medical Care at Two Hospitals in Bogor City (n = 890)

Deviant groups (IDR)	Frequency (n)	Percentage (%)
-4,708,500.00 to -255.00	5	0.6
-1.00 to 0.00	688	77.3
1.00 to 32,898,060.00	197	22.1

Table 3. Summary Statistics of the Deviant (197 Medical Care Episodes) at Two Hospitals in Bogor City (n = 890)

	INA-CBG Tariff Paid (IDR)	Deviant between the INA-CBG with the Hospitals' Fare (IDR)
Mean	7,896,767.40	6,068,355.99
Median	5,384,300.00	4,159,155.00
Modus	24,301,700.00	1,327,290.00
Standard deviation	5,758,627.12	6,483,870.71

the fiscal capacity of the region.¹⁸ The central government realized that there should be no region that cannot afford their citizens' medical care comprehensively to prevent the societal inequity issue and welcome the demographic bonus in the future.

While the INA-CBG fares have been set by the central government, which is led by the National Social Security Council/*Dewan Jaminan Sosial Nasional* (DJSN), the medical care in each health care facility, including the hospitals, is formed independently and depends on the hospital's ownership.⁹⁻¹⁰ This issue emerged when the payments in these domains were determined as being under the INA-CBG rates. Most of the medical care costs were higher than the INA-CBG rates.⁴ The autonomy and decentralization of the local government may lead it to develop its policies, including those related to health financing for the citizens. Thus, this study presented the platform for determining such according to the mean value of the calculated deviance to assist the local government in briefly setting a maximum value that can address the mismatch between INA-CBG rates and hospital fees.

Furthermore, *BPJS Kesehatan* was formed with the intention of anticipating fraud problems.¹⁹ This problem occurs at all levels of the health insurance process, resulting in misuse of funds and manipulation in the procurement process. The Audit Board of the Republic of Indonesia/*Badan Pemeriksa Keuangan* (BPK) noticed several common fraud activities, including procurement of goods and services, licensing, local elections, personnel, maintenance of public facilities, receipt of revenues, oversight, and accountability of regional heads.²⁰ These kinds of frauds were considered sensitive and got the government's attention. Because of this, it allowed *BPJS Kesehatan* to eliminate the exposure of fraud cases that can harm the excellent governance system, including in

the regions.

Regardless of the good intention of the Indonesian Government concerning equity in health care,²¹ *Jamkesda* of Bogor City has gained positive feedback from citizens, which is ensuring that all citizens acquire standard medical care, specifically in hospitals, free of charges.⁴ Bogor City has been awarded as one of the cities that can manage their health financing issues, including *Jamkesda*, in Indonesia.²² This achievement is basically because of its powerful resources as the nearest city to Jakarta, the capital of Indonesia. Bogor City has long been recognized as the leading vacation destination by not only domestic tourists but also tourists from all over the world.²³

During the integration period of *Jamkesda* into *BPJS Kesehatan*, Bogor City transformed to integrate the citizen database by social offices into health in enrolling as insurance-policy handed.²⁴ However, data redundancy emerged, which needs more time to decompose the database.⁴ Inadequate information systems and the lack of regulation indicated that the prior and current integration process should be done slowly but surely.^{19,25} In this case, patients would be affected by consequences of the integration process.

Bogor City develops public trust to ensure excellent governance by focusing on humankind's prosperity, including managing the prominent health issue that arises from the unestablished health financing caused by the *BPJS Kesehatan* integration period. The city is making the necessary policies to cover the citizens' health financing by integrating the *Jamkesda* financing system into *BPJS Kesehatan*. This policy enables a certain amount of fare to be contributed to support the current health financing system.

Since Indonesia has not yet officially confirmed the country as having entered a post-COVID-19 pandemic period, the two years of the aggregate data analysis used in this account were obtained based on the aggregate dispersion of data, and the structure of the data used was only analyzed in terms of the value of the average reimbursements. Thus, this study's findings cannot be used to compare the two hospitals. The study also cannot explain the disaggregated values, and the means and the standard errors were calculated for each case of mixed groups or differently mixed groups. Thus, this study presented the rationale of a value structure of the system of payments (INA-CBG) that seems to be defined in absolute amounts of money instead of in percentages concerning the reimbursement fee.

Conclusion

Almost one-quarter of medical care episodes in the hospital in the Bogor City of Indonesia demonstrated a deficit. This study recommends that further studies be

done to calculate the mean differences between the before- and post-COVID-19 situation once the Indonesian government has judged the COVID-19 pandemic to have passed. It is essential also to look closely at the hospital claims calculations from reimbursement fees set by the INA CBGs managed by *BPJS Kesehatan*, which would need to be paid by the Bogor City Government to cover the per medical care costs of each episode of hospital expenditures, which can be generated in light of the policies of Bogor City itself.

Abbreviations

NHI: National Health Insurance, COVID-19: Coronavirus Disease 2019; INA-CBG: Indonesian-Case Based Groups; *BPJS Kesehatan*: *Badan Penyelenggara Jaminan Sosial Kesehatan* (Social Security Administrative Body); ICD-10: The 10th revision of the International Statistical Classification of Diseases and Related Health Problems; IDR: Indonesian Rupiah; PEN: *Pemulihan Ekonomi Nasional* (National Economic Recovery Plan); *Jamkesda*: *Jaminan Kesehatan Daerah* (Regional Health Insurance); DJSN: *Dewan Jaminan Sosial Nasional* (National Social Security Council); BPK: *Badan Pemeriksa Keuangan* (The Audit Board of the Republic of Indonesia).

Ethics Approval and Consent to Participate

The study was approved by the local government Research Committee of the Bogor City Government (Ref. Nr. 2022-01).

Competing Interest

The authors declare that there are 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 datasets generated and/or analyzed during this study are not publicly available due to confidentiality but are available from the Bogor City Government upon reasonable request.

Authors' Contribution

AA was the project leader and was responsible for study and project design. Both MV and AA performed the data analysis to make conceptual contributions and prepare the first manuscript. RDA and LOHSS performed the data collection and calculated the study results. G and MHH were co-writing and involved in the revision of the manuscript. All authors approved the final manuscript.

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COVID-19 Prevention and Control: Mining Industry Responses to the Pandemic

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Abstract

The rapidly growing global Coronavirus Disease 2019 (COVID-19) pandemic crisis affects the labor-intensive mining industry. The industry is characterized by high worker mobility and 24-hour operations; thus, this continuous, mobile workforce increases the transmission risk of COVID-19 and has been a challenge for the mining industry during the pandemic. PT X, one of the largest mineral mining locations in Mimika District, Central Papua Province, Indonesia, was challenged to face the COVID-19 pandemic crisis. Therefore, this qualitative study aimed to analyze the COVID-19 handling efforts by PT X Concentrating Division using a descriptive-analytical method to describe the completion of PT X. The assessment aimed to examine nine critical factors formulated by the International Labour Organization and evaluated as practical steps to prevent and mitigate the virus spread in the division. Furthermore, an analysis was conducted on data related to COVID-19 handling. The results showed that the nine critical factors had an average value of 89.41%. These results indicated that the pandemic handling efforts in the division had been implemented well.

Keywords: control, COVID-19, handling, mining industry, practical steps

Introduction

During the present pandemic, Indonesia has faced three peak waves of COVID-19 cases.¹ The first wave occurred from January to February 2021 due to the Alpha variant, with daily cases reaching 14,528. From June to July 2021, the second wave occurred due to the Delta variant, with the highest cases reaching 56,757.² In 2022, the third wave was triggered by the Omicron variant, resulting in up to 63,956 cases.¹ A total of 6,055,645 confirmed cases were recorded as of June 2, 2022. These included 3,105 (0.1%) active cases, 5,895,940 (97.4%) recoveries, and 156,600 (2.6%) deaths.³

The rapidly growing global pandemic crisis has impacted health, political, economic, financial, and social aspects. This is in part triggered by the various policies issued by the government to overcome the spread.⁴ The declining productivity of the industrial and labor sectors has significantly impacted the community's economic activities. One of sectors affected by the COVID-19 pandemic is mining industry.⁵ Therefore, this sector must implement specific strategies for sustainable and safe production.

The pandemic has significantly affected the mining industry from a business standpoint, causing a decline in the prices of raw metal commodities, including gold, silver, and copper between 2020 and 2021.⁴ The impact is seen in the tight policies from operational aspects to human resources. In Mexico, mining industries shut down operations for three months in 2020, owing to the high COVID-19 prevalence. This was also experienced in mines in South Africa, where most workers were laid off because mining operations had to be stopped due to the pandemic. However, the policy was eventually adjusted to operational implementation with 50% capacity.⁴ In Indonesia, the impact decreased mining production figures by -2.18% in 2020.⁶ This indicates that the COVID-19 restrictions and control policies are a challenge for the mining industry.⁷

The physical distance between the mining industry from the general population prevents COVID-19 spread.⁸ However, the labor-intensive mining industry is characterized by high worker mobility and 24-hour operations, and this forces workers to work continuously, increasing the transmission risk. With the potential spike in COVID-19 cases, Indonesia's mining industries'

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management must make large-scale restrictions on human and operational activities.

Mining workers have various individual characteristics in terms of age, health status, and potential for comorbid symptoms related to the COVID-19. The productive-age population has varied potential for comorbid diseases in terms of prevalence. This includes 8.5%, 7.9%, 21.8%, 3.8%, and 34.1% for diabetes mellitus, stroke, obesity, chronic kidney disease, and hypertension, respectively.⁹ Furthermore, mining workers also can experience potential mental fatigue. For example, workers at seven coal-mining sites in Indonesia experienced a 32.3% prevalence of mental fatigue. This condition is caused by the increased work pressure on operators as the largest group in coal mining.¹⁰ Therefore, the mining industry must implement critical control and prevention aspects effectively, efficiently, and on target. This is because of the operational impact that affects the industry's production results.

Production and businesses that must run continuously have been challenging to operate during the pandemic. Mining industries must consider systems, empowerment, communication, health services, tracing, mobility and community management. This is stated in the guidelines and regulations regarding COVID-19 in the workplace. Some regulations governing the handling of COVID-19 in the workplace include the Decree of the Minister of Health No. 328 of 2020 concerning the Guidelines for the Prevention and Control of COVID-19 in Offices and Industry, and No. 413 of 2020 concerning the COVID-19 Prevention and Control. Additionally, guidelines for prevention and control in the workplace have been formulated by agencies worldwide, such as the International Labor Organization (ILO), Canadian Centre for Occupational Health and Safety (CCOHS), Mine Safety and Health Administration (MSHA), and *The Commission des Normes, de l'équité, de la Santé et de la Sécurité du Travail* (CNESST).

The ILO categorizes these points into nine critical factors in COVID-19 prevention and control in the mining industry.¹¹ The factors were developed by considering regulations, systems, resources, and health implementation aspects. Therefore, this study aimed to discuss the best practices of the PT X Concentrating Division in dealing with COVID-19 during the 2020-2022 period and beyond. This study focused on managerial and operational scopes based on prevention and control according to the ILO guidelines.

Method

This qualitative study used an analytical method to describe a case study through data collection from the ore processing industry located in Mimika District, Central Papua Province, Indonesia. Data were selected

from the company's COVID-19 daily positive cases, PT X Concentrating Division data within the COVID-19 period, and PT X internal COVID-19 publication on the company website. In-depth interviews with management were conducted to validate the data and deepen the analysis results. The data were assessed using the ILO COVID-19 checklist guidelines to evaluate the critical factors as practical steps to prevent and mitigate the spread of COVID-19 in the PT X Concentrating Division. The ILO guidelines were selected as they are a specific guide for discussing the handling of COVID-19 in the mining sector. In addition, the aspects covered in this tool are comprehensive in terms of regulations, systems, resources, and health implementation.

Each critical factor consists of several questions that delve deeper into their implementation. Planning, resources, and management systems has nine questions with an average of five sub-questions regarding commitment, company mitigation plans, response teams, risk management, and evaluation. Education and communication has six questions with three sub-questions regarding training, team communication, people management, and consultation. Worker health surveillance has seven single questions regarding self-monitoring and contact tracing, medical check-up management, health management for comorbid people, health facilities, tracing mechanisms, and isolation for sick people.

Hygiene and cleaning has ten single questions regarding public facilities, personal protective equipment (PPE) availability, and social distancing at the sites. Site access and work organization has eight questions with an average of four sub-questions regarding roster management, day-off policy, access limitation, public physical distancing policy, and crew management. Travel and mobility have eight questions with two questions and four sub-questions regarding airplane transportation and health measurement in transportation. The accommodation factor has seven questions regarding access limitations in barracks and physical distancing control in local transport. Suppliers and contractors have six single questions regarding contractor management during the COVID-19 pandemic and beyond. The last factor is mining communities and indigenous peoples, which consists of nine questions, with one question having six sub-questions regarding company efforts to prevent, communicate about, and control the spread of COVID-19 to indigenous people at the site.

These questions and sub-questions were then answered based on company statistics on the COVID-19, health promotion programs during the COVID-19 pandemic, company policies regarding the COVID-19, company best practices during the COVID-19 pandemic, and post COVID-19 policy, and were added to the results of in-depth interviews with management. The percentage

Seven of the nine indicators met the criteria and achieved 100% program compliance. These included reporting the COVID-19 to the management, the COVID-19 health services, monitoring the the COVID-19 program, completeness of PPE for workers in health facilities, COVID-19 risk assessment, and commitment to implementing COVID-19 policies in writing. However, two indicators had not reached 100% fulfillment. These are the COVID-19 Task Force, which has been formed in the division but has not been maximized in planning and carrying out tasks because of the busy schedule of each team, and the preparedness and response plan, which has not carried out evaluation activities optimally.

Figure 3 shows that the communication and education indicators have also met the requirement. Five of the six indicators met the criteria by achieving 100% fulfillment. These include mental health services, providing information to workers' families and workers leaving the site, calls for physical meetings, and information flow systems. The indicator scored less than 100% was the availability of training and publications. The only COVID-19-related training carried out in the PT X Concentrating Division was induction for workers who had just returned to work after taking self-quarantine. For the COVID-19 prevention, the only education available was through print and online media.

Figure 4 shows that the indicators for surveillance, contact tracing, and monitoring of individual workers have met the requirement. Four of the six indicators meet the criteria by achieving 100% fulfillment. These are case data recording and reporting, self-quarantine facilities and information, and surveillance systems. The indicators scored less than 100% are health screening and worker self-monitoring information. The health screening carried out at the PT X Concentrating Division was limited to temperature checks that occurred during every activity in that area, especially worship activities and physical meetings. Other health screening activities such as health questionnaires had not been conducted. The PT X Concentrating Division had also educated workers to be able to monitor independently if they experienced some symptoms of COVID-19, although the education was limited through electronic media.

Figure 5 shows that only two of six indicators met the criteria by achieving 100% fulfillment. The indicator of providing face masks and tissues regularly has a value of less than 100% because the activities of providing masks and tissues were only carried out at the beginning of the COVID-19 pandemic. When cases declined and handling began to be under control, the allocation of funds for the provision of masks was diverted to other activities, such as strengthening health screening. The indicator of providing hand washing and hand sanitizer had been carried out by the PT X Concentrating Division by

providing proper hand washing facilities in every office building equipped with hand soap and hand sanitizer, but hand washing facilities were limited in the field area.

Figure 6 shows that the access to sites and work organization indicators have met the requirement. Five of the six indicators meet the criteria by achieving 100%. The six indicators are access to sick leave and sick benefits, availability of hotline facilities, work planning for workers at risk of the COVID-19, efforts to reduce on-site workers, and limiting site access for less im-

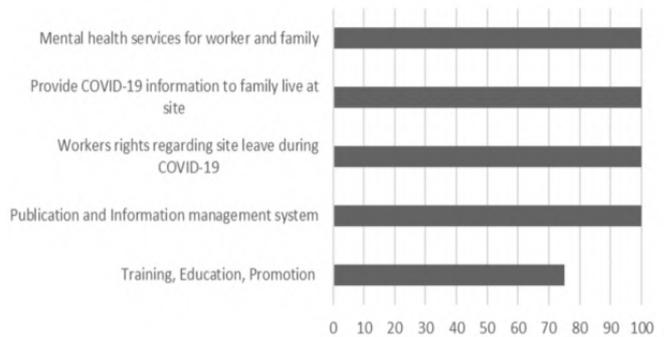


Figure 3. Education & Communication Overview

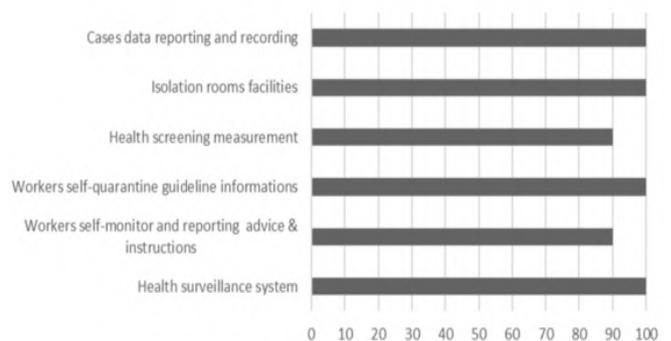


Figure 4. Worker's Health Surveillance, Self-Monitoring, and Contact Tracing Overview

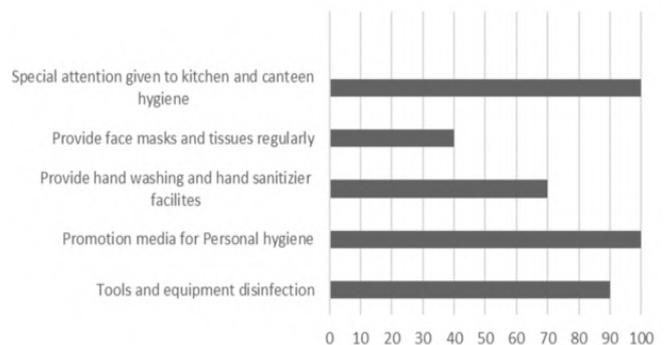


Figure 5. Hygiene and Sanitation Overview

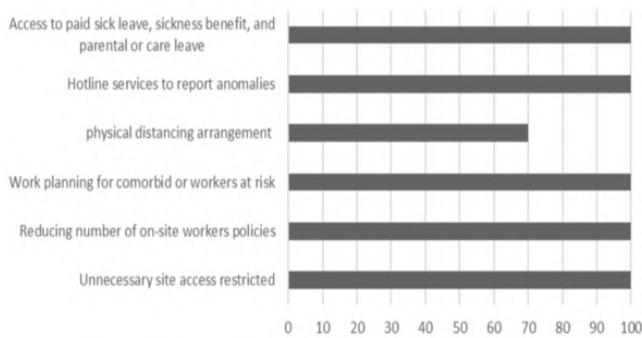


Figure 6. Site Access and Work Organization Overview

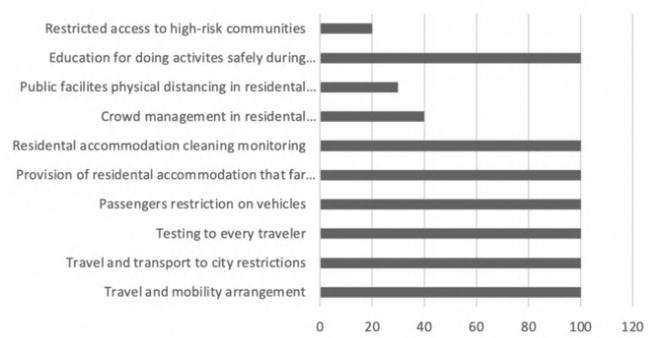


Figure 7. Travel, Mobility, and Accommodation Overview

portant matters. The one indicator whose fulfillment was less than 100% is the physical distancing arrangement. Physical distancing arrangement had been made by the corporate management, but raised awareness by workers is necessary to carry out physical restrictions.

Figure 7 shows the travel and mobilization indicators have met the requirement by reaching 100%. The four indicators include the COVID-19 checks for each traveler, travel restrictions to the city center, and travel and mobilization arrangements. Accommodation factors shows that three of the six accommodation indicators have fulfilled the program by reaching 100%. These include education for safe activities during the pandemic, monitoring the cleanliness of workers' residences, and providing a place to live far from the city center. Additionally, the three indicators with fulfillment of less than 100% were restrictions on access to high-risk communities, physical distancing rules in public facilities in areas where workers live, and crowd control in residential areas.

The high-risk community referred to in this study was the local community living near the site. Restrictions on local communities are difficult to do because their primary needs, such as clothing and food, are obtained from shopping centers located in the area of the site. The company has carried out restrictions on social activities in public spaces by closing various public facilities, such as sports and recreation centers, but the closure of these facilities resulted in increased crowds in open spaces. the crowd in an open space is referred to as a pedestrian area, which was used as a morning exercise path for workers.

Figure 8 shows that supplier and contractor indicators have met the criteria well. Three of the five indicators have met the criteria by reaching 100% program fulfillment. These are communication forums with contractors and suppliers, proactive management attitude in implementing health protocol practices, and relationship

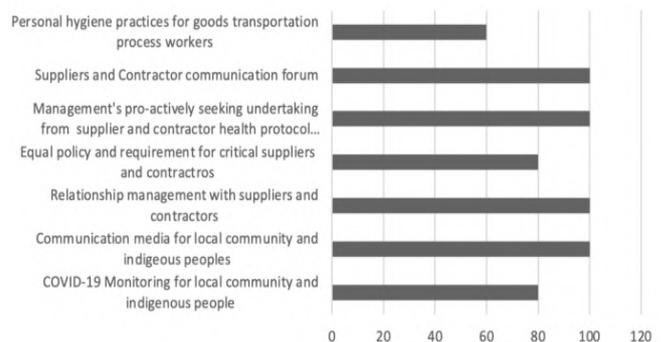


Figure 8. Supplier and Contractors and Mining Communities, and Indigenous People Overview

management with suppliers and contractors. The two indicators in which fulfillment was less than 100% are personal hygiene practices for workers in the goods transportation process and the same arrangements for important suppliers and contractors.

The indicators of mining and local communities are communication media with 100% compliance and monitoring of the COVID-19 for those around the sites with 80% compliance. The mining communities referred to in this study are all mining workers and their families left in the site's residential area and indigenous people, namely local communities living not far from the site's residential location and fulfill their basic needs from the shopping center located in the site's settlement. Communication media for the prevention of the COVID-19 for mining communities and indigenous people is carried out quite massively through print media (posters, banners, and billboards) and online media (websites and emails), and in every area of the settlements, recommendations have been made to implement health protocols to prevent the COVID-19. Monitoring of health protocols in mining communities can still be carried out

well, except for in the local communities because of the low level of awareness regarding COVID-19 and their location of residence, which is quite far and remote from the site location, making it difficult to carry out direct monitoring.

Discussion

COVID-19 Handling and Prevention at the PT X Concentrating Division for the 2020-2021 Period

The PT X Concentrating Division has made efforts to overcome the pandemic at the workplace. During monthly or daily lineup meetings, management's commitment and communications are conveyed regarding planning, resources, and the systems in place. Furthermore, the COVID-19 Task Force delegated tasks according to the regulations implemented by the Indonesian Government. This involves contact tracing, where workers identified as positive and active contacts, although not COVID-19-confirmed, must self-quarantine in their barracks for 14 days. The policy is effective, as evidenced by the stable number of cases below ten people per month in the early days of the pandemic.

The PT X Concentrating Division COVID-19 protocols have also been implemented in the field through awareness and training. A special induction discussing the COVID-19 materials for workers was attached to online safety training opportunities. Moreover, workers were given a brief induction regarding the necessary considerations when resuming work after self-quarantine. The peak time for the infection rate during the Alpha COVID-19 wave from June to August 2021 was due to the transition between workers who were on leave (school children's holidays).

At the PT X Concentrating Division, workers typically take the opportunity to take time off during this period. High infections occurred because in the previous month, there was no upward trend in the COVID-19, hence workers saw that there would be no potential for an increase in the number of cases. Written posters and interoffice memoranda were constantly being submitted and updated. The division implemented a policy of leaving the site for workers with potential comorbidities in the high-risk category. Healthy and productive workers were instructed to not leave the site for a certain period. Additionally, the 24-hour mental health services were provided to workers and their families living on-site.

The PT X Concentrating Division allocated three barracks, each with 100 people, for quarantine at Mile 68 and 72 residential locations. Disinfection was conducted weekly in the office and workshop areas. This policy is more intense than in the other divisions at PT X and was useful in reducing the number of COVID-19 cases among workers in the Concentrating Division.

The implementation of social restrictions on every

facility in this area must be improved, as described in the accommodation results. The division has implemented several policies, such as providing boundaries in the meeting areas, and hybrid meeting methods to standardize movement up and down stairs. Furthermore, workers used masks and the PPE to reduce the risk of COVID-19. The PT X Concentrating Division exhibited high COVID-19 awareness by sharing their active participation in tracing and communications through social media, such as WhatsApp groups and stories. Thus, it raised the workers' opportunity to avoid the COVID-19 infection.

In the early phase of the pandemic, public facilities such as mess halls, cooperatives, and restaurants were closed for on-site dining and workers were only allowed to eat at home. Mosques and churches have also been a concern for workers wishing to use public facilities. In addition, workers have used disinfectants because the PPE is a personal responsibility.¹¹

Initiatives have also been implemented by contractors or external subordinate company in the PT X Concentrating Division. Most contractors distributed masks and hand sanitizers during joint agendas such as safety meetings or divisional togetherness events. This was also supported by divisional management through the procurement of public facilities such as hand washing stations and sanitizers for public use and free of charge. The self-monitoring work by the PT X Concentrating Division was carried out daily using a standard self-checklist following the government's standards. The missed implementation was documentation and evaluation in the form of meeting minutes, which are monthly recapitulated.

Mobility has been adjusted to the COVID-19 conditions, such as when workers were detained and could not leave the site during the early pandemic. The management made a policy that only 75% of workers should be on site at a given time. However, the management also developed a roster policy of nine weeks onsite and three weeks of leave for each worker.¹² This was accompanied by a work-from-home policy during the increased wave of Alpha variants.

The accommodation on the site is also of concern to the PT X Concentrating Division that has implemented social restrictions on public facilities such as buses and light vehicles. The policy of providing IDR 1,500,000 to workers who did not transit to Timika City was implemented to reduce the risk of the COVID-19 virus exposure from outside the site area.¹² This was considered effective, as evidenced by the sloping curve of the pandemic wave in the Delta wave period. Crowd management was conducted by the PT X Concentrating Division at the beginning of the COVID-19 pandemic. The implementation had been carried out quite well, as

indicated by the presence of social distancing signs in every public place. However, over time, the behavior of workers loosened, which can be seen apart from the peak time due to the COVID-19 wave, namely, the trend of setting crowd management in the airport area as a transportation center for the PT X with outside areas.

A study by Manullang, *et al.*, revealed that the mental health impact of the pandemic has been greater among 18- to 24-year-olds than in older adults.¹¹ This age group also reported significantly greater loneliness and dropped positive mood, both of which were associated with greater mental health difficulties. During the COVID-19 pandemic, the company implemented a policy to limit social interaction with people outside the site. Interactions were carried out by workers trapped on site with their families through personal social media. Companies must consider social interactions as a critical factor in restoring workers's mental health.¹³

Access restrictions for residents around the site were already implemented prior to the pandemic. This is because Mile 74 is the PT X Concentrating Division's limited production area, which is accessible only for workers. However, the PT X Concentrating Division remains involved in the outreach by PT X management to the local community.¹² The challenge is that the community has trouble participating in the COVID-19 program due to differences in understanding and knowledge of the pandemic.¹⁴

Coping and Prevention of the COVID-19 at the PT X Concentrating Division 2022-Current Period

Policies have been readjusted by the management of the PT X Concentrating Division as COVID-19 cases decrease. The work roster has been changed to six weeks onsite and a two-week leave applied to each worker. Incentives for workers going to Timika City were also removed. Additionally, social restrictions on public facilities such as restaurants, churches, and mosques have eased.¹⁵

For "essential activities" such as mining, some of the more significant measures that are necessary to mitigate the spread of COVID-19 include periodic testing, case monitoring, and priority vaccination of all people working in this sector. In addition, the number of people infected and suspected cases in the sector must have been periodically disclosed because, as this study has shown, there is a higher risk of incidence and comparatively rapid spread of the disease in locations where minerals are produced. Priority attention must be paid to indigenous lands that overlap the mining areas.¹⁶

The key driver for implementing health protocols is top management commitment. Implementation of the COVID-19 response in the workplace through the corporate policies and procedures regarding the COVID-

19 and the establishment of a COVID-19 Task Force are key to navigating the COVID-19 pandemic.¹⁷ The assumption here is that when there is a change in policies and the easing of restrictions, it will not slack the workers' health awareness because they will continue using masks and hand sanitizers. Communications and outreach to maintain health and fitness should be continuously promoted. This can be conducted massively through the media and small meetings between sections within the division.

Limitation and Strength

The limitation for the present study is that the scope of study is only one division; therefore, the results of study are insufficient to assess the handling efforts made by the company. The existence of some confidential data is also a drawback in this study because it has affected the quality of study results and analysis. The strength of this study is novelty for the PT X Concentrating Division as well as for mineral companies. This study can also be used as input and evaluation material for continuous improvement in efforts to handle the COVID-19. The observation method used includes implementation by companies during the pandemic and post-pandemic.

Conclusion

The total average for all factors completion is 89.41%. The nine critical factors covering Planning, Resources, and Management Systems at the PT X Concentrating Division have been implemented well. Workers' active participation and awareness also support the implementation of policies and programs. The implementation of prevention and control by the PT X Concentrating Division is adequate, as indicated by the trend of peak numbers which may decline as soon as the PT X Concentrating Division implements the policies and programs.

Abbreviations

COVID-19: Coronavirus Disease 2019; ILO: International Labour Organization; CCOHS: Canadian Centre for Occupational Health and Safety; MSHA: Mine Safety and Health Administration; CNESST: *Commission des Normes, de l'équité, de la Santé et de la Sécurité du Travail*; PPE: Personal Protective Equipment; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2.

Ethics Approval and Consent to Participate

This study was approved by the Learning and Organizational Development, PT Freeport Indonesia, with a letter-number: 009/TA/JA/L&OD-CPM/II/2022.

Competing Interest

The authors declares that there are no significant competing financial, professional, or personal interests that might have affected the per-

formance or presentation of the work described in this manuscript.

Availability of Data and Materials

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Authors' Contribution

AS and AMK, conceived the idea, data collection, data analysis, interpreted the study results, and drafted the manuscript. AS, AMK, and MRI performed data collection, critically analyzing and interpreting the study results. EKP gave his expert opinion in sampling design and data collection. ADA gave her input in the manuscript drafting. All authors read and approved the final manuscript.

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Misperception of Vaccine Acceptance to the COVID-19 Vaccine in Indonesia: A Systematic Review

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Abstract

Vaccination is one of main steps to overcome the continuous increase in the Coronavirus Disease 2019 (COVID-19) pandemic. However, its implementation is hindered by various responses such as acceptance and refusal. This study aimed to describe the perception of the COVID-19 vaccine in Indonesia. A systematic review design was used, and the literature searches were carried out using Google Scholar, PubMed, Science Direct, and WHO COVID-19 databases following the PRISMA guideline process. The keywords used were coronavirus, COVID-19, vaccination, COVID-19 vaccination, vaccine response, vaccine acceptance, vaccine perception, and Indonesia in English or Indonesian articles published in 2020-2021. This study discovered 13 sample articles including six qualitative and seven cross-sectional studies. The responses showed varying results divided into positive, indicating vaccine acceptance, and negative responses that made hesitations to refusal. People with a good response and perception considered the vaccine an antibody to fight the virus. Meanwhile, others who hesitated or rejected were due to their concerns about side effects, safety, and effectiveness. Furthermore, inaccurate information or hoaxes circulating in the community significantly influence people's perceptions.

Keywords: COVID-19 vaccines, Indonesia, perception

Introduction

The first Coronavirus Disease 2019 (COVID-19) case was reported in Wuhan City, Hubei Province, China, in December 2019. From investigations and case identification, some of the initial cases were linked to the food market in Wuhan City indicating that the market played a role to the initial development of the pandemic.¹ Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was identified in early January 2020. Its complete genetic sequence from ancient human cases and other viruses from China and worldwide suggests that it has an ecological origin in the bat population. All available evidence also indicated that the virus is of natural animal origin and not a manipulated or manufactured virus.¹

On March 9, 2020, the COVID-19, which was spreading worldwide, was declared a pandemic by World Health Organization (WHO). Currently, 219 million cases have been recorded globally, with approximately 4.55 million death as of October 6, 2021.² While, Indonesia has reached 4.22 million positive cases, 142,000 deaths, and the average daily addition of 1,000–2,000 cases.²

The initial steps taken to reduce the transmissibility of the disease are preventive measures or Non-Pharma-

ceutical Interventions (NPI) as implemented in Indonesia by the 5M appeal: wearing masks, washing hands, keeping a safe distance, staying away from crowds, and reducing mobility for the community, and 3T for the government which includes testing, tracing, and treatment. To date, those steps are proven to slow down the infection, but the most promising strategy for limiting the pandemic, reducing mortality and morbidity is still in the capacity of medical technology, including effective, safe, and affordable antiviral agents and vaccines.³

Many scientists and pharmaceutical companies develop vaccines from various sources, such as attenuated or inactivated viruses, deoxyribonucleic acid (DNA) or ribonucleic acid (RNA), replicating and non-replicating viral vectors, and sub-protein units combined with virus-like particles. Each vaccine candidate can use one of these mechanisms with details on the outcome.⁴ In Indonesia, several COVID-19 vaccine products have been made and used to control the spread of the virus.⁵ The vaccination program began on January 13, 2021, after issuing an emergency use authorization by the National Agency of Drug and Food Control (NADFC)/ *Badan Pengawas Obat dan Makanan* (BPOM).⁵

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Based on the Decree of the Minister of Health of the Republic of Indonesia No. H.K.01.07/Menkes/9860/2020 of 2020 on Stipulation of Vaccine Types for the Implementation of Coronavirus Disease 2019 (COVID-19) Vaccination, six vaccine product by PT Bio Farma (Persero), AstraZeneca, China National Pharmaceutical Group Corporation (Sinopharm), Moderna, Pfizer Inc. and BioNTech, and Sinovac Biotech Ltd are permitted to use in Indonesia.⁵ The Indonesian Government continues to strive by setting policies, educating, socializing campaigns on the vaccine on social media platforms, and collaborating with various influencer parties for public acceptance. Responses and positive behavior to the COVID-19 vaccination process are very important to achieve a herd immunity and control the pandemic effectively.

Vaccination was carried out in two periods. The first period run from January to April 2021, prioritizing 1.3 million health workers and 17.4 million public officers in 34 provinces. While, the second period expectedly started to start from April 2021 to March 2022 to reach 181.5 million people and achieve the herd immunity.⁶ From a survey by the Indonesian Ministry of Health, Technical Advisory Group on Immunization (ITAGI), the United Nations Children's Fund (UNICEF), and the WHO on the receipt of the COVID-19 vaccine in Indonesia, around 65% of respondents were willing to receive vaccines as provided by the government, 8% refused, and 27% expressed hesitations about the government's plan in distribution.⁷ The most common reasons for vaccine refusal are safety, effectiveness uncertainty, lack of trust, fear of side effects such as fever and pain, and religious beliefs.⁷ Study by Cascini, *et al.*,⁸ discovered that vaccination hesitations in some countries vary among different populations. While, various factors contributing to the high level of hesitation include concerns about vaccine efficacy, safety, side effects, convenience, price, and the belief that vaccines are unnecessary and insufficient testing.

Previous studies analyzed the Indonesians' interest, response, perception, and willingness to vaccinate. However, they have not been systematically examined to summarize this topic comprehensively. Policymakers need to consider the fact about the COVID-19 vaccine response in order to expand the COVID-19 vaccine coverage in Indonesia. Thus, this study aimed to describe the perception of the COVID-19 vaccine in Indonesia.

Method

The study used a systematic review following the guidelines of preferred reporting items for systematic review and meta-analysis (PRISMA). A systematic review is a design method to identify, evaluate, and interpret all relevant results related to certain questions, topics, or

phenomena of concern.⁹

The search was conducted through Google Scholar, PubMed, Science Direct, and WHO COVID-19 databases. This review used keywords and keyword combinations. The keywords used with Boolean operators (AND, OR) were "coronavirus" OR "COVID-19" AND "vaccination" OR "covid vaccination" OR "vaccine response" OR "vaccine acceptance" OR "vaccine perception" AND "Indonesia". On google scholar, the keywords used were "coronavirus" OR "COVID-19" AND "vaccination" OR "covid vaccine" OR "vaccine response" OR "vaccine acceptance" OR "vaccine perception" AND "Indonesia."

The inclusion criteria were original studies in English and Indonesian language, published in open access journals from 2020 to 2021 in Indonesia to determine the response, acceptance, and public perception of the COVID-19 vaccine, and having qualitative and quantitative methods from analytical or descriptive studies such as case-control, cross-sectional, prospective, and retrospective cohort studies. While, the exclusion criteria were paid articles from non-open access journals and not conducted in Indonesian. After obtaining the results, the total articles obtained were entered into the Mendeley application for duplicate checking, and the articles were selected based on the title and abstract. Subsequently, a full-text assessment is carried out for study feasibility, where successful articles were subjected to a quality assessment until the final was achieved.

Information on the initial screening was done. In case there were differences in the number of articles obtained, the third party's assistance was provided. Any differences in opinion were resolved through discussion, and the final decision was made. The search strategy was based on participants, intervention, comparison, and outcome (PICO) approach.

The quality assessment was carried out using the Joanna Briggs Institute (JBI)'s Critical Appraisal Checklist adapted to this study design. This study had two types of designs: qualitative and cross-sectional. Therefore, the JBI assessment sheet was used. Studies that scored above 50% were included in the sample, while those below were excluded to avoid bias.

The qualitative and quantitative studies were extracted into an Excel table with details, including author and year of publication, title, study site, population size, design, positive response/acceptance, and negative response/refusal of the COVID-19 vaccination. To minimize the biases, the inclusion criteria was clearly described to avoid inconsistent application in study selection.

Data synthesis involves quantitative data presented as textual descriptions and collected with qualitative data. They were collected to determine people's response to the COVID-19 vaccine.

Results

A total of 2,046 studies were obtained; 979 from Google Scholar, 1,000 from Science Direct, 32 from PubMed, and 35 from the WHO COVID-19 database. After checking, 17 were obtained as duplicates. Then, 2,029 studies were screened based on titles and abstracts until 20 studies were left for full-text and feasibility assessment, where two were paid articles, four were not full text, and one was not located in Indonesia. Subsequently, the remaining 13 articles were assessed qualitatively using the JBI's Critical Appraisal Checklist. Of these articles, only 13 obtained an assessment score above 50%. Therefore, they were used as samples (Figure 1).

The characteristics of this study were six articles with qualitative design and seven with cross-sectional design (Table 1). While, the populations in four articles were less than 50; more than 100 in seven articles; and two articles had the general population in one specific area. The average age was in the range of 18-59 years. However, one article focused on the elderly aged 60-74 years, with a majority of females.

The quality assessment using the critical appraisal checklist assessment sheet from the JBI scored above 50%. For the qualitative studies, four scored 80%, one scored 70%, and another was 60%. While, for the cross-sectional study, five scored 100%, one scored 87.5%, and another one was 75%.

After summarizing several studies taken as samples, the positive responses from the people taking the COVID-19 vaccine were as an antibody or immune booster to reduce the virus transmission, morbidity, mortality, and can form a herd immunity (n = 5), the desire to seek valid and reliable information about the vaccine (n = 5), and the belief in the benefits, safety, the effectiveness of vaccines and reduce in worry (n = 4). The government's role also affected the interest of the people in vaccines because they were motivated after seeing the president as the first person to be vaccinated. Moreover, accurate information from the government increased people's willingness to vaccinate and most of them also willing to be vaccinated when it is provided freely (n = 3). People feeling more susceptible to COVID-19 were more likely to receive the vaccine because they perceived the virus as a threat to their health (n = 2).

The negative response results (Table 2) were that people with low interest in vaccination doubted and rejected the COVID-19 vaccine because they worried about the side effects, safety, and effectiveness (n = 7). It is questioning whether the COVID-19 vaccine was halal (n = 3), assuming that the COVID-19 vaccine was a conspiracy, the government's propaganda, and business field (n = 4). To believe that COVID-19 was only a common cold (n = 2) and the vaccines would not suppress the virus spread (n = 2). Furthermore, inaccurate information or hoaxes about the COVID-19 vaccine also affect people's perceptions and willingness to receive vaccines (n = 3).

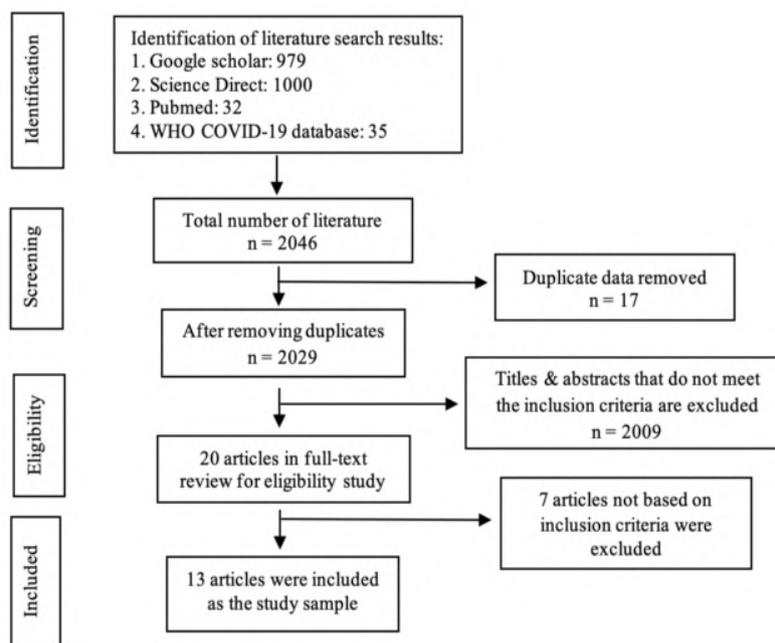


Figure 1. PRISMA Sample Flow Chart

Table 1. Description of Selected Papers with Positive Response

Author	Year	Population	Design	Positive Response
Calista and Shihab, ¹⁰	2021	7 Informants	Qualitative	<ol style="list-style-type: none"> 1. The COVID-19 vaccine as an antibody. 2. Looking for information on the COVID-19 vaccine and educating others. 3. Motivated because the president is the first person to be vaccinated and believes that vaccines are the best solution for preventing the virus in Indonesia.
Indriyanti, ¹¹	2021	38 Sample informants	Qualitative	<ol style="list-style-type: none"> 1. Vaccines can reduce viral transmission, morbidity, and mortality, and also promote herd immunity. 2. Status as a health worker makes it easier to get vaccines. 3. Good for vaccination after getting information/training.
Izmi, et al., ¹²	2021	General	Qualitative	Vaccines can become antibodies or immune boosters to block the COVID-19 from family.
Martini, Kusumawaty and Yunike, ¹³	2021	10 Informants	Qualitative	<ol style="list-style-type: none"> 1. Vaccines can protect against the COVID-19. 2. Family and friends support vaccines.
Ganafi and Afrizal, ¹⁴	2021	General	Qualitative	<ol style="list-style-type: none"> 1. High awareness of seeking real information about the vaccine. 2. Vaccination as a form of protection from the pandemic.
Muhammad, et al., ¹⁵	2021	7 Informants	Qualitative	<ol style="list-style-type: none"> 1. Vaccines can form herd immunity. 2. Seek valid information on vaccines and support the government's efforts. 3. 86% of respondents gave a positive response to the distribution of the vaccine.
Arumsari, Desty and Kusumo, ¹⁶	2021	200 Samples	Cross-sectional	<ol style="list-style-type: none"> 1. 52.7% of respondents disagree that the too-short vaccine's clinical trial makes them underestimate the effectiveness. 2. 55.4% do not agree that the COVID-19 vaccine causes side effects such as fever and pain sensation after being injected.
Puspasari and Achadi, ¹⁷	2021	382 Samples	Cross-sectional	<ol style="list-style-type: none"> 1. 93% of Indonesians stated that they were willing to get vaccinated. 2. The vaccine reduces the chance and worry of infection/complications.
Linda Prasetyaning Widayanti, ¹⁸	2021	188 Samples	Cross-sectional	<ol style="list-style-type: none"> 1. 87.2% of respondents have a good perception of vaccine effectiveness. 2. 77.7% agree to take part in the vaccination.
Erawan, et al., ²⁰	2021	452 Samples	Cross-sectional	<ol style="list-style-type: none"> 1. The perception that COVID-19 is a severe threat to health by assuming that they are very vulnerable and are willing to receive vaccinations. 2. The perceived benefits of the COVID-19 vaccination are also a predictor that makes them interested in vaccination.
Ichsan, et al., ²¹	2021	266 Samples	Cross-sectional	79.3% of respondents believe in the safety and effectiveness of the vaccine.
Harapan, et al., ²²	2020	1,068 Samples	Cross-sectional	93.3% of participants want to be vaccinated when it is provided free of charge by the government.

The rest refused to pay for the COVID-19 vaccine (n = 1).

Discussion

Positive Response to Vaccines

Several studies stated that the COVID-19 vaccine was an antibody or immune booster that reduces virus transmission, morbidity, and mortality and also forms herd immunity.^{11,12,15,21} These positive factors are needed to achieve the vaccination target in Indonesia because people are aware of its importance in overcoming the pandemic. A study conducted in Jordan by El-Elimat,³ also discovered that 66.5% of participants stated that vaccine is important to fight the COVID-19. Similarly, a study by Saied, et al.,²³ which assessed the perception of Egyptian medical students, stated that approximately 90.5% believed vaccination is important to overcome the pandemic. Meanwhile, antibodies are the soldiers in the body's

defense system trained to recognize one particular antigen. When an antigen enters the body for the first time, it takes time for the immune system to respond and produce specific antibodies against the antigen. The vaccine consists of small and harmless fragments of an attenuated organism, including its antigenic portion, which enables the body to recognize an antigen and form antibodies. Therefore, when the actual organism's antigen enters the body, the body can easily defeat it.²⁴ It also helps in achieving herd immunity which varies across the country, since not all individuals, such as infants, people with health problems, or those who are unwilling, can be vaccinated. In a study by Cihan,²⁵ the number of people fully vaccinated against COVID-19 was estimated to analyze the adequacy of herd immunity in the US, Asia, South America, Africa, Europe, and globally. The results showed that the United States reached its highest level of complete vaccination rate on June 1, 2021, while other

Table 2. Description of Selected Papers with Negative Response

Author	Year	Population	Design	Negative Response
Calista and Shihab, ¹⁰	2021	7 Informants	Qualitative	1. Refused to pay for vaccines. 2. Refused because of health/disease.
Indriyanti, ¹¹	2021	38 Sample informants	Qualitative	1. Worried about adverse event following immunization (AEFI). 2. Hesitation about the benefits of vaccines after reading the news that vaccines are not a guarantee of being COVID-free. 3. Hesitation about the safety of vaccines after traveling long distances.
Izmi, <i>et al.</i> , ¹²	2021	General	Qualitative	Vaccines are dangerous for the body because they can be deadly; hesitation about the vaccine trials and assume that it is the government's duty.
Martini, Kusumawaty and Yunike, ¹³	2021	10 Informants	Qualitative	1. Do not believe in the COVID-19 and assume it is a fabrication of political interests and a common cold. 2. Vaccines are useless. 3. Many died after getting the vaccine.
Ganafi and Afrizal, ¹⁴	2021	General	Qualitative	1. Hesitation about vaccine safety. 2. Hesitations about the effectiveness of the vaccine. 3. Distrust of vaccines. 4. Concerns about side effects such as fever and pain. 5. Questioning the halalness of vaccines. 6. Statement that pandemic is a conspiracy.
Muhammad, <i>et al.</i> , ¹⁵	2021	7 Informants	Qualitative	Hesitation because of a lot of confusing news on the COVID-19 vaccine on social media, the remaining 14% are still unsure about the vaccine distribution.
Arumsari, Desty and Kusumo, ¹⁶	2021	200 Samples	Cross-sectional	1. 54.1% of respondents disagree that the vaccine is safe to use. 2. 59.5% feel that vaccines cannot suppress the virus's spread. 3. 42.6% are unsure about the effectiveness of the vaccine. 4. 50% question the halalness of vaccines. 5. 58.1% agree that humans do not need vaccines. 6. 52.0% also agree that the Coronavirus would disappear by itself. 7. 47.3% agree that only 3M can suppress the virus spread. 8. 51.4% agree that the pandemic is a conspiracy. 9. 57.4% do not believe that the government can properly handle the pandemic.
Puspasari and Achadi, ¹⁷	2021	382 Samples	Cross-sectional	Concerns about vaccine side effects.
Linda Prasetyaning Widayanti, ¹⁸	2021	188 Samples	Cross-sectional	24 people (12.8%) stated that the vaccines are ineffective in dealing with the COVID-19, affecting their attitude toward receiving vaccines.
Putri, <i>et al.</i> , ¹⁹	2021	399 Samples	Cross-sectional	1. Anxiety about possible side effects after vaccination. 2. Anxiety after receiving inaccurate/hoax information.
Ichsan, <i>et al.</i> , ²¹	2021	266 Samples	Cross-sectional	1. Most respondents in Central Sulawesi stated that the COVID-19 vaccine was safe and effective, but only 35.3% of respondents were willing to receive the vaccination. 2. 11.7% stated that it was not safe. 3. 4.9% stated that it was not effective. 4. 13.5% expressed fear of side effects. 5. 1.1% stated that it is against religious values.
Harapan, <i>et al.</i> , ²²	2020	1,068 Samples	Cross-sectional	Vaccine interest tends to decrease when its efficacy is only 50%.

countries were quite far from the threshold level of herd immunity.

The desire to obtain valid and reliable information on the COVID-19 vaccine is essential because it prevents people from careless absorption of any information they receive. Many inaccurate information circulating in the community affects their perceptions and the implementation of vaccinations carried out by the government. It also creates a negative view and worries, while those who are not easily influenced by information will try to find justified information from reliable sources. In a survey of vaccine acceptance in Indonesia, approximately 54% of respondents chose to receive information about the vaccine through social media such as WhatsApp, Facebook, Instagram, and Twitter, followed by print and mass me-

dia such as television and newspapers. While, almost 13% prefer to receive information through telecommunication channels such as short message services and telephone.⁷ Therefore, to overcome the spread of hoax news, the government established a positive law regulating the crime of spreading hoax information in Indonesia, which is contained in Articles 14 and 15 of Law No. 1 of 1946 concerning Criminal Law Regulations, Law No. 19 of 2016 regarding Amendments to Law No. 11 of 2008 concerning Information Technology and Electronic Transaction (ITE) is regulated in Article 28 Paragraph (1) in conjunction with Article 45 (A). For those posting hate speech to incite people or participate in cornering a group on their social media platforms, they will be subjected to Article 45A Paragraph 2 of the ITE Law.²⁶

Some people also hold onto vaccines' benefits, safety, and effectiveness to reduce their anxiety. This condition also indicated a positive response or belief toward vaccines, whereas some hesitate about its safety and side effects. A previous study showed that the COVID-19 vaccine, which can be accepted in Indonesia, should have three characteristics: effective, safe, and halal. In terms of effectiveness, the efficiency of the Sinovac in Indonesia is only 65.3%, which is lower than Brazil (78%) and Turkey (91.25%). There is no evidence that it can protect a person from the COVID-19 infection. However, clinical trials showed that people vaccinated with the CoronaVac have a three times lower risk of infection. While, the efficiency of Pfizer in Indonesia is significantly greater than Sinovac (95%). This difference is influenced by the host (human), agent (vaccine), and environment (regional conditions). Adverse events after immunization (AEFI) that can occur after the vaccine include pain, swelling, irritation, redness, myalgia, fatigue, arthralgia, fever, and dizziness.²⁷ Furthermore, there was a relationship between perceived benefits and willingness to vaccinate in a cross-sectional study, including by Puspasari, *et al.*,¹⁷ where vaccination indicators reduce the possibility of infection, complications, and worry. The study by Erawan, *et al.*,²⁰ reported that perceived benefits and perception of the vaccine effectiveness have a significant relationship with the willingness to be vaccinated.¹⁸

The government's role also affected the people's interest in vaccines, where some who were willing to receive vaccines were motivated because the president was the first person to be vaccinated. Furthermore, the government's accurate information and free-charge vaccine influenced people's willingness to vaccinate due to their trust and confidence in the government. According to Trent, *et al.*,²⁸ in Sydney and Melbourne, higher trust and confidence in the government are associated with a greater possibility of being willing to receive the vaccine. This is significantly different from New York and Phoenix, where trust in the government is relatively low, but individuals with higher trust tend to reject the vaccination. This condition is caused by some preventive measures such as masks and vaccines that have been politicized in the US. The willingness to receive vaccines in the US also depends on people's political affiliation with the government in power during the survey. Moreover, responsible governments must promote preventive policies based on ethics to increase public trust and reduce the mistrust of the COVID-19 vaccines. The decision not to be vaccinated is due to their fear and disbelief of its health benefits. Therefore, the government must implement several initiatives to strengthen public confidence.²⁹

People more susceptible to the COVID-19 showed a positive response and tended to receive the vaccine more

because they assumed the virus poses a threat to health. They also felt that their immune systems were weak or had a higher risk of virus exposure. While, a previous study on the Health Belief Model (HBM) approach also assessed the relationship between perceived susceptibility to vaccine acceptance as stated in study by Puspasari, *et al.*,¹⁷ an indicator of worrying about infecting the COVID-19 and getting infected with the COVID-19 is possible, from the perception of severity with indicators of severe complications and fear of being infected. A study by Harapan, *et al.*,²² also stated that the relationship between people with a high perceived risk of infection had a twice probability of receiving the vaccine than those who did not have. This result is supported by the study by Hawlader, *et al.*,³¹ in four South Asian countries: Bangladesh, India, Pakistan, and Nepal, where participants worrying about infecting the COVID-19 were more willing to receive the vaccine. This showed that participants with perceived susceptibility to disease were significantly more inclined to receive the vaccine. While, the Indonesian Ministry of Health stated that the vulnerable groups targeted for the third phase of vaccination in the Regulation of the Minister of Health of the Republic of Indonesia No. 10 of 2021 are based on the Implementation of Vaccinations against the COVID-19 included vulnerable communities from geospatial, social, and economic aspects.⁷ The Spokesperson for the Indonesian Ministry of Health for Vaccination also verbally stated the criteria for vulnerable communities as targets for the third phase of vaccination are 1) living in the COVID-19 red zone, 2) weak socioeconomic condition, 3) less fortunate, 4) capital city marginal groups, 5) persons with disabilities, and 6) people with mental disorders.³¹

Negative Response to Vaccines

Concern on vaccine side effects, safety, and effectiveness is a negative response from most people who doubt and reject to be vaccinated. This is similar to the results from the COVID-19 vaccine acceptance survey in Indonesia, where people concerning on vaccine safety by 30%, doubts about its effectiveness at 22%, low confidence in vaccines at 13%, and fear of side effects such as pain and fever at 12%.⁷ Furthermore, a study by Puspasari, *et al.*,¹⁷ stated that concern about vaccine side effects and ineffectiveness with a p-value = 0.0005 had a relationship that hindered vaccine acceptance. This response was responsible for the refusal by most people in several countries due to the less certainty about the safety and the potential for unknown side effects. At the same time, misinformation from social media can also affect their perception.²³ Study on the relationship between general vaccine attitudes and intention to vaccinate discovered that confidence in safety is the most significant determinant of vaccine acceptance.³² The public trust in

the COVID-19 vaccine can also vary based on the community's sources of information. This is because a vaccine acceptance survey in Indonesia showed that people obtain more information from social media (54%). This indicated that social media greatly influences public perception and trust in the vaccine. Therefore, the government must direct the people to choose reliable sources to obtain information. This also poses a challenge for the government and those with the relevant authority because the information spread in the community varies according to their geographical area and economic status.

The issue of the halal vaccine has become public doubt to get a vaccine in Indonesia. A study by Puspasari, *et al.*,¹⁷ showed that worrying about whether the vaccine is halal or not had a p-value of 0.0005, an obstacle to vaccine acceptance. Since most Indonesians are Muslims, they become more careful in selecting a consumption that does not conflict with religious values, such as questioning whether the production and handling of vaccines are appropriate with Islamic religious rules. For the halal vaccine, there has been a statement from the Indonesian Ulema Council/*Majelis Ulama Indonesia* (MUI) that the vaccine products by Sinovac Life Sciences Co. Ltd. China and PT Bio Farma are halal. At the same time, AstraZeneca is haram because of the pork trypsin content. However, it can be used permissibly due to an urgent need and unavoidable emergency conditions related to the fulfillment of the COVID-19 vaccine to overcome the pandemic.³³

Many people believe that the COVID-19 infection and its vaccine are conspiracies, propaganda, and a business field for the government. There is also an assumption that it is a fabrication that is deliberately made and exaggerated for political purposes, while some say that it is only a common cold. While, this showed that the belief is generated from hoax information circulating among the community and disseminated through stories told between individuals and groups. The belief in the conspiracy is not only in Indonesian community but also several countries. These groups are more prevalent among individuals from ethnic minority backgrounds, with lower levels of education, annual incomes, poor knowledge, and adherence to the COVID-19 guidelines.³⁴ A study conducted in Jordan showed that many campaigns launched by anti-vaccines spread on social media with fictitious, false, and misled Arabic translations that gave credence to the conspiracy. However, those who do not believe tend to receive the vaccine.³

The perception of people feeling that vaccines cannot suppress the virus spread also reduces their interest in receiving vaccines. One factor that makes people think that the vaccine is useless includes the confirmation of ten positive cases of those vaccinated. Those who do not

believe in vaccines are people with low awareness and incorrect information about vaccines.³⁵ While, the perception that the public knows about COVID-19 and its vaccine results from the information obtained. This is because the information obtained affected their response due to their education and income level. People with low education and income levels are more easily influenced by information and their behavior to disseminate the information without prior verification. Experience on the internet or social media also determines a person's attitude in disseminating information. Therefore, the more experienced someone has in using the internet, the higher their ability to discover, share, and verify information.³⁶ According to Juditha,³⁷ three critical approaches can be taken to anticipate the spread of hoax news in the community: technological, institutional, and literacy approaches. A technological approach using the hoax checker application to determine the truth of the news, the institutional is by continuously promoting the anti-hoax community. The literacy approach is the anti-hoax news movement and socialization that continues to be encouraged by the people.

There is also a response from people refusing to be vaccinated when they have to pay. This statement is supported by the study of Puspasari, *et al.*,¹⁷ This issue was circulating in the community that a paid COVID-19 vaccine was announced by the Indonesian Ministry of Health and borne by the company for all of its employees to receive the vaccine immediately and achieve the herd immunity. However, the government had announced a free vaccine for the public to silence the issue. Similarly, a study by Adigwe,³⁸ in Nigeria showed that most participants (85.1%) stated that the vaccine needed to be provided free because only a quarter of the participants (26%) were willing to pay. While, the groups that were likely to pay for vaccinations include the elderly and those who had previously been infected. According to Wang, *et al.*, most respondents were willing to pay part of the vaccination, indicating a high demand for vaccinations to control and overcome the pandemic in China.³⁹

Other Factors Related to Vaccine Acceptance

The cross-sectional study showed several other factors influencing people's willingness to receive the COVID-19 vaccine. In a study by Harapan, *et al.*,²² the status as a health worker was twice more likely to receive the vaccine due to their higher risk of exposure. Similarly, Chew, *et al.*,⁴⁰ also stated that more than 95% of healthcare workers in Asia were willing to receive the vaccine. While, the main reasons for vaccination are the perceived vulnerability to pandemics and the presence of a pro-social mindset. Age was also associated with receiving the vaccine, as shown in a study by Putri, *et al.*,¹⁹ where the respondents were in the productive age group

and actively working. This made them willing to vaccinate to remain active according to their age. Furthermore, Ichsan, *et al.*,²¹ discovered that age was related to willingness to vaccinate. Therefore, the older a person ages, the higher the willingness to receive the vaccination. The younger age group tends not to be vaccinated since age is positively associated with willingness to accept the COVID-19 vaccine.²⁸ However, willingness tends to be greatest among adults aged 65 years and above and those in 18-24. This indicated that the relationship between age and willingness to be vaccinated is also influenced by other factors based on their need to be vaccinated.

Strength and Limitations

This study tries to summarize the responses to the COVID-19 vaccine in Indonesia comprehensively. The study uses combined data from both qualitative and cross-sectional designs, which makes them the strength of this study. However, the present study has limited selected papers because of the restricted access from the non-open access journal. Nevertheless, this study utilizes the open access journal well to cover the problems.

Conclusion and Recommendation

Some factors related to people's responses to the COVID-19 vaccine are different. The average response of people accepting the vaccine reports that because it is an antibody that fights against the virus. Its acceptance also raises among those who already believe in the benefits, safety, and effectiveness. Moreover, the role of the government can affect people's perception and acceptance of vaccines due to the vulnerability feeling among individuals. Other factors such as status as a health worker and age are also related to vaccine acceptance.

People with a negative response to vaccines are concerned about side effects, safety, and effectiveness, which can be due to a lack of information and certainty. The halal status of the vaccine also plays a significant role besides the issues of conspiracy and paid vaccine. The government needs to pay attention to these factors to expand the COVID-19 vaccinations coverage. Further study should explore not only the review in response to the COVID-19 vaccine in Indonesia, but also the reason for people who have positive and negative responses to it.

Abbreviations

COVID-19: Coronavirus Disease 2019; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2; WHO: World Health Organization; NPI: Non-Pharmaceutical Interventions; DNA: Deoxyribonucleic Acid; RNA: Ribonucleic Acid; NADFC: the National Agency of Drug and Food Control; BPOM: Badan *Pengawas Obat dan Makanan*; ITAGI: Technical Advisory Group on Immunization; UNICEF: United Nations Children's Fund; PRISMA: Preferred Reporting Items for

Systematic Reviews and Meta-Analysis; PICO: Participants, Intervention, Comparison, and Outcome; SMS: short message services; AEFI: Adverse Events After Immunization; HBM: Health Belief Model; MUI: *Majelis Ulama Indonesia*.

Ethics Approval and Consent to Participate

No applicable.

Competing Interest

The authors declare that there are 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 is publicly available from Google Scholar, PubMed, Science Direct, and WHO COVID-19 databases in 2020-2021. The data of this study are 13 eligible articles that included in the reference.

Authors' Contribution

SH conceptualized the study design, acquired the raw data for analysis and HI conceptualized the article and prepared the original draft of the manuscript.

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The Effect of COVID-19 Pandemic-Induced Stress on Reproductive-Age Women's Menstrual Cycle Regularity

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Abstract

Intense stress resulting from major life events can affect women's menstrual cycle. The current Coronavirus Disease 2019 (COVID-19) pandemic, impacting various sectors, is considered a major form of stress. During May-November 2020, some women in Iraq have experienced menstrual disruptions, which can happen whether they get infected with the COVID-19 or simply deals with pandemic-induced stress. Thus, this study aimed to evaluate the effect of the COVID-19 pandemic-induced stress on menstrual cycle regularity of reproductive-age women. This study used an observational cross-sectional design conducted in Iraq from May to November 2020. A sample of 500 reproductive-age women filled out an online questionnaire about their menstrual records and psychological stress levels using a Perceived Stress Scale-10 for three months during the pandemic. A comparison between menstrual cycle irregularity and stress levels before and during the pandemic was done with a p-value of <0.05 and statistically significant. It was found that 47.72% of women had irregular menstrual cycles and high perceived stress scales during the pandemic compared to 20.94% with irregular cycles and high-stress levels before the pandemic. In brief, the high-stress level induced by the COVID-19 pandemic is associated with the irregular menstrual cycle in the sampled reproductive-age women.

Keywords: COVID-19 pandemic, menstrual cycle, Perceived Stress Scale

Introduction

It is well known that intense stress resulted from major life events such as wars, separation from family, and moving to a new place can all affect women's menstrual cycle.¹ The current Coronavirus Disease 2019 (COVID-19) pandemic is considered a major form of stress as it impacts various sectors, from public health to the economy sectors.² Based on the authors' initial study, in Iraq, some women have experienced menstrual disruptions (irregularity, menorrhagia, hypomenorrhea, oligomenorrhea, and polymenorrhea) during the period of strict quarantine (May-November 2020), which can occur either they get infected with the COVID-19 or simply dealing with pandemic-induced stress. A normal menstrual cycle is 28 days long and ends with the shedding of endometrium and bleeding. This cycle indicates a healthy hypothalamic-pituitary-ovarian axis with a normal out-flow tract.³⁻⁵

The Neuroendocrine system plays a vital role, influencing the reproductive organs and endocrine systems to help adapt to the increased stress and high cortisol levels. This condition may adversely affect the normal luteinizing hormone rhythm and thus disrupt the regular men-

strual cycle.⁶ Moreover, stress may even cause amenorrhea.⁷ Menstrual cycle irregularity is an important sign of anovulation associated with decreased ovarian hormone production, which may lead to infertility, heart disease, and type 2 diabetes mellitus (T2DM).⁸

The ongoing COVID-19 pandemic is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and was first recognized in December 2019 in Wuhan City, Hubei Province, China. The World Health Organization (WHO) announced the outbreak as a Public Health Emergency of International Concern (PHEIC) in January 2020 and a pandemic in March 2020. As of March 24, 2021, more than 124 million cases had been diagnosed, with more than 2.73 million COVID-19 deaths globally.⁹

The WHO expresses concerns over the psychosocial and mental health consequences secondary to the pandemic and assumes that new precautions such as quarantine have adversely affected people's daily activities and economy, which may increase anxiety, depression, and insomnia.¹⁰ The psychological and mental health of health care providers is an emerging concern, where they practice their work under stressful and resource-limited

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settings and are constantly exposed to the risk of infection.¹⁰

The Perceived Stress Scale (PSS) is the most widely-used psychological tool for measuring stress awareness. Items are designed to measure how unexpected, out of control, and burden the respondents find their lives. It includes several questions asking about the level of stress and focusing in general perspective and are devoid of contents specific to any subpopulation group. Each participant is asked to indicate how frequently they felt or thought in a particular way.¹¹ Thus, this study aimed to demonstrate the effect of the COVID-19 pandemic-induced stress on different aspects of the menstrual cycle in healthy reproductive-age women with a previously normal cycle with a subgroup of health care workers who were in close contact with the COVID-19 cases compared to those who were not.

Method

This study used an observational cross-sectional design conducted in Iraq during the period of strict quarantine between May and November 2020. The sample included 500 women aged 18-44 years. Furthermore, the data collection was conducted using an online self-administered questionnaire (Google Forms) distributed via Facebook, WhatsApp, and Telegram. The questionnaire consisted of four parts, with a total of 36 questions. The written consent of the participants was obtained during the survey, and their anonymity was maintained throughout the study.

The first part collected participants' demographic data (age, country of residence, education level, marital status, financial status, contraceptive use, lactation status, and chronic disease during the pandemic). The second included questions on the menstrual records within three months during the period of strict quarantine in Iraq (March, April, and May 2020). The third part assessed the risk factors for menstrual cycle irregularities in the six months preceding the pandemic, and the last measured the psychological stress levels of the participants before and during the pandemic.

The stress was measured retrograde depending on the participants' recall of their psychological condition before the pandemic. Then they reported their psychological status during the pandemic using the Perceived Stress Scale-10, which is a Likert type of scale where 4 = Very often, 3 = Fairly often, 2 = Sometimes, 1 = Almost never, and 0 = Never. In the four positively-stated items (4, 5, 7, and 8), the scores were obtained by reversing responses (e.g., 0 = 4, 1 = 3, 2 = 2, 3 = 1, and 4 = 0) and then summing across all the scale items. The resulting values were divided into two intervals (≤ 20 = low-stress and > 20 = high-stress).

The women older than 44 years and younger than 18

years old, lactating women, women on hormonal contraception, and those with chronic diseases (hypertension, diabetes, hepatic, cardiac adrenal disease) were excluded from the study, as these factors may be associated with anovulation or oligo-ovulation. The data were tabulated and statistically analyzed using Minitab 18 free version. The participants made a comparison between menstrual cycle irregularity and perceived stress scale before and during the pandemic with a p-value<0.05, which was statistically significant.

Results

Table 1 shows the demographic characteristics of the participants. Of 500 sampled women, 95 were excluded from the study as they did not meet the inclusion criteria (healthy women aged 18-44 years with normal menstrual cycle parameters before the pandemic). This study revealed that 34.81% of participants were aged 18-26 years, 52.09% were aged 27-36 years, and 13.08% were aged 37-44 years. The majority were living in Iraq at the time of the survey (88.88%). The education level showed that those attaining bachelor's degrees were 58.76%, 29.38%, 10.37%, and 1.48% were postgraduate, secondary school, and primary educational levels, respectively.

Furthermore, it was found that 60.49% were married, and 37.28% were single, 0.49% and 1.72% were widows and divorced, respectively. The financial status showed that 41.48% had a stable income and 58.51% did not have. Most of the sampled reproductive-age women were not using hormonal contraceptives (73.06%), while (26.93%) were using it. Only 17.14% of the sampled reproductive-age women were lactating, while 82.85% were not. Chronic disease was detected in

Table 1. The Demographic Characteristics of the Participants (n = 405)

Variable	Category	n	%
Age group (year)	18-26 years	141	34.81
	27-36 years	211	52.09
	37-44 years	53	13.08
Country of residence	Inside Iraq	360	88.88
	Outside Iraq	45	11.11
Educational level	Primary education	6	1.48
	Secondary	42	10.37
	Bachelor's degree	238	58.76
	Master's and Doctoral	119	29.38
Marital status	Married	245	60.49
	Single	151	37.28
	Widow	2	0.49
	Divorced	7	1.72
Financial status	Stable income	168	41.48
	Unstable income	237	58.51
Contraceptive use	Use contraceptive	66	26.93
	Non contraceptive user	179	73.06
Lactation status	Lactating	42	17.14
	Non-lactating	203	82.85
Chronic diseases	Present	28	6.91
	Absent	377	93.08

6.91% of participants, while 93.08% enjoyed good health.

This study showed that 22.72% of women had irregular menstrual cycles before the COVID-19 pandemic. During the pandemic, it was raised to 43.21% (Figure 1). Before the COVID-19 pandemic, 20.94% of the reproductive-age women had an irregular menstrual cycle with a PSS of >20, and 25.15% with a score of ≤20, the p-value was 0.13. During the COVID-19 pandemic, 47.72% of the reproductive-age women had an irregular cycle with PSS more than 20; while, the reproductive-

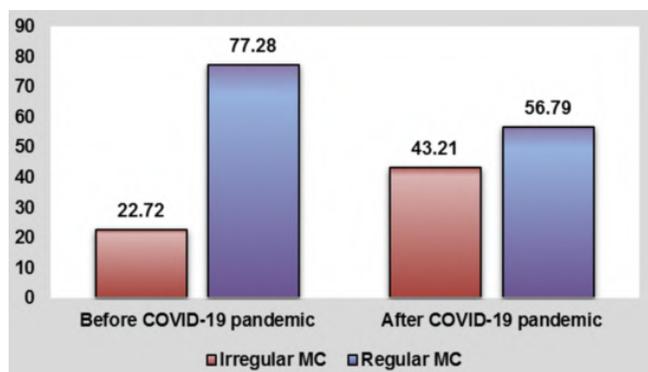


Figure 1. The Percentage of Menstrual Cycle Irregularity Before and During the COVID-19 Pandemic

age women with a score of ≤20 who had an irregular menstrual cycle was 36.59% (Table 2).

This study showed that a higher percentage of reproductive age women with PSS higher than 20 had dysmenorrhea compared to women with low PSS, 54.36% and 32.93%, respectively, with a p-value of 0.001. Similarly, the higher percentage of women with high stress level developed hypomenorrhea compared to those with low stress level, 53.94% and 33.33% (p-value = 0.001), respectively. The p-value was also significant (0.002) for menorrhagia in association with high stress level. Although the higher percentage of women with high stress level developed oligomenorrhea (28.22%), the p-value was not significant (0.06). Similarly, the p-value was not significant for high stress and polymenorrhea (0.29). Some participants reported to have more than one menstrual disorder in their response to the questionnaire (Table 3).

The health care workers who had contact with COVID-19 cases and PSS score of less than 20 were 19 (11.59%), while those who had not and had a PSS score of more than 20 were 145 (88.41%). At the same time, the PSS score of more than 20 revealed that 41 (17.01%) health care workers had contact with COVID-19 cases and 200 (82.99%) had not (Table 4). There were 60 health care workers who had contact with the COVID-19 cases. However, 33 experienced irregular menstrual

Table 2. The Association between High-Stress Levels and Menstrual Irregularity Before and During the COVID-19 (n = 405)

Menstrual Irregularity	Before COVID-19				Menstrual Irregularity	During COVID-19			
	PSS≤20		PSS>20			PSS≤20		PSS>20	
	n	%	n	%		n	%	n	%
Irregular (n = 92)	43	25.25	49	20.94	Irregular (n = 175)	60	36.59	115	47.72
Regular (n = 313)	128	74.85	185	79.06	Regular (n = 230)	104	63.41	126	52.28
p-value	0.13				p-value	0.021			

Note: PSS = Perceived Stress Scale

Table 3. The Association of High-Stress Level and Menstrual Cycle Changes During the Pandemic

Characteristic of the Menstrual Cycle	Category	Perceived Stress Scale				p-value
		≤20		>20		
		n	%	n	%	
Dysmenorrhea	Present (n = 185)	54	32.93	131	54.36	0.001
	Absent (n = 220)	110	67.07	110	45.64	
Hypomenorrhea	Present (n = 185)	55	33.33	130	53.94	0.001
	Absent (n = 220)	109	66.67	111	46.06	
Menorrhagia	Present (n = 112)	39	17.68	85	34.44	0.002
	Absent (n = 293)	135	82.32	185	65.56	
Oligomenorrhea	Present (n = 101)	33	20.12	68	28.22	0.06
	Absent (n = 304)	131	79.88	173	71.78	
Polymenorrhea	Present (n = 45)	15	9.15	30	12.45	0.29
	Absent (n = 360)	149	90.85	211	87.55	

Table 4. The Association of Health Care Workers' Contact with COVID-19 Cases and High-Stress Level

Contact with COVID-19 Cases	Perceived Stress Scale			
	<20		>20	
	n	%	n	%
Present (n = 60)	19	11.59	41	17.01
Absent (n = 345)	145	88.41	200	82.99
p-value	0.68			

Tabel 5. The Association of Health Care Workers' Contact with COVID-19 Cases and Menstrual Cycle Irregularity

Contact with COVID-19 Cases	Menstrual Irregularity			
	<20		>20	
	n	%	n	%
Present (n = 60)	27	9.44	33	35.87
Absent (n = 345)	286	90.56	59	64.13
p-value	0.0001			

cycles, while the remaining 27, still had regular ones (Table 5). Meanwhile, health care workers who had no contact with the COVID-19 cases mainly experience a regular menstrual cycle (90.56%).

Discussion

This study intended to demonstrate the effect of stress on menstrual cycle parameters in healthy reproductive-age women with previously regular menstrual cycles. The demographic characteristics showed that more than half of the participants were less than 36 years old and living Iraq during the survey. Most participants had bachelor's degrees, were married, did not use contraceptives, but enjoyed good health. However, less than half had a stable income and were lactating.

The findings of this study revealed that the sampled women experienced irregular menstrual cycles with a high-stress level of PSS>20 with a p-value of 0.021. These results were similar to the study by Nagma, *et al.*,¹² which showed an association between irregular menstrual cycles and high-stress levels in undergraduate medical students (PSS score>20). This study showed that high-stress level was associated with dysmenorrhea in the sampled women with a p-value of 0.001. This condition was in line with a study focusing on female medical students of Universitas Padjadjaran Bandung, West Java Province, Indonesia, which showed an association between the severity of stress and dysmenorrhea in the last menstruation.¹³ However, the study by Nagma, *et al.*, stated different findings which did not show an association between high-stress levels and dysmenorrhea.¹²

This study showed that women with high-stress levels were more likely to develop disruption in the amount of menstrual blood loss, whether increased loss (menorrhagia) or decreased loss (hypomenorrhea) (p-value = 0.02 and 0.01, respectively). However, these findings were subjective and dependent on the patient's appreciation of the amount of loss. Another study supporting these findings stated that higher stress was associated with painful periods, heavy menstrual bleeding, and premenstrual symptoms.⁶ The association between high-stress levels

and changes in menstrual cycle intervals, whether increased interval (more than 35 days) oligomenorrhea or decreased interval (less than 21 days), did not show in this study. While, Fenster, *et al.*, found that women working in high-stress jobs were twice as likely to have a short interval between menstrual cycles compared to women working in non-stressful jobs.¹⁴ However, larger sample size and more extended follow-up period are needed to confirm or negate this finding.

Another study of female American and Italian nurses experiencing stress demonstrated an association between high-stress levels and both longer cycles and anovulation.¹⁵ In the present study, although a higher percentage of contacts with COVID-19 had high-stress scores (PSS>20), the p-value was not significant (0.68). It might be because of the small sample size and the number of women in contact with COVID-19 positive cases in Iraq during the survey. Additional studies are needed to demonstrate the effect of contact with COVID-19 cases on stress levels among health care workers.

This study showed an association between health care workers' contact with COVID-19 cases and irregular menstrual cycle (p-value = 0.0001). This finding might be explained by higher demand in the work setting with increasing shifts in quantity and quality. A Korean study shared a similar result and stated an association between irregular menstrual cycles and the professional specifications of female workers.¹⁶

Stress stimulates the hypothalamic-pituitary-adrenal (HPA) axis, and the hypothalamus will release corticotrophic-releasing factor (CRF) hormone, which stimulates the pituitary to release adrenocorticotrophic hormone (ACTH) into the blood. In turn, the ACTH stimulates the adrenal glands to produce cortisol. These hormones control stress response in the body and can suppress the release of normal levels of reproductive hormones leading to irregular ovulation, anovulation, or amenorrhea, depending on the degree of gonadotrophin-releasing hormone (GnRH) suppression.¹⁷⁻²¹ Thus, stress adversely affect menstrual cycle regularity by stimulating the HPA axis which may suppress GnRH release.

Conclusion

The high stress induced by the COVID-19 pandemic is associated with menstrual cycle irregularity in the sampled reproductive-age women. Moreover, the high stress and dysmenorrhea, hypomenorrhea, and menorrhagia show a relationship in the present study, but not for oligomenorrhea or polymenorrhea. Health care workers who have direct contact with COVID-19 cases relate to the irregular menstrual cycle. However, larger sample size and more extended follow-up period are needed to confirm or negate this finding.

Abbreviations

COVID-19: Coronavirus Disease 2019; T2DM: type 2 Diabetes Mellitus; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2; WHO: World Health Organization; PHEIC: Public Health Emergency of International Concern; PSS: Perceived Stress Scale; HPA: Hypothalamic-Pituitary-Adrenal; CRF: Corticotropin-Releasing Factor; ACTH: Adrenocorticotrophic Hormone; GnRH: Gonadotrophin-Releasing Hormone.

Ethics Approval and Consent to Participate

Ethics approval was obtained from the scientific committee in the College of Medicine, University of Mosul, 2020. The written consent of the participants was obtained during the survey, and their anonymity was maintained throughout the study.

Competing Interest

The authors declare that there are 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

Data and complementary findings are available when requested by the publisher.

Authors' Contribution

RAH, ZNF, and RMAW made substantial contributions to the study's conception, design, acquisition, analysis, and interpretation of data. RAH, ZNF, and RMAW took part in the critical revision of the study for intellectual content, gave the final approval for this version to be published, and agreed to be accountable for all aspects of the work.

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Susceptibility Antibiotics of Bacteria Causing Urinary Tract Infection in Pregnant Women Infected with COVID-19

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Abstract

Urinary tract infections (UTIs) are a significant issue in women of all ages, but they are especially common during pregnancy. Co-infection of the Coronavirus Disease 2019 (COVID-19) with UTIs in pregnant females is a hot topic today, as it may be linked to various conditions. Furthermore, understanding the types of bacteria that cause UTIs and related antimicrobial resistance may aid the clinician in selecting the appropriate empirical treatment. This study aimed to isolate and characterize causative agents of UTIs and determine antimicrobial treatment sensitivity patterns among pregnant women diagnosed with the COVID-19 admitted to Teaching Hospital X in Iraq. Antimicrobial drug resistance testing was performed on 42 mid-stream urine samples that had been prepared for culture. *Escherichia coli* (18/42.85%), *Klebsiella pneumoniae* (9/21.45%), *Streptococcus galactica* (7/16.66%), and *Proteus mirabilis* (4/9.52%) were the bacteria isolated and diagnosed from pregnant women. The infections *Pseudomonas aeruginosa* and *Staphylococcus aureus* were the least common (2/4.7). In conclusion, the isolated uro-pathogens showed high resistance to Gentamicin, Cefuroxime, Ceftriaxone and sensitive to Ampicillin and Nitrofurantoin. The common cause of UTIs among pregnant women infected with the COVID-19 was discovered to be *Escherichia coli*. Before recommending therapy, culture and sensitivity testing of isolates from urine tests should be conducted on a regular basis.

Keywords: antimicrobial susceptibility pattern, COVID-19, pregnant women, urinary tract infections

Introduction

The Coronavirus Disease 2019 (COVID-19) is gradually spreading globally, and the World Health Organization (WHO) declared the COVID-19 pandemic on March 11, 2020.¹ The first outbreak was discovered in Wuhan City, Hubei Province, China and quickly spread across the world.² The COVID-19 has resulted in about 420,000 confirmed patients and 18,887 deaths worldwide since around March 25, 2020, with 81,852 reported cases and 3,287 deaths in China.³ The COVID-19 outbreak and pregnancy in terms of clinical features and consequences were observed.⁴ The COVID-19 is especially dangerous for pregnant women who are older, obese or have post-medical issues like hypertension (high blood pressure) or diabetes mellitus.

Pregnant women infected with the COVID-19 require extra care. There is currently insufficient evidence on the COVID-19 and pregnancy, with most cases occurring late pregnancy, posing a danger to both the mother and fetus. A COVID-19-infected mother's late pregnancy may result in negative urological consequences. When working with some of these patients, an interdisciplinary

team approach should be used because it allows for the effective acquisition of information, skills, and responsibility.⁵

Urinary tract infections (UTIs) are frequent in pregnant women. Pyelonephritis is by far the most detected medically diagnosed condition in pregnancy, and it can present itself in that way as UTIs, with poor treatment leading to complications. As a result, practitioners must be able to tell the difference between the normal and abnormal urinary tract and kidney results, assess anomalies, and cure diseases.⁶

Urinary contamination was documented in nearly 10% of primary care appointments among expectant mothers, and thus more about 15% of women had a single episode of UTI at some point in their lives. UTIs frequently occur as a result of an escalating infection.⁷ Due to ureteral dilation, increased bladder capacity, and reduced bladder tone, as well as reduced ureteral timbre, which contributes to higher urine stagnation and ureterovesical reflux, pregnant people, are more likely to have UTIs. Glycosuria, which affects 70% of pregnant women, stimulates bacterial development in the urine.

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With significant functional physiological and hormonal variations, as well as the position of the inguinal mucous, pregnant women, are more susceptible to urinary tract infection. Bacterial infections found in rectal plants can now enter the vagina via the genitals.⁸ The *Enterococcus* family, which contains *E. coli*, *Klebsiella spp.*, *Proteus spp.*, and *Enterobacter spp.*, is the most common cause of bacterial infection. Inability to recognize bacteremia during pregnancy raises the risk of acute pyelonephritis by 25% and can lead to problems such as preterm birth, temporary kidney failure, pulmonary fibrosis, sepsis, shocks, and hematological disorders. Women who have an untreated UTI during their third trimester are already at risk of giving birth to a child with mental disorders or developmental delays.⁹ This study aimed to isolate and identify the bacteria causing UTIs in the COVID-19-infected pregnant women and then assess the impact of antibiotics on the microorganisms isolated from urine samples.

Method

A total of 42 samples of urine were collected from pregnant women infected with the COVID-19 at Teaching Hospital X in Misan City, Iraq. The age of patients was categorized into three groups: 25–30, 31–35, and 36–45 years old. A mid-stream urine sample was taken for each woman in sterilized test tubes for the period from February 2021 to July 2021. All samples were cultured on nutrient agar, MacConkey agar, 5% blood agar, mannitol salt agar and incubated overnight at 37°C aerobically for 24 hours.

All urine samples were examined under a microscope. First, colonies were diagnosed initially depending on the phenotypic and culture characteristics. Identification of the isolated bacteria was done according to standard microbiological methods,¹⁰ including cultural characters, and gram stain then isolates were diagnosed by VITEK® 2 Compact Automated Systems with ID-GN and ID-GP cards based on the manufactures instructions.

Antimicrobial susceptibility tests were performed using the Kirby–Bauer disk diffusion method recommended by the Clinical and Laboratory Standards Institute

(CLSI).¹¹ All aspects of the Kirby–Bauer procedure are standardized to ensure consistent and accurate results. The media used is Mueller-Hinton agar at only 4 mm deep, poured into either 100 mm or 150 mm Petri dishes. The pH level of the agar must be between 7.2 and 7.4. Bacterial inoculum is prepared by diluting a broth culture to match a 0.5 McFarland turbidity standard, which is equivalent to approximately 150 million cells per mL.¹² The antibiotics tested were Ampicillin, Amikacin, Ceftriaxone, Cefotaxime, Ciprofloxacin, Gentamicin, Erythromycin, Nalidixic, and Nitrofurantoin.

The statistical analysis of the obtained results was performed using the SAS statistical package v.9.2. Statistical analyses were based on the model of analysis of variance (ANOVA) and Tukey's multiple tests (or confidence interval) at the assumed significance level of 0.05. The statistical averages were compared according to the Least Significance Difference (LSD) test.²⁴

Results

A total of 42 urine samples were positively cultured. The result of this study showed the pathogen isolates and their respective percentage shown in Table 1; positive culture included the most frequent organism; *E. coli* (18/42.85%) followed by *Klebsiella pneumoniae* by nine isolates (21.45%), *Streptococcus galactica* (7/16.66%), and *Proteus mirabilis* (4/9.52%), *Pseudomonas aeruginosa* and *Staphylococcus aureus* were the least identified pathogens (2/4.7).

The age range for the selected samples was classified into three categories as shown in Table 2 in which the highest infected age is 36-45 years old represented by 30 isolates (71.42%) While, there was no difference between the age groups of 25-30 and 31-35 years. The UTI was determined based on the general urine lab examination including Pus Cells, RBCs, and Epithelial cells that revealed significant relationships between the bacterial isolates and the UTIs problems.

Figure 1 presents the number of pregnancies among the samples studied. The highest sector infected by identified bacteria was (4 to 5) by 20/47.61% followed by (1 to 3) by 15/37.71%, and finally, the least number of iso-

Table 1. Distribution of Bacteria Isolated from Urine Samples of Pregnant Women Presenting with Symptoms of Urinary Tract Infection and General Urine Examination

Bacterial Isolate	n	%	Pus Cell	RBC	Epithelial Cell
<i>Escherichia coli</i>	18	42.85	30	10	18
<i>Klebsiella pneumoniae</i>	9	21.45	22	2	20
<i>Streptococcus galactica</i>	7	16.66	18	2	18
<i>Proteus mirabilis</i>	4	9.52	16	4	14
<i>Pseudomonas aeruginosa</i>	2	4.76	15	2	14
<i>Staphylococcus aureus</i>	2	4.76	14	4	10
LSD at 0.05	1.779		1.751	1.699	1.677

Notes: RBCs = Red Blood Cells, LSD = Least Significant Difference

lated strains was for (6 to 7) by 7/165.6%. The result of this study also showed that the percentage of Gram-negative bacteria is higher than the percentage of Gram-positive bacteria (66.6%) (33.3%), respectively (Table 3).

Discussion

Urinary tract infections are among the most predominant infectious illnesses, impacting 150 million people across the globe each year.¹ In 2007, there had been approximately 10.5 million appointment visits for symptoms (representing 0.9% of all outpatient visits) and 2–3 million urgent care visits 2–4 in the United States alone. In the Western world solely, the societal costs of the diseases, including wellness costs and lost time at work, are conservatively believed to be around USD 3.5 billion each year. Urinary tract infections are quite a deadly disease in children, elderly men, and women of all ages.¹³

Urinary tract infection is a relatively prevalent condition and its early diagnosis has significant consequences for personal health, antimicrobial resistance, and medical expenses.¹⁴ Because the incidence of bacteria and their characteristics might fluctuate with temporal and spatial location, monitoring of local UTIs aetiology, as well as antibiotic susceptibility, is deemed valuable to guide temporal structure.¹⁵ Using demographic and clinical data, efforts should really be made to improve the prediction of causal uropathogens. Along with the worldwide COVID-19 pandemic, UTIs in pregnant women should be monitored and evaluated on a regular basis.

Urinary tract infections are caused by a variety of microorganisms, which includes both gram positive and gram-negative ones. In a study, *E. coli* (42.85%) was pre-

dominant isolate followed by *Klebsiella pneumoniae* (21.45%), *Streptococcus galactica* (16.66%), and *Proteus mirabilis* (9.52 %) respectively. This finding is similar to many reports indicating that gram-negative bacteria mostly *E. coli* and *Proteus spp.* are the most common pathogens isolated in a patient with UTIs. A study showed that 42 samples collected and screened from patients infected by the COVID-19 and UTIs yielded positive bacteria cultures and it has again confirmed UTIs to be a common infection in women.¹⁶ The UTI patients might have a correlation to the COVID-19 pandemic side effects or risk factors.

In this study, bacteria were gram-negative most common at 66.6% and the gram-positive bacteria at 33.3.1%. The incidents were found similar in rural areas of Tanzania.¹⁷ Gram-negative and gram-positive organisms, and certain other types of fungi, can cause UTIs. Uropathogenic *E. coli* diseases are the major cause of both simple and complex UTIs. *K. pneumoniae*, *S. saprophyticus*, *Streptococcus galactica*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Candida spp.* are the most common agents involved in simple UTIs.^{3,6,12,13} This fact is clearly demonstrated in the current study in Table 3, *E. coli* was the main pathogenic isolated from urine samples accounting for 18 (42.8% out of all isolates) with big bacteremia. *E. coli* was to be a diuretic due to count of the factors of the spectra of colonialism invasion of urinary epithelium such as Adhesions fiber (P) and fiber (S).¹⁸ *Klebsiella pneumoniae* was the second most common isolated bacteria coagulant negative.

Urinary Tract Infection Relation to Age and the COVID-19 in Pregnant Women

Obviously, age is a risk factor that plays an important role in transmitting UTIs in pregnant women where 30 isolates out of 42 (71.42%) appeared in the age range of 36 to 45 years, whereas younger age was recorded with a low number of isolates (12 /-28.58%). This fact is in line with the study by Rowe and Mehta in 2013,¹⁹ who stated that in the elderly, UTIs and subclinical bacteriuria are prevalent It is difficult to tell the difference between a severe UTI and asymptomatic bacteriuria in older persons, especially those in long-term care institutions because

Table 2. Distribution of Isolates with Age Range and Their Respective Percentage

Age Range (years)	n	%
25-30	6	14.28
31-35	6	14.28
36-45	30	71.42

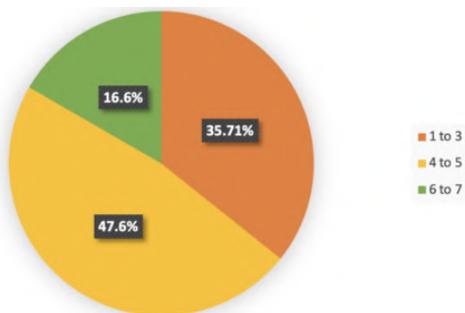


Figure 1. The Number of Pregnancies among the Samples Studied

Table 3. Gram-negative and Gram-positive Bacteria and Their Respective Percentage

Bacterial Isolate	Status	%
<i>Escherichia coli</i>	Negative	66.6%
<i>Klebsiella pneumoniae</i>	Negative	
<i>Proteus mirabilis</i>	Negative	
<i>Pseudomonas aeruginosa</i>	Negative	
<i>Staphylococcus aureus</i>	Positive	33.3%
<i>Streptococcus galactica</i>	Positive	

Table 4. Resistance of Organisms to Antibiotics (%)

Bacterial Isolate	Ampicillin	Amikacin	Ceftriaxone	Cefotaxime	Ciprofloxacin	Gentamicin	Erythromycin	Nalidixic	Nitrofurantoin	LSD at 0.05
<i>Escherichia coli</i>	27	24	55	80	78	80	22	26	38	2.33
<i>Klebsiella pneumoniae</i>	12	40	80	72	80	77	27	53	27	2.31
<i>Streptococcus galactica</i>	22	25	46	70	40	70	12	22	22	4.40
<i>Proteus mirabilis</i>	40	38	50	58	35	72	38	46	35	2.56
<i>Pseudomonas aeruginosa</i>	25	27	70	70	42	76	40	50	20	2.45
<i>Staphylococcus aureus</i>	40	30	22	82	50	82	20	70	35	3.21

they are less likely to have localized gynecologic symptoms.

Patients with urine incontinence and chronic intermittent cystitis/bladder pain syndrome exhibit higher urinary inflammatory cytokines than healthy controls, according to earlier study. As a result, it is postulated that the COVID-19-associated cystitis can arise in the COVID-19, accompanied by de novo acute urinary symptoms, and is induced by elevated inflammatory cytokines secreted into the urinary and/or produced in the bladder.²⁰ Thus, the relation between the COVID-19 and UTIs in pregnant women could be a highly important topic that needs in-depth investigations.

Pseudomonas aeruginosa revealed good sensitivity to Ampicillin, Amikacin and Nitrofurantoin while showing low resistance against Gentamicin (75%), Cefotaxime and Ceftriaxone (70% for each antibiotic). In general, Ceftriaxone, Cefotaxime, Gentamicin and Nalidixic were the most resistant to the pathogens (Table 4). These findings are in line with a study by Rodhe, *et al.*²¹ Women who have four to five pregnancies had the highest rate of UTI, which is consistent with previous study by Malekzadegan, *et al.*²² At the ages of 24, 40, and 50, one out of every three women will require antibiotic treatment for UTIs.²³

Most bacterial isolates are susceptible to routinely-used antibiotics, such as Ceftriaxone, Cefotaxime, Gentamicin, Ciprofloxacin, and Nalidixic, which were found in 80% of the germs identified. Ampicillin, Amikacin, Erythromycin, and Nitrofurantoin sensitivity were found in the majority of bacterial isolates. As a result, rather than following global principles, the empirical antibiotic choice should be based on awareness of specific bacterial species' prevalence and antibiotic sensitivity.

Early detection of the causal agent of UTIs and determination of their drug sensitivity pattern in pregnant mothers infected with the COVID-19, according to this study, can aid in ensuring effective treatment of UTIs and preventing additional complications in the mother and fetus. Pregnant women should be given health information on the causes of UTIs and drug usage. Ampicillin, Amikacin, Erythromycin, and Nitrofurantoin are examples of antibiotics. When there are no facilities for doing

culture and susceptibility testing in their location, it might be utilized for empirical therapy of UTIs. However, it should be administered with caution to prevent the establishment of new drug resistance, particularly in patients with the COVID-19 risk factors.

Conclusion

The progression of UTIs is shown to be caused by gram-negative and gram-positive bacteria in this investigation. In pregnant women infected with the COVID-19, the most frequent pathogenic bacteria from the urinary system, *E. coli*, is the most prevalent cause of UTI. The isolated uropathogens showed high resistance to Gentamicin, Cefuroxime, Ceftriaxone and sensitive to Ampicillin and Nitrofurantoin. It is suggested to monitor the most efficient bacteriostatic medications against UTIs pathogenic bacteria, such as Ampicillin, Amikacin, Erythromycin, and Nitrofurantoin.

Abbreviations

UTI: Urinary Tract Infections; COVID-19: Coronavirus Disease 2019; WHO: World Health Organization; CLSI: Clinical and Laboratory Standards Institute.

Ethics Approval and Consent to Participate

All procedure of study was conducted with allowance and permission of the Faculty of Health Sciences, University of Misan and Maysan Health Directorate, in means of medical ethics.

Competing Interest

The authors declare that there are 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

Data and complementary findings are available when requested by the publisher.

Authors' Contribution

Single author presented in this paper.

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Analysis of COVID-19 Preventive Behavior in Diabetes Mellitus Patients: A Literature Review

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Abstract

The Coronavirus Disease 2019 (COVID-19) is a new human-infected coronavirus causing respiratory problems. The COVID-19 can affect people of all ages, but those with a record of chronic disease (comorbidity) are at higher risk of poor outcomes with the COVID-19. This study aimed to review COVID-19 preventative behavior in diabetes patients. Diabetes Mellitus (DM) is one of the comorbidities that aggravates COVID-19 in patients. Such patients are at risk of deteriorating critical conditions in the intensive care units (ICUs) and even death. Prevention is the best measure to avoid COVID-19, although it is currently considered adequate. This article reviewed 22 papers focusing on COVID-19, DM, COVID-19 in DM patients, COVID-19 preventive behavior, and COVID-19 knowledge, attitude, and practice in patients with chronic disease, while primary focusing on DM. It is revealed that diabetes patients at high risk of COVID-19 need to practice good preventive behaviors. Furthermore, it emphasizes that improving knowledge, encouraging positive attitudes, and implementing good COVID-19 preventive behaviors in DM patients requires education and access to the COVID-19 related health information.

Keywords: attitude, COVID-19, diabetes mellitus, knowledge, preventive behavior

Introduction

The ongoing COVID-19 pandemic impacts the health sector and the world's socioeconomic system.¹ Based on World Health Organization (WHO) data, on June 9, 2022, there were 531,550,610 confirmed cases of COVID-19 and 6,302,982 deaths globally.² The Ministry of Health of the Republic of Indonesia verified that, on June 8, 2022, there were 6,058,180 confirmed cases of COVID-19, with 5,897,630 recovered and 156,628 deaths.³

Based on data from the Indonesian COVID-19 Handling Task Force data as of June 20, 2021, around 4,332 patients had comorbidities. Diabetes Mellitus (DM) is the second-highest comorbid disease by 36.5%. Of the 4,322 COVID-19 patients with comorbidities who died, 9.7% were related to DM.⁴ Thus, this study addresses the challenge of identifying issues related to COVID-19 and DM. To attain this end, data were obtained from reported research on COVID-19 pertaining to various countries.

Existing evidence suggested that elderly people with a record of chronic disease (comorbid) are at increased risk and experience worse complications.⁵ Nearly 30% of

COVID-19 deaths can be attributed to diabetes, hypertension, obesity, and smoking.⁶ In Indonesia, three of most prevalent comorbidities in COVID-19 patients are hypertension, DM, and cardiovascular disease,⁷ wherein diabetes is the second most common non-communicable disease (NCD) in COVID-19 patients which worsens disease severity and mortality.⁸ Other prevalent comorbidities include hypertension, diabetes, and thyroid diseases.⁹ Although the prevalence of DM in COVID-19 patients is generally lower compared to the general population, it has a more severe impact than on those without the disease.¹⁰ However, the results obtained from the preliminary analysis showed that elderly male patients with diabetes exhibited a higher likelihood of having severe COVID-19 symptoms than those without such characteristics.¹¹ Hyperglycemia, imbalances in pathways involved in viral entry into cells, and impaired immune and inflammatory responses cause this COVID-19-induced mechanism in DM patients.¹⁰ Uncontrolled blood sugar levels and complications related to DM critically affects this group of COVID-19 patients, whose prognosis was observed to be poor.¹²

As for the situation in Indonesia, the country's gov-

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ernment announced measures to be implemented to help DM patients during the COVID-19 pandemic on March 28, 2020.¹³ To reduce the likelihood of contracting the disease, the most effective step is to follow COVID-19 preventive behavior. It should be noted that knowledge, attitudes, and behavior regarding COVID-19 largely affect community compliance with guidelines and regulations.¹⁴ If people in Indonesia possess good knowledge and exhibit positive attitudes, they can be expected to take effective preventive action.¹⁵ It is imperative that those at a higher risk of contracting COVID-19 must maintain adequate COVID-19 preventive behavior. However, the key problem is that insufficient knowledge among patients with DM and hypertension affects their preventive behavior, thus increasing their risk of contracting COVID-19.¹⁶ Notably, COVID-19 prevention behavior is closely related to age, sex, and employment.¹⁷ As explained above, it is evident that one must also focus on DM prevention to avoid DM complications arising from COVID-19 infection and reduce its incidence.¹⁸ However, there is a gap in the literature regarding discussions on COVID-19 preventive behavior in DM patients in Indonesia, suggesting that further research and investigations are required to control and prevent COVID-19 in such patients. This study aimed to fill this gap by conducting a literature review of COVID-19 preventive behavior in diabetic patients.

Method

The literature searched for this review focused on study relevant to COVID-19 preventive behavior in patients with chronic illness, specifically DM. Relevant articles were searched for and identified on PubMed and ProQuest. About 22 of the 73 shortlisted articles met the exclusion and inclusion criteria. The inclusion criteria were articles published in the last three years based on the keywords COVID-19 and DM as well as COVID-19 preventive behavior in DM patients. The exclusion criterion was articles whose summary of contents did not correspond to the relevant keywords. An article was considered for this study if it was either a review or a research article that was available for open access. Articles that were unavailable for open access were excluded. The search terms used in Medical Subjects Headings (MeSH) were (COVID-19 AND Diabetes Mellitus), (COVID-19 in Diabetes Mellitus patients), AND (Preventive Behavior of COVID-19).

The eligibility of the papers based on their title and abstract was assessed independently by the first two authors. Additionally, if needed, the full paper was acquired to determine its eligibility status. In case of any disagreement, a consensus was reached by consulting the third author. Papers in languages other than English were excluded if their translations were unavailable. The full text

of the papers that met the eligibility criteria for the review was then assessed. The authors then pooled the results of the studies focusing on COVID-19 preventive behavior in diabetic patients. Finally, the articles were reviewed and discussed thoroughly, critically, and objectively using the same method from the related previous study.¹⁹

Results and Discussion

Article Selection

After searching with the selected keywords, the authors identified 73 research articles on PubMed and ProQuest, after removing duplicate entries. Based on the inclusion and exclusion criteria, 22 articles were finally selected and examined based on their relevance to the topic. COVID-19, diabetes mellitus, and COVID-19 in DM patients were the subjects of five articles. Additionally, 17 studies were based on preventive behavior for COVID-19, including knowledge, attitude, and practice (KAP) in patients with chronic illnesses, particularly those with diabetes. Finally, the articles were reviewed and discussed using objective and comprehensive analysis with regard to COVID-19, diabetes mellitus preventive behavior, and COVID-19 KAP in patients with chronic illness, specifically in diabetic patients.

This review analyzes articles dealing with the prevention of COVID-19 in diabetics and COVID-19 preventive behaviors. Areas for further study that emerged from the articles have been identified, including knowledge, attitudes, and characteristics in relation to COVID-19 among diabetics. While, the relative lack of publications regarding preventative behavior among diabetic COVID-19 patients can be regarded as a limitation and weakness of the present review. The strengths of this review are twofold: one, it has employed reputable databases (PubMed and ProQuest) consisting of recent publications to select relevant articles; and two, it has facilitated the review of publications on COVID-19 preventive behavior in diabetic. This study recommends that COVID-19 preventive behavior is the most effective strategy to avoid COVID-19, and further emphasizes the need for improving COVID-19 health education programs for DM patients to encourage knowledge development, positive attitudes, and efficient preventative behaviors among them.

Prevention of COVID-19 in Diabetics

To prevent COVID-19, clinicians advise DM patients to wash their hands frequently with soap and avoid touching their faces, except when necessary, to minimize their exposure to virus carriers. Wearing a mask outdoors is also strongly recommended. In addition, DM patients are advised to maintain a healthy diet and stay active. Furthermore, when following a diabetic treatment, patients should check their blood sugar levels regularly,^{20,21} and consult a doctor in case of discrepancies. Since pa-

tients must handle both oral and injected drugs, it is imperative for them to wash hands frequently to prevent COVID-19 infection.²¹ DM patients' increased risk of suffering from severe diseases is primarily due to uncontrolled blood sugar levels; therefore, it must be monitored regularly.²¹ Moreover, healthy lifestyle choices and consistent administration of medication are also advised for DM patients. Besides, taking advantage of telemedicine facilities may further reduce the risk of exposure.

COVID-19 Preventive Behaviors

Behavior and lifestyle significantly affect health status. To reduce patient risk factors and comorbidities public policies should promote healthier lifestyles, including healthier diets and regular physical activity.⁶ Since there is no effective treatment for COVID-19 yet, prevention is the best way to minimize infection. Under such circumstances, knowledge and attitude are fundamental for preventive behavior. Sulistyawati, *et al.*,¹⁵ found that in Indonesia respondents with good knowledge and positive attitudes practiced preventive behaviors. Similarly, good knowledge and positive attitudes among the majority of a population indicated a higher likelihood of appropriate COVID-19 preventive behaviors.^{14,22} Based on Lee, Kang, and You's study in South Korea, knowledge about COVID-19 related to preventive behaviors, such as wearing masks, hand hygiene, and avoiding crowds impelled people to adopt preventive practices.²² However, having good knowledge and attitudes to COVID-19 does not necessarily result in improved health practices, as was found for the people of Sudan.²³ To avoid misleading information, adequate information on COVID-19 precautions is essential.¹⁵

Although a large number of patients with comorbidities, such as diabetes and hypertension, are aware of the symptoms of COVID-19 and have implemented appropriate behaviors, many are yet to make routine changes for preventing infection.²⁴ Contrary to this, patients in Vietnam and Ethiopia exhibit strong knowledge, positive attitudes, and performed COVID-19 prevention well.^{25,26} As mentioned before, sufficient knowledge and a positive attitude in patients with chronic diseases are significant for preventing COVID-19.²⁶ In comparison, many patients with chronic conditions had low perceptions and willingness to carry out COVID-19 intervention behaviors.²⁷ Akalu's study (2020) in Ethiopia found that patients with chronic diseases demonstrated poor preventive behavior, such as failing to use masks outdoors as well as unwillingness to avoid crowds and maintaining a distance. In general, patients with chronic diseases and low level of knowledge are less likely to practice COVID-19 preventive behaviors.⁵

The risk of COVID-19 for DM patients must be encountered by appropriate preventive behavior. A study

on DM and hypertension patients found that inadequate knowledge increased their risk of COVID-19 infection.¹⁶ COVID-19 knowledge and attitudes were observed to be high in type 1 diabetes mellitus (T1DM) patients in a study involving young adults in India.²⁸ However, many young adult patients with T1DM were less aware of the risk of COVID-19 compared to those with other kinds of diabetes.²⁸

To date, it is unclear whether DM patients comply with COVID-19 preventive measures. Extra and optimal preventive practices were rarely observed in Pakistan.²¹ In a Chinese study, DM patients were reportedly more anxious about COVID-19 than non-DM people. In the same study, it was reported that infection was avoided during the COVID-19 pandemic primarily due to behavioral changes, such as maintaining a healthy diet, using medication, and exercising.²⁹ Furthermore, an Indian study showed that only 28% of DM patients regularly monitored their blood sugar levels during the COVID-19 pandemic.³⁰

Knowledge

Sources of verified accurate information are the utmost importance in increasing public knowledge on COVID-19. Fixing hoax circulating in the community will also help reduce inappropriate preventive behavior.¹⁷ Social media is widely used to find information on COVID-19 in Indonesia.¹⁵ To provide error-free and appropriate COVID-19 preventive practices, the overall health education programs regarding COVID-19 must be improved.¹⁴ Although COVID-19 is a new disease, Indonesia, Malaysia, South Korea, China, and Sudan all seem to possess some amount of prior knowledge about it.^{15,22,23} Knowledge of COVID-19 is related to COVID-19 attitudes and preventive practices.²² As an example, DM patients in Ethiopia had adequate knowledge of COVID-19.¹⁶ Meanwhile, results have been inconclusive with regard to appropriate knowledge of COVID-19 and its preventive behavior among patients with chronic diseases like diabetes, hypertension, and chronic lung disease.⁵ Considering that effective prevention practices are associated with possessing sufficient knowledge of the same, health sectors should cooperate to increase access to COVID-19 information.¹⁶

Attitude

Assessment and measurement are essential tools for understanding human attitudes and behavior.³¹ Studies related to COVID-19 have shown that communities are becoming increasingly aware of COVID-19.^{15,17,22,23} A positive attitude to protection against COVID-19 influences preventive behavior.² Since people with DM face an increased risk of being infected with COVID-19 during the pandemic, they took sufficient preventive action

to avoid infection.²⁹ Findings with regard to DM and hypertension patients as well as T1DM patients showed positive attitudes to COVID-19 preventive behavior.^{16,28} These patients maintained social distance and washed their hands frequently to protect themselves.²⁸

Characteristics

With an increase in education, knowledge can also be better received and understood. Knowledge of COVID-19 is, therefore, closely related to the level of education.^{22,23} Lower levels of education significantly impact knowledge of COVID-19 among patients suffering from chronic diseases. A study on DM and hypertensive patients found that inadequate knowledge and appropriate behavior related to COVID-19 was associated with low educational attainment.¹⁶ The demographic characteristics related to the KAP could serve as a compass for policymakers to focus health education programs toward appropriate target groups.³² The evaluation of the diabetes KAP has become essential for directing behavioral changes among individuals with diabetes and those at risk.³³ Furthermore, a study on patients with chronic diseases shows that socio-economic characteristics, such as age, education, employment, and income, are connected to low knowledge and poor preventive behaviour.⁵

Conclusion and Recommendation

This study concludes that COVID-19 preventive behavior is the best strategy to avoid contracting the disease, especially in view of its harmful effect on DM patients and the lack of treatment considered adequate for COVID-19. Although vaccination is one of the main steps to avoid transmission, severity of infection, and death as a result of contracting COVID-19 among high-risk patients (comorbid), it is still necessary to practice protective behavior to reduce the risk of transmission of COVID-19. Therefore, future studies on the current topic are recommended, so that health education programs regarding COVID-19 in DM patients can be improved to increase knowledge, help encourage positive attitudes, and implement appropriate COVID-19 prevention behaviors.

Abbreviations

COVID-19: Coronavirus Disease 2019; DM: Diabetes Mellitus; ICU: Intensive Care Unit; KAP: Knowledge, Attitude, and Practice; WHO: World Health Organization; NCD: Non-communicable Disease; MeSH: Medical Subjects Headings; T1DM: Type 1 Diabetes Mellitus.

Ethics Approval and Consent to Participate

Not applicable.

Competing Interest

The authors declare that there are 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 authors have full access to all the data in the study and take responsibility for the data integrity.

Authors' Contribution

HH and GP conceptualized, investigated, wrote the draft of the manuscript, and validated the study. HH and PD wrote the main manuscript text. PD edited the draft, and all authors contributed to interpreting the results. All authors read and approved the final manuscript.

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Psychological Distress among Parents due to Their Children Having Cancer: A Systematic Review

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Abstract

As a result of their children's cancer, parents are at risk of experiencing psychological distress. Parental stress will affect their roles in providing emotional support for their children. This systematic review aimed to identify the psychological distress of parents having children with cancer. EBSCO, PubMed, Science Direct, and Research Gate were applied to conduct electronic searches. The terms "parents," "children," "cancer," and "psychological distress" were combined using the Boolean expressions "OR" and "AND." The inclusion criteria were non-experimental studies published in English within the last 10 years (2010-2020). Risk of bias assessment was conducted for each included study using the Joanna Bridge Institute critical appraisal tools to build transparency of findings. A total of 12 articles were included in the study to determine the prevalence of psychological distress among parents and the symptoms and factors that influence it. The high category of parental distress reached 17.6%, while the very high category reached 5.8%. Thus, it needed more concern. Suicidal ideation, insomnia, and poor health were all connected to psychological distress, with the age of children and parents, the number of children, occupation, education level, depressive history, and time of diagnosis all being predictive factors.

Keywords: cancer, children, distress, parents, psychological distress

Introduction

Cancer in children continues to increase. According to statistics collected from 62 countries in 2001-2010, the cancer rate among children aged 0 to 14 years was 140.6 million per year, and 155.8 million children aged 0 to 19 years per year.¹ In the high-income nations, the cure rate for cancer in children approaches 80%, but in low-income, it can be as low as 20%.²

For patients and their families, cancer in children is a difficult phenomenon and potentially devastating.³ As families witness their children being extremely ill and in agony, with repeated hospitalizations and emergency visits, parents find it difficult to cope with this situation. Other concerns include cancer treatment and adverse effects such as baldness and financial difficulties.⁴ As a result, families accept a series of stressors and manage emotional pressure with family members, especially parents, who are the children's primary source of emotional support.⁵⁻⁷ When their children are diagnosed with a life-threatening condition or injury, parents may endure great distress. Despite the fact that many families show psychological resilience when their children are diagnosed with cancer, some children and their parents are more

prone to experience psychological distress.^{5,8}

The National Comprehensive Cancer Network (NCCN) defines psychological distress as an unpleasant, multifaceted emotional experience of psychological, social, and spiritual nature that can impair physical ability.⁹ Depression and anxiety are the two main forms of psychological distress.^{10,11} Sadness, diminished excitement, loneliness, hopelessness, worthlessness, sleeping difficulty, sobbing, and inability to cope, are symptoms of depression. While, anxiety is characterized by being tensed, restlessness, irritability, and fear. Identifying these signs and symptoms is important to determine the individual's level of distress.¹²

Parental pain can occur at the time of caring for children with cancer, particularly children at the advanced stage of this disease.¹³ Many studies recorded in Sloper's study has found that parents of children with cancer experience significant psychological distress at the time of diagnosis and during the early phases of cancer treatment. This anguish can last for a year or more.⁷ Longer treatment, more frequent hospitalizations, relapses, workplaces, and financial issues can be exacerbated by the burden of care during the therapy phase. This effect

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can increase the burden on families. They can come across various stressors; as a result, they pose as risk factors for significant parental distress during their child's therapy.⁷

In the setting of pediatric cancer, parental distress is a crucial component to assess since it affects the child's quality of life as well as other psychosocial outcomes.¹⁴ Significant parental distress can have far-reaching consequences, impacting both the sick child and the rest of the family.⁸ Parental distress also affects parents' ability to manage their careers and care for their children.⁸ Also, parents with emotional problems face serious difficulties adjusting to their child's cancer. Parents' health is negatively affected by anxiety and depression and their manifestations.⁶ Identification of the level of parental distress is needed to prevent, reduce, or provide treatment according to its severity.¹⁵

The parents faced an uphill battle and felt an unstable situation after the disclosure. Even after the child's treatment is completed, parents experience the challenge of transitioning back to life before diagnosis and needing psychological support.¹⁶ The number of studies on psychological distress, particularly depression and anxiety in parents of children with cancer as a special group, is still limited; most of them are primary studies.¹⁶ The previous literature review on the factors and consequences of parental distress related to childhood cancer was conducted in 2015; however, the review did not specifically identify depression and anxiety but stress in general.⁵ Furthermore, there have been many changes in the evidence related to prognosis, the survival rate in cancer children, and other factors that may affect the burden on parents in this decade. Treatment effectiveness and efficiency have improved over the last decade, which may positively impact parental distress. Although it is unclear to what extent this will have an impact. As a result, a review is required to capture the most recent updates on parental distress, particularly on anxiety and depression issues. The general aim of this review was to identify parents' psychological distress due to having cancer children, while the specific purpose of this review was to determine the prevalence, symptoms, impact, and factors influencing psychological distress.

Method

The systematic review provided a comprehensive overview and significance of the issues discussed by identifying and summarizing existing study.¹⁷ This approach was used to identify the prevalence of psychological distress associated with having a child with cancer and to examine its symptoms, effects, and influencing factors. Templier and Pare's steps are adapted for the review stage.¹⁷ The primary objective of the review was to answer the research question: how is parents' psychological

distress related to having a child with cancer based on prevalence, symptoms, impact, and related factors?

The electronic search strategy was carried out by the first two authors. An extensive search was conducted using index terms and keywords across four databases: EBSCO, PubMed, Science Direct, and Research Gate. An initial search on PubMed combined the main concepts from the research aims: ('child' OR 'children') AND ('parent') AND ('cancer' OR 'neoplasm') AND ('psychological distress' OR 'emotional distress'). Each database's keyword truncation was done individually. The search was conducted for three months, between March to June 2021. The initial search for articles published in English with no year limit to obtain a thorough study.

The articles that met the study's inclusion criteria were written in English and reported the prevalence of psychological distress among parents. The studies with a non-experimental quantitative design were chosen. Only literature published between 2010 and 2020 was considered. Articles that did not have a full text, an experimental quantitative research design, or a qualitative study were eliminated. Importing articles and deleting duplicates were done with the reference manager. The title and abstracts were then independently reviewed by the first two authors. The complete texts of the shortlisted articles were then checked against the inclusion and exclusion criteria. Joanna Bridge Institute (JBI) appraisal tools for cross-sectional and cohort studies were used in the quality appraisal. Any discrepancies in judgment are settled through discussion until an agreement is reached. The data extraction included the author, year of publication, country, study design, sample size, instrument, prevalence of psychological distress, symptoms, impact, and factors influencing psychological distress. The prevalence of psychological distress among parents of cancer children was expressed as a percentage. Sugiyono's criteria are then used to categorize the prevalence of psychological problems, with 0–20% being very low, 21–40% low, 41–60% moderate, 61–80% high, and 81–100% very high.¹⁸

Results

The search and screening process for studies is shown in Figure 1. Four databases provided 357,235 articles from the year 2010 to 2020. After excluding duplicates and applying inclusion and exclusion criteria, 184 articles remained. After full-text examination, 12 articles remained for quality appraisal, receiving a quality score above seven. Overall, the study quality was acceptable.

Table 1 provides information about the characteristics of the included studies. Studies were conducted in Iran, the United States, Australia, India, the Netherlands, Jordan, Sweden, Lebanon, Singapore, and Indonesia. By region, there were two studies from Southeast Asia, two

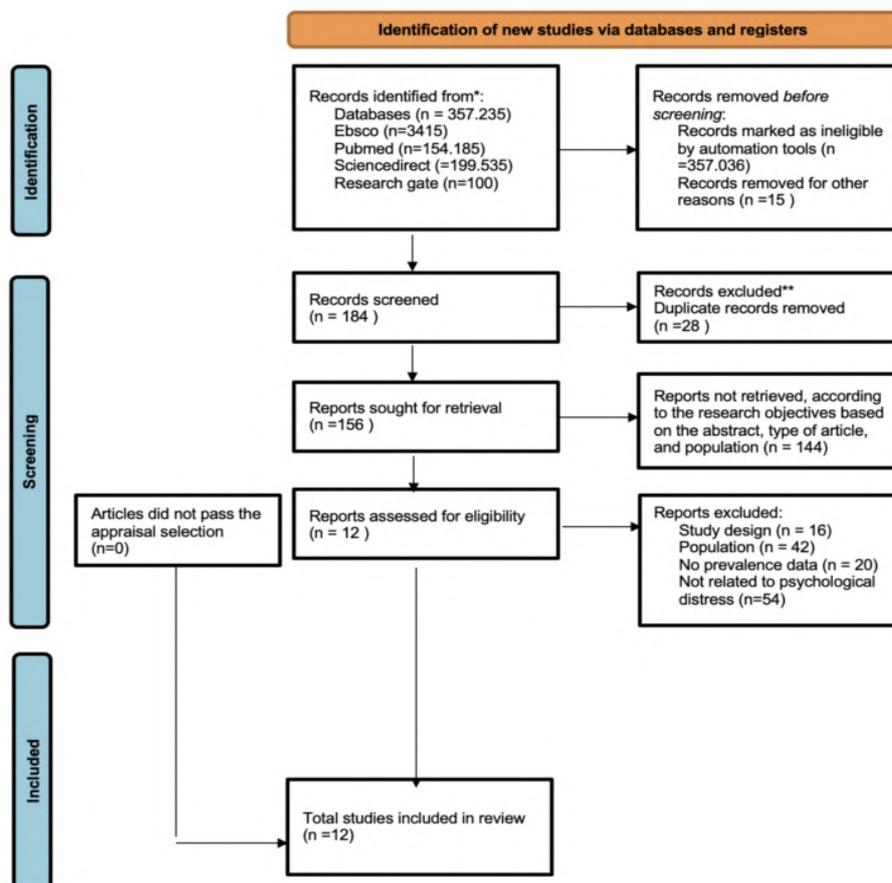


Figure 1. Article Selection Flow

from Europe, one from Australia, two from America, three from the Middle East, and one from South Asia. The instruments used to measure psychological distress varies, including the Depression Anxiety Stress Scale, the Beck Depression Inventory (BDI), the Beck Anxiety Inventory (BAI), the Hospital Anxiety and Depression Scale, The Hamilton A and B scales, as well as the Distress Thermometer for Parents (DT-P), the Kessler Psychological Distress Scale, the General Health Questionnaire (GHQ), and the Kessler Psychological Distress Scale.

Prevalence values were analyzed using grading criteria adapted from Sugiyono,¹⁸ with very low, low, moderately high, high, and very high outcome categories. The results of classifying the prevalence of psychological distress according to Sugiyono's criteria in each included study are shown in Table 2.

The study's findings revealed 17 prevalence values of distress, which include anxiety and depression. The largest prevalence was in the moderately high value group, with six studies (35.2%), while the lowest was in

the very high category, with one study (5.8%). Details about the prevalence, criteria, symptoms, impact, and factors that influence parental psychological distress are provided in Table 3. Out of the 12 included, one study discussed the signs and symptoms of psychological problems. The study found that parents with psychological distress, such as anxiety and depression, had respiratory symptoms, gastrointestinal symptoms such as indigestion, and symptoms of cardiovascular palpitations and headaches.¹⁹ In general, the prevalence of anxiety was higher than the prevalence of depression. The average prevalence of anxiety ranged from 17.1% to 63%. However, the prevalence of depression reached 85.14% in India, but this percentage represented the total of all categories of depression. In developed countries, the rate of depression reached 12.2% in Australia, while in Sweden, it reached 14%. In Indonesia alone, the percentage of depression reached 25%, but it was lower than the prevalence of depression in Iran, reaching 32.4%.^{2,6-10}

Based on Table 3, two studies discuss the impact of

Table 1. Characteristic of Studies

Author	Year	Objective	Country	Study Design	Instrument	Sample Size
Rahmani, et al., ⁶	2018	Study of anxiety and depression among Iranian parents of cancer children.	Iran	Cross-sectional	The Hospital Anxiety and Depression Scale (HADS)	148 parents with child cancer.
Collins, et al., ²⁰	2019	Assess the impact of unifocal and multifocal retinoblastoma on depression, anxiety, and stress in parents of these patients.	USA	Cross-sectional	The BDI II, Beck Anxiety Inventory (BAI), The Parental Stress Index	38 parents of children with retinoblastoma.
Vernon, et al., ²¹	2017	Knowing the prevalence of PTSS/PTSD, depression, and anxiety in mothers and fathers of children with cancer, and the relationship between parental demography, disease-related characteristics, and parental distress symptoms.	Australia	Cross-sectional	The Depression Anxiety, Stress Scales short form	66 parents, 41 mothers, and 25 fathers.
Srivastava, et al., ¹⁹	2020	Determine the level of anxiety and depression in cancer children undergoing chemotherapy and clinical and sociodemographic factors.	India	Cross-sectional	Hamilton A and Hamilton B Questionnaire	101 parents
Schepers, et al., ¹⁵	2018	Assess maternal and paternal distress and level of family psychosocial risk after diagnosis of childhood cancer.	Netherland	Cross-sectional	The Distress Thermometer for Parents (DT-P)	192 parents, 119 mothers, and 98 fathers.
Al Qadire, et al., ²²	2018	Assess anxiety, depression, and their predictors among parents of children with cancer.	Jordan	Cross-sectional	The Hospital Anxiety and Depression Scale (HADS)	222 parents
Wikman, et al., ²⁵	2018	Determine the prevalence and determinants of anxiety and depression in cancer-affected and bereaved parents five years after treatment stopped, or the child died, as well as the comorbidity of anxiety, depression, and PTSS.	Sweden	Longitudinal study	Beck Anxiety Inventory and Beck Depression Inventory	132 (68 mothers, 64 fathers).
Lakkis, et al., ²⁴	2016	Determine the prevalence of psychological distress among parents of Lebanese children with cancer as well as the causes of stress and coping strategies.	Lebanon	Cross-sectional	The General Health Questionnaire (GHQ-12)	114 (29 fathers, 85 mothers)
McCarthy, et al., ¹⁰	2016	Determine the prevalence of psychological distress in adolescent and young adult cancer patients and their parents and its determinants.	Australia	Cross-sectional	The Kessler Psychological Distress Scale (K10)	204 parents
Rosenberg, et al., ²⁵	2014	Determine the prevalence and factors that lead to psychosocial distress in parents of children with advanced cancer.	USA	Cohort Study	The Kessler-6 Psychological Distress Scale	104 parents
Isabel Tan, et al., ²⁶	2021	Determine the level of distress and associated factors among Singaporean parents of children with cancer.	Singapore	Descriptive correlational	The Distress Thermometer for Parents (DT-P) tool	81 parents
Aziza, et al., ²⁷	2019	Determine the demands and factors that lead to parents' psychological distress when caring for children with cancer in Indonesia.	Indonesia	Cross-sectional	The Hospital Anxiety Depression Scale	100 parents

Notes: PTSS = Post-traumatic Stress Syndrome , PTSD = Posttraumatic Stress Disorder

distress on parents. Some of the impacts identified included suicidal tendencies, insomnia symptoms such as difficulty falling asleep, waking at night, early morning awakening, and difficulty going back to sleep, as well as the effect on patients and their families' health status. Two major factors affect the level of psychological dis-

tress, and parents' psychological distress was influenced by parent and child factors. Parental factors included age, employment status, education level, record of depression, number of children, parental perception of the child's recovery, and the presence or absence of chronic diseases suffered by parents. At the same time, the child factors

included age and time since diagnosis.

Discussion

The Prevalence and Symptom of Psychological Distress

The results of the prevalence analysis based on the level criteria showed that the prevalence of distress in parents with children with cancer was mostly in the moderately high category. Rahmani,⁶ and Aziza,²⁷ give a high level of anxiety and low depression. Despite a tendency for higher anxiety levels in mothers, gender differences in parents had no significant effect on the level of parental distress.^{6,21} Parents of children with cancer who have siblings have higher rates of depression and anxiety than the general Australian population. They have higher

rates of depression than parents of children with cancer who do not have siblings. This supports the family systems theory, which states that families with more difficulties experience cumulative stress, which leads to increased anxiety and despair.²¹ Positive coping mecha-

Table 2. Percentage of Psychological Distress due to Having Children with Cancer

Prevalence Category	Frequency	Percentage
Very low	2	11.7%
Low	5	29.4%
Moderate	6	35.2%
High	3	17.6%
Very high	1	5.8%

Table 3a. Distress Prevalence, Criteria, Symptoms, Impact, and Factors Affecting Distress

Author	Distress Prevalence	Prevalence Category	Symptom of Distress	Distress Impact	Factor Affecting Distress
Rahmani, <i>et al.</i> , ⁶	Anxiety and depression were reported by 41.2% and 32.4% of parents with child cancer children, respectively.	Anxiety: moderately high Depression: low	N/A	N/A	Working fathers' depression levels varied significantly depending on their occupation.
Collins, <i>et al.</i> , ²⁰	Parents suffered from depression in 26.7% and anxiety in 35.8% of cases.	Anxiety: low Depression: low	N/A	N/A	High anxiety is influenced by educational attainment and a history of depression.
Vernon, <i>et al.</i> , ²¹	In 26.7% of cases, parents were depressed, and 35.8% were anxious.	Anxiety: very low Depression: low	N/A	N/A	The number of children and the length of time since diagnosis are risk factors for depression.
Srivastava, <i>et al.</i> , ¹⁹	85.14% of parents experienced depression, and	Anxiety: moderately high Depression: very high 56.4% experienced anxiety.	32.7% of parents experience indigestion and cardiovascular symptoms such as palpitations, migraines, and respiratory symptoms.	61.4% of parents had suicidal thoughts, and 86.1% had insomnia, which included difficulty falling asleep, awakening at night, waking up early, and falling back asleep.	Education level has a significant relationship with anxiety level.
Schepers, <i>et al.</i> , ¹⁵	Compared to parents of healthy children, parents of cancer children are more distressed. Fathers are in anguish at 59.2%, while mothers are in distress at 63%.	Distress in father: moderately high Distress in mother: high	N/A	N/A	N/A
Al Qadire, <i>et al.</i> , ²²	79.7% of parents suffered moderate to severe depression, while 26.6% suffered from anxiety.	Anxiety: low Depression: high	N/A	N/A	Parents of younger children had higher anxiety levels. Furthermore, parents with work difficulties and at least one chronic ailment scored higher than the depression score.
Wikman, <i>et al.</i> , ²³	Anxiety and despair affect up to 20% of parents of cancer patients children.	Anxiety: very low	N/A	N/A	N/A

Table 3b. Distress Prevalence, Criteria, Symptoms, Impact, and Factors Affecting Distress

Author	Distress Prevalence	Prevalence Category	Symptom of Distress	Distress Impact	Factor Affecting Distress
Lakkis, et al., ²⁴	Psychological distress affects up to 56% parents.	Psychological distress: moderately high	N/A	N/A	N/A
McCarthy, et al., ¹⁰	Anxiety and depression affect up to 28% of parents.	Anxiety: low Depression: low	N/A	N/A	N/A
Rosenberg, et al., ²⁵	More than 50% of parents experience high psychological distress.	Psychological distress: Moderately high	N/A	Parents' distress impacts the health of their children and their families.	Distress is linked to the parents' age and their sense of their ability to recover. According to studies, young parents experience a lot of stress.
Isabel Tan, et al., ²⁶	67.9% of parents who have children with cancer reported being distressed.	Distress: high	N/A	N/A	N/A
Aziza, et al., ²⁷	Anxiety affects 49% of parents, while depression affects 25%.	Anxiety: moderately high Depression: low	N/A	N/A	N/A

nisms may help prevent depression, according to studies describing low rates of depression. Relationships with friends, family, and religion have all been cited as helpful coping mechanisms.²¹

Chemotherapy undertaken by children also has a high level of impact, resulting in high levels of depression and anxiety among parents, with 85.14% and 56.4%, respectively. Loss of appetite and mood swings in children is the most distressing side effects of chemotherapy for parents, and parents' stress levels are increased because of these adverse effects.¹⁹ Although this contradicts the study by Sloper,⁷ the level of distress of parents whose children have completed treatment is not significantly reduced compared to those whose children are still receiving treatment. By six months of following diagnosis, fathers and mothers' psychological distress was quite significant. This could be a time when clinical indications of illness are more likely to appear. In the first year after the child's diagnosis, parents frequently experience extreme distress, according to Norberg and Boman.²⁹ Parenting children with progressing illness has been shown to have a significant impact on mental health, with distress rates ranging from very low to very high. This highlights the necessity of continuing to pay attention to the psychosocial needs of parents of children with cancer.^{6,21}

Gastrointestinal problems such as dyspepsia and indigestion, palpitation, headaches, and respiratory problems are all symptoms of psychological distress. Gastrointestinal problems are thought to result from brain-gut axis interactions involving many factors, including psychological disorders.^{30,31} In a group of 32 functional dyspeptic patients, Sari and Murni,³² found that digestive

problems are a sign of distress, with 37.5% of the patients reporting anxiety and 12.5% reporting depression. According to Alijaniha, et al.,³³ 80% of people who suffer from anxiety feel symptoms of palpitations; while, depressed clients were 23.6%. Another symptom that is closely related to anxiety and depression is respiratory issues. The nature and underlying mechanisms of the relationship between mental health and respiratory symptoms are still unknown.³⁴

Impact of Distress on Parents of Children with Cancer

Suicidal thought was described by 61.4% of parents, while 86.1% of parents reported insomnia.¹³ Suicidal inclinations is a word to describe someone who may be suicidal, has suicidal ideation, or has attempted suicide. Suicidal tendencies have a positive correlation with depression. Depression can affect individuals' performance in their daily lives and increase the emergence of suicidal thoughts.³⁵ Insomnia is sometimes used as a term to describe the presence of evidence of a sleep disorder such as long sleep latency, frequent awakenings during the night, prolonged periods of wakefulness during periods of sleep, or even frequent temporary awakenings are considered evidence of insomnia.³⁶ Parenting and psychological distress are the strongest predictors of sleep disorders in parents.³⁷ Adults with high levels of psychological distress are more likely to have poor health, lose productivity at work, and die as a result. Psychological distress can affect a person's capacity for work, family life, and welfare activities. It is the most prevalent symptom of the emotional difficulties that characterize human psychological responses to environmental changes.³⁸

Factors Affecting the Distress of Parents of Cancer Patients

Many factors influence psychological distress, including parents' and child factors. Parents' factors that contribute to distress are age, education level, occupation, depressive records, recovery perception, and chronic illness suffered by parents. While, age, number of children, and time since diagnosis are child factors that are connected to parental distress. Parental occupation is associated with a rise in depression scores because work is connected to the availability of financial support. Anxiety and depression symptoms are made worse by a lack of financial support.²² The reason is that families with children with cancer must pay a lot of additional costs.^{39,40}

Parents with a record of depression had higher anxiety levels, according to Collins, *et al.*, study.²⁰ Parents attaining a secondary school education or lower worried more than those with tertiary education or higher, by 29.2% and 10.9%, respectively. This may be due to the difficulty of understanding the disease by less formally-educated parents.¹⁹ Furthermore, according to Collins, *et al.*,²⁰ anxiety levels were related to parents reporting developmental delays in their children. Parents' perceptions of their child's delay and the small possibility of their child recovering have a significant impact on this, according to Rosenberg, *et al.*,¹³ Parents believing that their child is benefiting from cancer-directed therapy today are less upset. In contrast, those who believe their child is suffering are more upset. Additionally, parents thinking that their child is depressed or anxious have higher distress scores and are more likely to suffer from a severe psychological distress.¹³ Furthermore, Rosenberg, *et al.*,¹³ discovered those younger parents are more distressed than older parents. This could suggest a lack of maturity, and financial and social resources cause distress.

Strength and Limitations

The limitations of this review study are that the primary study was only quantitative non-experimental, and limited English articles. In the analysis process, the prevalence of anxiety and depression in the father, mother, or both parents has not been separated, because not all primary studies provide complete data on parental psychological distress (father, mother, father and mother). The country of origin of the preliminary study is still limited. It cannot represent developing or developed countries because each region has not been represented, hence the analysis cannot be based on country. However, the strength of this study is that it focused on two main symptoms of psychological distress, including anxiety and depression. Furthermore, this study suggests the need for further analysis to determine the average prevalence

of anxiety and depression through meta-analytical studies, respectively.

The relatively-high rate of distress among parents of cancer patients indicates that parents may be more susceptible to psychological problems, highlighting the significance of recognizing and treating anxiety and depression for parents.^{21,22} As a result, health care providers must pay close attention to the basic needs of parents of children with cancer, as well as coordinate and collaborate to provide comprehensive and holistic care. To provide high-quality care and improve treatment results for children with cancer and their families, it is essential to support parents as they cope with the heavy burden of caring for a child with cancer. Parents should receive psychosocial support during the initial stages of treatment to prevent psychological distress, and their mental health needs must be continuously assessed. To provide emotional and psychosocial support for children and their families while not just focusing on physical requirements, doctors, nurses, psychologists, public health professionals, and social workers must work collaboratively across disciplines. Additionally, parents must also be supported by health professionals who listen to their worries, touch and physically be present with them, and share their perspectives on their issues.^{26,27}

Conclusion

Parents who have children with cancer are at risk of psychological distress. Psychological distress negatively impacted the patients and the health of their families. Parents are at risk of having suicidal tendencies, experiencing insomnia symptoms such as difficulty falling asleep, waking at night, waking up early in the morning, and difficulty going back to sleep, affecting the health of patients and their families. Several factors influence psychological distress, including parents and children-related factors. Health practitioners must prioritize early detection and provide efficient intervention to support parents experiencing psychological distress. Increasing information, creating peer-support groups, and promoting mental health, especially among at-risk groups like families of cancer patients, are ways to increase promotive and preventive efforts at the community level, which are more crucial.

Abbreviations

NCCN: The National Comprehensive Cancer Network; JBI: Joanna Bridge Institute; BDI: Beck Depression Inventory; BAI: Beck Anxiety Inventory; DT-P: The Distress Thermometer for Parents; GHQ-12: The General Health Questionnaire; HADS: Hospital Anxiety and Depression Scale; K10: The Kessler Psychological Distress Scale (K10); NCCN: National Comprehensive Cancer Network. PTSS: Post-traumatic Stress Disorder; PTSD: Post-traumatic Stress Disorder; USA: the United States of America.

Ethics Approval and Consent to Participate

This review article involved no subjects; hence, no ethical approval was required or attached.

Competing Interest

The authors declare that there are 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

Data included in this article are openly available and may be accessed by accessing the links in the reference section.

Authors' Contribution

IN contributed to the collection of studies, assessing the qualities of included studies in this article using the JBI Critical Appraisal tools and drafted the article. RKD contributed to the studies collection, selected the articles, and drafted and revised the article. NOH assessed the qualities of included studies using JBI tools for cross-sectional studies and critically reviewed the draft of this article. SP critically reviewed and revised the draft of this article.

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Evaluation of Vitamin D and Anti-Müllerian Hormone Levels in Iraqi Infertile Women

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Abstract

Although the mechanism underlying the relationship between vitamin D insufficiency and reproduction is unknown, research suggests that it may have a direct deleterious impact on ovarian function. This is primarily because vitamin D insufficiency can affect gonadal function. The anti-müllerian hormone (AMH) is one of the most important biomarkers produced by granulosa cells and plays a key role in folliculogenesis. This study wanted to look at and compare vitamin D and AMH levels in infertile and fertile women, as well as the relationship between them in both groups. A hundred infertile and fertile women participated in the study. Anti-müllerian, prolactin, follicle-stimulating, and luteinizing hormones, as well as 25 hydroxyvitamin D, were estimated. Vitamin D deficiency was found in 72% of infertile women (n = 36), compared to 48% (n = 24) of the fertile group. There was no significant link between 25-hydroxyvitamin D and AMH in both groups. Infertile women exhibited a significantly lower serum AMH and higher body mass index. This study's findings suggested that the correlation between vitamin D and ovarian reserve markers was unlikely to present. However, the infertile group has a more significant vitamin D deficiency and insufficiency rate.

Keywords: anti-müllerian hormone, reproduction, vitamin D

Introduction

Infertility is a complex illness with substantial medical and emotional consequences. It is a common condition characterized by the inability to get pregnant after a year or more of unprotected sex.¹ Vitamin D insufficiency is a serious health issue affecting people of all ages worldwide because of its critical role in bone health.² Vitamin D levels have been linked to various illnesses in numerous studies, and it has an enormous consequence on gene expression in reproductive organs, implying that it has a role in fertility. The mechanism underlying this relationship is unknown. However, the discovery of the Vitamin D receptors and the enzyme 1-hydroxylase in organs such as the uterus, ovary, and placenta may explain how vitamin D shortage affects gonadal function. As a result, vitamin D is becoming a new factor in reproductive health.³

The most frequent approach for determining vitamin D levels is to check the blood concentration of 25-hydroxyvitamin D. It is the most accurate measure of vitamin D levels, which has a half-life of three weeks and hence is a correct indicator of vitamin D status.⁴ Accord-

ing to several studies summarized in Grzechocinska, *et al.*,⁵ vitamin D interacts with the anti-müllerian hormone (AMH) gene, directly altering its synthesis, and hence ovarian activity is sustained longer in women with higher vitamin D levels. According to some study, AMH production may be positively regulated by vitamin D,⁶ while others found no link.⁷

The AMH is a granulosa cell-produced dimeric glycoprotein thought to be one of the most important ovarian reserve markers.⁸ Its main role in the ovary is to prevent early stages of ovarian follicle growth, preserve ovarian reserve, and regulate the influence of follicle-stimulating hormone (FSH) on follicles.⁹ Thus, this study aimed to look at and compare vitamin D and AMH levels in infertile and fertile women and the relationship between serum AMH and vitamin D levels in both groups

Method

This study was conducted in Mosul City, Iraq, at various centers. The Medical Research Ethics Committee of the College of Medicine at the University of Mosul, Iraq, approved this study. Before collecting data, all partici-

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pants were informed about the study's goals and received their agreement.

This was a case-control study with 100 women ranging from age 18 to 40 years old. They were split into two categories: control, which consisted of 50 seemingly healthy fertile women, and case, which consisted of 50 infertile women with unexplained infertility. Records of smoking, usage of steroids, hormonal drugs, or oral contraceptive pills, vitamin D insufficiency, endometriosis, autoimmune disease, polycystic ovarian syndrome, thyroid disorders, tubal cause, or male cause were all ruled out.

After an overnight fast, a sample of five mL of venous blood was drawn from each woman on the second day of her menstrual cycle to assess the biochemical markers 25-hydroxyvitamin D, AMH, FSH, luteinizing hormones (LH), and prolactin hormone. The mini VIDAS assay, a bioMérieux automated quantitative enzyme-linked fluorescent assay (ELFA) technology, was used to measure all parameters.^{10,11} The body mass index (BMI) = weight (kg)/height² (m²), and according to the World Health Organization (WHO), a BMI of less than 18.5 kg/m² is considered underweight, 18.5-24.9 kg/m² is considered normal weight, (25-29.9 kg/m²) is overweight, and a BMI of 30 kg/m² or above is considered obesity.¹²

The Institute of Medicine and the Endocrine Society Clinical Practice Guidelines stated that 25-hydroxyvitamin D values below 20 ng/mL indicate a deficiency, between 20 and 30 ng/mL suggest insufficiency, and over 30 ng/mL indicate normal.⁴ The data in this study were analyzed using the SPSS Program, and the mean and standard deviation were used to express the findings. The differences between the groups were investigated using the Student's t-test, and Pearson's correlation test was used to identify the link between vitamin D and AMH.

Results

A case-control study has been handled on 100 women, 50 fertile and 50 infertile, both groups having ages ranging from 18 to 40 years. The controls had a BMI between 19.4-26.6 kg/m², while the patients had a BMI between 18.9-35 kg/m². Table 1 displays descriptive statistics for each of the groups studied using the Student's t-test. In some cases, the BMI was considerably greater (p-value = 0.019). There was no discernible age difference between the two groups.

Table 2 shows that the case group has an elevated %age of vitamin D deficiency than the control. Table 3 demonstrates that 62% of the case group were overweight and obese (40% overweight and 22% obese), while only 26% of the controls were overweight. Table 4 demonstrates that the amount of serum AMH in patients is significantly lower than in controls (p-value = 0.0001). Vitamin D had no significant link with AMH in both groups, according to Table 5 using Pearson's correlation test.

Discussion

The importance of vitamin D in fertility becomes more widely recognized. Several studies have pointed to a link between efficient infertility therapies and adequate vitamin D levels.¹³ Ovarian function and AMH production may be affected by vitamin D, according to study.¹⁴ In young women, serum levels of AMH are thought to rise quickly after a high-dose vitamin D supplement.¹⁵

The BMI in the case group of this study (mean±SD = 25.38±5.09) was significantly higher than that of the controls (mean±SD = 23.6±2.29) with a p-value = 0.019, and 40 % of infertile women were overweight, with 22% obese, compared to 26% of the fertile group were overweight. This followed Dağ and Dilbaz's study, which

Table 1. Characteristics of Respondents Based on Age and Body Mass Index

Variable	Case (n = 50)			Control (n = 50)			p-value
	Category	Mean	SD	Category	Mean	SD	
Age	18-40	31.20	5.72	18-40	32.58	6.35	0.259
Body mass index (kg/m ²)	18.9-35	25.38	5.09	19.4-26.6	23.6	2.29	0.019

Note: SD = Standard Deviation

Table 2. The Percentage of Vitamin D Levels in Both Groups

Vitamin D	Case (n = 50)		Control (n = 50)	
	n	%	n	%
Deficiency (<20 ng/mL)	36	72%	24	48%
Insufficiency (20-30 ng/mL)	10	20%	9	18%
Normal (>30 ng/mL)	4	8%	17	34%

Table 3. The Percentage of Body Mass Index in Both Groups

Body Mass Index	Case (n = 50)		Control (n = 50)	
	n	%	n	%
18.5-24.9 kg/m ²	19	38%	37	74%
25-29.9 kg/m ²	20	40%	13	26%
≥ 30 kg/m ²	11	22%	0	0

Table 4. Characteristics of Respondents Based on Age and Body Mass Index

Variable	Case (n = 50)		Control (n = 50)		p-value
	Mean	SD	Mean	SD	
Vitamin D (ng/mL)	17.576	0.187	19.584	7.455	0.187
Anti-müllerian hormone (ng/mL)	1.159	0.767	1.754	0.554	≤0.0001
Prolactin (ng/mL)	19.816	9.135	18.438	7.476	0.437
Follicle-stimulating hormone (m IU/mL)	6.813	3.946	5.75	3.155	0.122
Luteinizing hormones (m IU/mL)	4.208	2.471	3.880	4.208	0.416

Table 5. Anti-Müllerian Hormone and Vitamin D Relationship

	Case (n = 50)		Control (n = 50)	
	r	p-value	r	p-value
Anti-müllerian hormone	0.221	0.12	0.115	0.425

found that being overweight and obese can impair fertility.¹⁶ This could be owing to a negative relationship between BMI and the amount of estradiol generated, resulting in a reduction in estradiol concentration as BMI rises.¹⁷

In this study, 72% of women in the case group were vitamin D deficient, 20% had insufficient vitamin D, and 8% were of normal vitamin D levels, which were similar to the findings of Lata, *et al.*, finding that 64.28 % of infertile women had vitamin D insufficiency.¹⁸ Dressler, *et al.*, discovered that 98.2 % and 81.3 % of infertile women in two different clinics had vitamin D insufficiency or deficiency.¹⁹

In this study's investigation, it was found that vitamin D levels in the case and control groups were not significantly different. Even though the case group's levels were lower, implying that vitamin D may play a function in fertility. According to the Rudick, *et al.*, study, Caucasian women with vitamin D insufficiency have a lower pregnancy rate (37%) than women with adequate vitamin D (78%).²⁰

The case group had a considerably lower level of AMH than the controls (p-value = 0.0001). This was in line with the findings of Lata, *et al.*, 's study, which discovered lower AMH in cases (p-value = 0.003),¹⁸ that may be a factor in infertility in this group because AMH is a reflection of ovarian reserve and responsiveness, which influence reproduction in women, excluding other sources of infertility. The FSH, LH, and prolactin hormone levels did not differ significantly among the groups studied, and they were all within normal ranges.

Despite the fact that there is no concurrence on whether vitamin D affects AMH generation, it has been suggested that it directly affects ovarian function. Vitamin D has a positive correlation with AMH; accord-

ing to Merhi, *et al.*,²¹ The AMH stimulant was also found to be influenced by vitamin D in another investigation of human granulosa cells.²² These studies clashed with this study, which established no significant linkage between AMH and vitamin D. This was in line with the results of Lata, *et al.*, which established no connection between vitamin D levels and AMH.¹⁸ This study's findings were also consistent with Drakopoulos, *et al.*, 's study,²³ also a retrospective analysis of 340 polycystic ovary syndrome and ovulatory women revealed that AMH levels were not linked with serum vitamin D concentrations.²⁴

Conclusion

Finally, this study's results revealed no significant correlation between AMH and vitamin D levels in both fertile and infertile women. Even though the infertile group has an elevating percentage of vitamin D deficiency. Therefore, to do a routine of vitamin D testing and therapy for deficient individuals to avoid depletion of ovarian reserve appears to be ineffective. Nonetheless, vitamin D may have a role in human reproduction, and ongoing prospective and translational research initiatives are desperately needed to investigate the possible impact of vitamin D insufficiency on reproductive outcomes.

Abbreviations

AMH: Anti-müllerian Hormone; BMI: Body Mass Index; FSH: Follicle-Stimulating Hormone; LH: Luteinizing Hormones; ELFA: Enzyme-linked Fluorescent Assay; WHO: World Health Organization.

Ethics Approval and Consent to Participate

All process of this study was recognized by the ethical committee of University of Mosul (Reg. MREC/2018-8).

Competing Interest

The authors declare that there are 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

All raw or complementary data are available upon request.

Authors' Contribution

SKH, ZMAH, and BHA did the experimental process, analysis, and manuscript writing.

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Patients' Experiences in Using Diabetes Self-Management Application: A Scoping Review

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Abstract

Diabetes cases continue to increase and burden the nursing system worldwide. Diabetes Self-Management application software (DSM apps) can enable patients to manage their disease independently while simultaneously reducing the burden of the system. These apps are already available, yet global patients' interests in using them are still low. This study aimed to describe the global tendencies of diabetes apps usage as an effort to manage diabetes cases by exploring the perceptions of diabetes patients on the use of DSM apps. This study summarized journal searches from the Elsevier, Wiley, BMC, and JMIR database with the search terms "web-based and mobile technology," "digital health intervention," "diabetes management mobile application," "mobile health for diabetes self-management," "tablet-based self-management," and "diabetes self-management qualitative." A total of nine journals published between January 1, 2018, to December 31, 2020, that meet the inclusion and exclusion criteria were selected. The study concludes diabetic patients in Asia, Africa, Europe, Australia, and America stated that the DSM apps used was helpful in managing diabetes. Other demographic factors such as age, level of education, and economic status have influenced the perception and tendency to use the DSM apps.

Keywords: application, community nursing, diabetes, diabetes self-management, scoping review

Introduction

Diabetes is a chronic disease and, to date, is expressed as one of the global health emergencies of the 21st century.¹ Currently, the number of people with diabetes worldwide is recorded at 463 million people, and it is estimated that the number will reach 700 million by 2045.^{2,3} This condition is due to prediabetes now being diabetic, including those who have long suffered from diabetes and have not been able to control it well.^{4,5}

On the other hand, the nursing system cannot accommodate the growth of diabetes cases. The number of available nurses is not proportional to the number of diabetic patients. By 2030, the need for health workers to be fulfilled will only reach 65 million, while the predicted health workers should be reached 80 million.⁶ It is necessary to find a way out, so that diabetic patients are able to carry out diabetes care independently. In line with Korzs' statement in 2020, diabetic patients need to engage in continuous self-management in self-care activities.⁷

Nowadays, as technology advances, there is a technology for self-care activities, and Diabetes Self-

Management application software (DSM apps) can enable patients to manage their disease independently while reducing the burden on the nursing system.⁸ The presence of technology can reduce the burden of health costs by 700 billion USD in 2017.⁶ Cost of lost productivity due to disability, absenteeism, complications, and death due to diabetes.^{3,9} Since 2013, there have been various internet-based apps (mobile and web apps) designed to help diabetes patients in self-management of disease, control, treatment, and convenience that can be tailored to the needs of each patient.¹⁰ Also, patients can discuss disease progression with health professionals.¹¹

Several studies predicted that there would be an increase in the use of technology for diabetes care, such as diabetes treatment applications and digital diabetes self-management.^{9,12} The apps are equipped with features including eating, physical activity, the use of diabetes drugs, and monitoring blood glucose using an insulin calculator.¹² The apps can help reduce the risk of developing diabetes complications, such as chronic renal failure disease, diabetic retinopathy, neuropathy, and diabetic wounds, improving glycemic control and quality

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of care.^{3,9}

Since many constraints affect, it is necessary to conduct a scoping review that explores the tendencies of diabetic patients' perceptions on those apps. However, in-depth studies that led to the patients' perception of using the DSM apps to manage their Type 2 Diabetes Mellitus (T2DM) were very limited,¹³ especially focused on comparing patients' perceptions in different continents of the world. Henning in Kelly, *et al.*, study stated that even in the last 30 years of qualitative studies, only a quarter have looked at aspects of self-management, with a smaller number looking specifically at the experience of using digital apps to aid self-management.¹⁴ Therefore, the authors are considering using qualitative studies to fill the academic gap.

This study hypothesized that there were technical and non-technical barriers (globally only) affecting the use of the apps. Therefore, this study designed three study questions: (1) How do patients from different continental regions perceive the DSM apps? (2) What factors influence patients' tendency to use the DSM apps? (3) Which features do the patients want in the DSM apps? The aim of this study was to see the global tendencies of patients' experience in using the DSM apps. Therefore, the objective of this study would be reached by analyzing articles about those issues from five continents: Africa, Asia, America, Australia, and Europe. Moreover, this study hopes that it could empower families, healthcare supporters, community groups, practitioners, nurse educators, and regulators to support patients in using the DSM apps. Furthermore, this study also hopes it could give developers suggestions to create apps designed according to diabetic patients' needs.

Method

This study used a scoping review to find out more about the experiences of diabetic patients using DSM apps. There were five steps of the scoping review methodology according to Sargeant, *et al.*,¹⁵ including (1) Identifying the question, (2) Identifying the studies, (3) Selecting relevant study, (4) Charting the data, and (5) Summarizing/result.

For the first step, the authors have identified three questions in the scoping review, especially about patients' perceive the DSM apps, patients' tendency to use the DSM apps, and the DSM apps features that patients need. The articles were searched and selected to answer all three questions. As step of identifying the studies, in this study, searching for articles manually through Google Scholar has collected journal articles representing Asia, Africa, America, Australia, and the European continents. Five databases were used in the search: Science Direct, Wiley, BMC, Elsevier, and JMIR journals for studies published between January 1, 2018, and

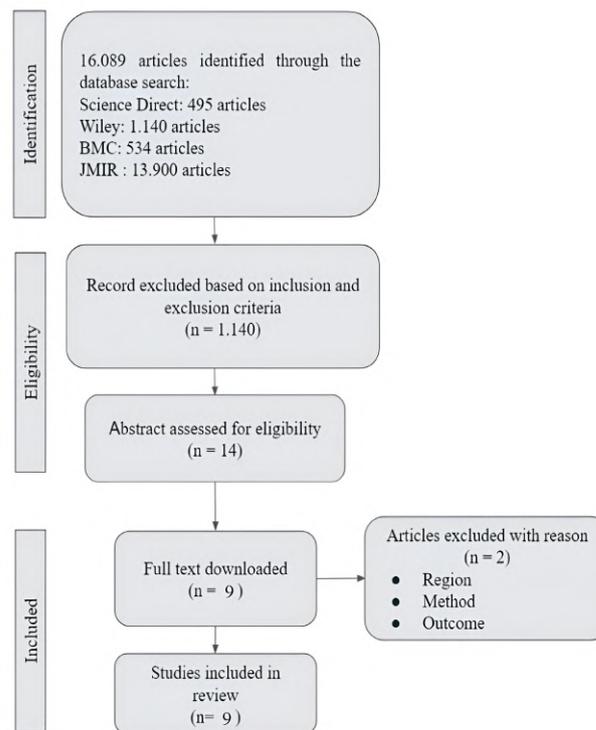


Figure 1. Flowchart of PRISMA-ScR

December 31, 2020. The terms "web-based and mobile technology," "digital health intervention," "diabetes management mobile application," "mobile health for diabetes self-management," "tablet-based self-management," and "diabetes self-management qualitative" were used during the search. The identification process is described through a flowchart of PRISMA-ScR on Figure 1.

The third step was selecting relevant study. The journal articles that met the inclusion criteria: (1) the journal articles analyze patients' experiences, opinions, and/or perceptions of the diabetes application, (2) use qualitative or mixed study methods, (3) study participants have been diagnosed with T1DM and T2DM, and (4) the internet-based diabetes self-management programs are accessed in tablets and/or mobile phones were chosen. Journal articles were taken using a mixed-method approach, and qualitative analysis was selected for this scoping review. Studies that did not meet the criteria were excluded.

The following step was charting the datas. The title and abstract of each article that met the inclusion criteria were then downloaded. The title, abstract, objectives, methods, and study results were read thoroughly. The authors have identified nine selected and relevant articles for scoping review. Then it was arranged as shown in

Table 1. The last step was summarizing the data finding.

Results

Of the nine selected journals, three analyzed themes describe the patient's experience, including the patient's

Table 1. Summary of Selected Studies (n = 9)

No.	Author	Year	Type of DM	Study Design	Sample	Purpose	Result
1	Pal, et al.	2018	T2DM	Focus group discussion	20 patients in the United Kingdom. The average age of patients: 57 years. Duration of diabetes: 0 - >10 years. Sex of patients: 8 female, 12 male.	To explore T2DM patients' perspectives on their needs for self-management.	Patients felt digital health intervention (DHI)/DSM apps could solve their existing problems.
2	Kelly, et al.	2018	T2DM	In-depth interview	15 patients in the United Kingdom. The average age of patients: 55.4 years. Duration of diabetes: 3 months to 24 years. Sex of patients: 10 female, 5 male.	To understand the impact of using web-based and mobile technologies to support the management of T2DM patients.	Web-based and mobile technologies have had a positive impact.
3	Rossmann, et al.	2019	T2DM T1DM Pre-diabetes	Semi-structured interview	21 patients from Singapore and 16 patients from Germany. The average age of patients: 48.35 years (Singapore); 44.5 years (Germany). Duration of diabetes: 1 to 38 years (Singapore); 0 to 49 years (Germany). Sex of patients: 10 female, 11 male (Singapore); 9 female, 7 male (Germany).	To examine T1DM or T2DM patients integrate mobile technology into their diabetes self-management.	T1DM or T2DM patients with long-term users tend to perceive DSM apps as applicable while the rest does not. Diabetic patients in Germany felt the need for DSM apps.
4	Petersen, et al.	2019	Uncategorized	Semi-structured interview	131 patients from South Africa. The average age of patients: not specified. Duration of diabetes: not specified. Sex of patients: not specified.	To explore patients' challenges and barriers to the adoption of ICT tools for diabetes self-management.	Patients' tendency to use ICT tools for diabetes is influenced by educational factors.
5	Zhang, et al.	2018	T1DM	Mixed-methods study	18 diabetes patients from China. The average age of patients: 6 to 33 years. Duration of diabetes: 0 to 12 years. Sex of patients: 11 female, 1 male (adult patients), 4 female, 3 male (young patients)	To investigate the perspectives and needs of T1DM patients and diabetes experts in China concerning diabetes apps.	T1DM patients use HCP-recommended apps.
6	Baptista, et al.	2020	T2DM	Focused interview	19 diabetes patients from Australia. The average age of patients: 14-60 years. Duration of diabetes: less than 5 years to 20 years. Sex of patients: 8 female, 11 male.	To investigate the Australian T2DM patients' daily experiences with the My Diabetes Coach application.	T2DM patients tend to use DSM apps when it is encouraged by HCPs.
7	Jeffrey, et al.	2019	T2DM	Semi-structured telephone interviews	16 applications and 14 non-application users (patients) in Australia. The age of patients: 30-79 years. Duration of diabetes: >6 months. App use: 17, Non-app use: 13. Sex of patients: 14 female, 16 male.	To understand the experiences, barriers, and facilitators for the use of applications in people with T2DM.	Both users and non-users show that the application is very useful for health and self-management.
8	Franklin, et al.	2019	T1DM	Semi-structured interview	8 patients in the United Kingdom. The age of patients: 27-57 years. Duration of diabetes: more than one year. Sex of patients: 4 female, 4 male.	To explore how mobile technology can support self-management in adults with T1DM.	T1DM patients who have used DSM apps have found it easy, decision-making saving time and enabling them to easily share their data with their consultant.
9	Alkawaldeh, et al.	2020	T2DM	Semi-structured interview	12 patients in the United States of America. The average age of patients: 68.65 years. Duration of diabetes: 5 to 20 years. Sex of patients: 7 female, 5 male.	To analyze elderly patients' perceptions in using the tablet-based application for 30 days as a routine component of diabetes self-management care.	The table-based application can help T2DM to become self-dependent and more accountable for their actions.

Notes: T2DM = Type 2 Diabetes Mellitus, T1DM = Type 1 Diabetes Mellitus, DHI: Digital Health Intervention, ICT = Information Communication and Technology, HCP = Health Care Professional.

perception of using the apps, the tendency of the patient to use the apps, and the apps features of interest.

a) Perception

From the statements (Table 2), the majority of patients feel that the DSM apps has a positive impact on disease management and health. Comply with using the apps, especially if HCPs or doctors re-

commend the apps.

b) Tendency

The factors influencing the patient's tendency to use the DSM apps can be reviewed in Table 3.

c) Feature

Advanced features as preference by the patients who has been already using the apps (Table 4).

Table 2. Patients' Perception toward Diabetes Self-Management Application

Article	Quotation	Analysis
1	"..If you just put that diabetes is such and such but can be controlled or managed or whatever word you want to use, through very simple means, I think that's a huge relief to people"	Patients felt that digital health intervention digital health intervention (DHI)/DSM apps could solve their existing problems.
2	"...The apps on my phone has a graph and how many steps is your target for walking in a day, how much water intake and what you are eating so you can record that. So it's easy to trace that way."	Web-based and mobile technologies have had a positive impact on the management of T2DM patients.
3	"Not all patients would be willing to pay." "If you put medical information in the cloud, then this becomes a... data-privacy issue".	The perception of patients in the use of DSM apps is not fully accepted, and they find some obstacles in their use.
4	"I don't always have the money to buy" "If technology were cheaper, I would use it every day."	The DSM apps are also perceived as expensive.
5	"I tried once to make an appointment with a doctor in the Weltang apps. But for his few minutes he needed to charge, so I exited. An unfamiliar doctor, you consult him, but you need to pay. Maybe you have a sense of..."	Apps were preferred because they were more effective and efficient. Meanwhile, consulting a doctor, requires a limited amount of time.
6	"If I did it my own way, I wouldn't have done it. I think an appointment (with HCPs) time kept me accountable."	Self-discipline and commitment to flexible digital consulting encourage by HCPs.
7	"I also don't see the need to have to use technology because I have my family around me for support."	The application was felt because there was support from the family.
8	"...my GP and all that, I'm extremely confident in them; they haven't mentioned it to me at this stage..."	Patients' good experiences were obtained from GPs' application recommendations.
9	"It helps me improve my management; I can see the connection to what I did that day."	Patients have positive acceptance of the DSM apps.

Notes: T2DM = Type 2 Diabetes Mellitus, DHI = Digital Health Intervention, DSM = Diabetes Self-Management, HCP = Health Care Professional, GP = General Practitioners.

Table 3. The Factors Influencing the Patient's Tendency to Use Diabetes Self-Management Application

Article	Quotation	Analysis
1	"...but sometimes it's a question of having too much information, and you can't take it all on board, and you can't make all the changes overnight."	There is a need to improve its conditions, so they are willing to use the apps.
2	"..I can keep track of my carbohydrates, and, more importantly, I can keep track of my sugar, so I know, if it tells me the sugar"	Continuous use of the apps to study daily patterns of blood glucose levels.
3	"How motivated is the patient...somebody who's...very energetic,...it's interesting, you know, something that's new to them, they'll do it." "You always have to put your glasses on your mobile phone."	There are limitations in using the apps.
4	"I also don't see the need to use technology because I have family around me for support."	DSM apps were less desirable. Patients depend on their families and HCPs.
5	"if I go to the hospital, I feel I have no time. Because if I learn on a mobile apps, videos can be saved; I can learn when I have time. I think the apps is better."	Apps are more efficient than direct consultations with the clinic.
6	"I'm interested in the technology of diabetes care. I'm interested in stuff all over the place, like reading about the impact of sugar on muscle."	Patients are interested in the application for consideration in making decisions in diabetes care.
7	"I also don't see the need to have to use technology because I have my family around me for support."	The family has supported the patient.
8	"If there were something that combined the 3, the blood glucose, the insulin amount, and the carbs altogether, that would be quite interesting... So I don't do it because there isn't really an easy way of doing it."	Patient decision-making is strengthened by the apps.
9	"It's a great application; It keeps me on track. It definitely does discipline me."	Improve their discipline skills in daily diabetes activities.

Note: HCP = Health Care Professional

Table 4. Patients' View According to the Features of Diabetes Self-Management Application

Article	Quotation	Analysis
1	"I suppose I'd want something that was a bit, kind of, an A to Z of one's life."	The apps has provided "one-stop shop" information for managing diabetes.
2	"I like the alarm [on the CBG monitor]. I often have it off at work, not because I am at work, just because my blood sugar is usually higher at work....",	Alarm feature to control blood sugar.
3	"Every device does its own things."	Required application with full features.
4	"They could use more pictures and less text on the applications."	The apps displays more visualizations than writing is in great demand.
5	"I consulted once. Because the doctor was busy, the response was not timely. Describing our condition by typing words may not be so good in meeting the needs of patients. After all, they are not our familiar doctors, and they don't know our condition. I hope to communicate directly with the doctor."	It would be even better if the communication with HCPs feature is linked to the electronic medical record for sustainability and direct consultation.
6	"It has to be reliable because that's my expectation now of apps and other things, and I can always find an alternative these days."	Information is presented by games or quizzes that are interesting, unique, and more interactive.
7	"What I wanted was like, a reading for the day, like a total reading and, and how much insulin I'd had each day and then sort of to see over a month what my average reading was..."	Visual representations of trends, particularly graphs for a month.
8	"I think the simplest way is really a line graph of the glucose levels..."	Blood glucose, where the display is a line graph visualization with the interpretation of high, low, or average trends.
9	"The opportunity to have reminders, I'm more consistent with taking medications."	Alarm feature to remind self-management schedule.

Note: HCP = Health Care Professional, CBG = Capillary Blood Glucose

The quality of the studies in this review was analyzed, and the risk of bias was assessed using the CASP Checklist.¹⁶ Ten questions were filled out to ensure qualitative compliance with the study and were categorized as low, moderate, or high risk of bias. All nine articles were selected at low risk of bias.

Discussion

Perception

Several interesting things have been found in this study. Sociocultural differences have led to different patient perceptions of diabetes management apps. There are differences in cultural principles in the group of developed countries that are members of the European, Australian, and American continents compared to countries in Asia and Africa.

The principle of individualism is very prominent in diabetic patients in Europe,^{12,14,17,18} Australia,^{20,21} and America,²² was the principle that emphasizes more on personal choice and freedom.²³ The selection of diabetes apps is determined by the needs of each diabetic patient. There is no consideration of groups such as families or HCPs.

On the other hand, Asian diabetes patients (in the article represented by Singapore and China),^{17,19} tend to hold the principle of collectivism, which is a social principle that prioritizes groups or communities over individuals.²⁴ One of the principles rooted in collectivism is the Confucian principle embraced by the majority of Chinese in Singapore and China. Confucianism believes

that good moral character would create a harmonious society.²³ The perception and tendency of diabetic patients in Singapore and China to use diabetes apps are strongly influenced by groups (both families and HCPs).^{12,19} The collectivist culture also prevails in Africa; self-managed apps are used when they receive support from families and recommendations from HCPs.²⁵

Tendency of several factors influence the patient's tendency to use the DSM apps:

a. Age

Young diabetic patients were more technologically literate. They had no barriers to using the DSM apps than older diabetic patients. Meanwhile, older diabetic patients found it difficult to use the apps.¹⁹ Their mobile devices were old and out of technology. The small mobile phone screen makes it difficult for elderly diabetic patients to type words describing their condition on the screen.¹⁷ Thus, the lack of exposure to technology leads to feelings of lack of confidence and fear of using new technology. In the end, the perception of older diabetics tends to be less supportive or less interested.²⁶

b. Motivation

The internal motivation to use the apps grows when they desire to learn about diabetes problems since they were diagnosed with diabetes by a doctor.^{20,21} However, external motivation comes from health care professionals who recommend using the app.²⁰ Features perceived as useful or facilitated use included the visual representation of trends, encouragement of self-motivation, convenience and user-friendly designs.

c. Data security factor

The DSM apps is made to track and store the patient's daily blood glucose data as well as other important information, like diet and health data, that can be used for self-management and monitoring. Patients' daily data, such as blood glucose (obtained via the blood glucose metres, insulin pumps, or other diabetes sensors through Bluetooth), together with other biometric, food, and exercise data, are gathered by the patient's phone via a specialised smart apps. Studies confirmed that running self-managed apps connected to healthcare providers requires high funding and infrastructure investment and takes data security and privacy into account.^{27,28}

d. Level of Education

Patients are interested in using the apps if they are trained, and facilities are available from the local clinic.¹⁹ From a literacy perspective, technology is more readily accepted by patients with secondary education.^{25,29,30} Personalized education is an under-represented feature in diabetes mobile apps. The patients liked different modes of educational materials. Patients are interested in using the appd if they are trained, and facilities are available from the local clinic.

Desired Features

Advanced features are selected by the tech-savvy patients using the apps. One-stop apps are preferred because it is more complete.^{12,14,20-22} Alarm and feature graph as an evaluation of the DSM apps feature with the meaning high, low, or normal trends.^{18,26}

Limitation

Diabetic patients in this study were mostly representatives of the continents of Europe, America, and Australia, and very few studies were conducted in the Asian and African continents. Internal and external barriers have not been studied in depth.

Conclusion

Patients' experiences in this study have positive and negative perceptions and tendencies using the DSM apps. This tendency is influenced by sociocultural factors, where the patient is located, age, education, and motivation. This study recommends future study to explore the perceptions of other stakeholders (health professionals and local/national authorities) on the implementation of diabetes self-management.

Abbreviations

DSM apps: Diabetes Self-Management application software; USD: United States Dollar; T2DM: Type 2 Diabetes Mellitus; PRISMA: Preferred Reporting Items for Scoping Reviews and Meta-Analyses; T1DM: Type 1 Diabetes Mellitus; DHI: Digital Health Intervention; ICT: Information Communication and Technology; CBG: Capillary

Blood Glucose; HCP: Health Care Professional; GP: General Practitioner.

Ethics Approval and Consent to Participate

Not applicable.

Competing Interest

The authors declare that there are 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 dataset used and analyzed are available in published documents and on the internet.

Authors' Contribution

The first author (SK) is the main contributor to the article, while the rest (SLP, SP, BFA) help with supervision and guidance.

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Maternal Coping Strategies for Premature Infant: A Systematic Review

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Abstract

A mother's stress due to the birth of her premature baby results in obstacles to the mother's role, hence it requires appropriate coping strategies. This review aimed to identify coping factors, explore coping strategies by mothers with premature babies, and identify interventions for enhancing maternal coping strategies. The article navigation utilized Boolean Operator of "or" and "and" with keywords of [preterm or premature or LBW, coping, and mother. Databases included ScienceDirect, EBSCOhost, PubMed, SAGE, ProQuest, and Scopus. The 529 articles obtained were screened by reading the focus of journals and addressing the topic and suitability of the journal content, selecting 10 articles. The first result reported factors influencing coping strategies: delivery method, income, available information, knowledge, support, and maternal self-efficacy. The second result presented maternal coping strategies for closely handling premature babies: belief in God, support-seeking, and the babies' condition progress. The third result showed two interventions: mother's empowerment program and group discussions with health workers. These two interventions to improve coping strategies play an important role in supporting mothers by facilitating their participation in caring for their babies.

Keywords: maternal coping, mother, premature

Introduction

Premature infants refer to live births before 37 weeks of gestation. Preterm birth is a worldwide epidemic, with a global incidence of 15 million per year.¹ Data reported that the estimated global preterm birth rate in 2014 was 10.6%, showing 14.84 million premature births in 2014.² Premature babies are typically born before the body system reaches the perfect condition, indicating certain physical characteristics and additional needs of different support and care for survival compared to the normally-born babies.³ Therefore, hospitalization of premature infants immediately after birth is unavoidable in most cases.³

A premature baby's birth leads the mother to get stressed due to uncertainty concerning the baby's survival, increased risk of medical complications, long-term effects of prematurity, hospitalization with various medical devices and procedures, and home care.^{4,5} In general, parents expect to discharge their babies from the hospital upon delivery; however, having a premature baby at home presents a huge challenge for the mother and family. The premature baby requires special care, creating tension and stress for the mother. Mothers perform high-

stress levels during their infant's hospitalization, even persisting upon the hospital discharge, which sometimes requires a longer duration of hospitalization (for six months or longer).⁶

Maternal anxiety needs to be under control because the mother acts as the primary care provider for the baby. The mother's emotional state potentially hinders the achievement of the mother's role and ability, which in turn affects the quality of care and the baby's growth and development process.^{7,8} Maternal stress can especially hinder the development and growth of the baby, causing feelings of rejection of the baby's presence and further leading to mental changes, emotional problems, and inappropriate activity levels.⁶ The mother experiencing stress also has low sensitivity to the baby, thereby affecting the interaction between mother and baby.⁹

Coping strategies provide solutions when dealing with stress. Lazarus and Folkman classify coping strategies into problem-based and emotion-based coping strategies.¹⁰ The application of efficient coping strategies will be able to regulate the mother's emotions, reduce the negative effects of stress due to premature birth, and improve the ability and interaction with the baby.¹¹ Thus far, the abil-

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ity of stress reduction leads to better maternal behavior, such as the ability to provide good care for the mother.¹² Coping exhibits an essential indicator of maternal response and behavior.¹³ Mothers with premature babies may have obstacles to carry out the mother's role, thus appropriate coping strategies are needed to deal with unexpected situations.¹⁴

Several articles report common coping strategies for mothers with preterm infants. This article does not classify coping as the problem-focused or emotion-focused, such as building a closer bond with the baby and seeking support.¹⁵⁻¹⁷ Only one study classified problem-focused and emotional-focused coping coping.¹⁴ To date, no articles summarize the research results of coping strategies for mothers with premature babies as an essential part of maternal health and care for premature babies. Thus, this study is a pioneer, contributing significantly to knowledge of coping strategies for mothers with premature babies. This review aimed to identify factors of coping, explore coping strategies implemented by mothers with premature babies, and identify interventions to enhance maternal coping strategies.

Method

This systematic review used six science databases: ScienceDirect, EBSCOhost, PubMed, SAGE, ProQuest, and Scopus, also was adjusted using the PRISMA guidelines. The search process applied three major keywords: coping, mother, and premature baby. For the population, mothers with premature babies were taken. The search strategy in ScienceDirect was coping AND mother AND premature, and in EBSCOhost was coping AND mother AND premature; (("coping"[All Fields]) AND ("mother"[All Fields]) AND ("premature"[All Fields])) in PubMed; coping AND mother AND premature in SAGE; coping AND mother AND premature in ProQuest; and coping AND mother AND premature in Scopus as the keywords. In the filter process, the study included full text, journal article type, dates of publication from last one-year, English language, open access, and original research.

The inclusion criteria were original study, published in 2015-2021, samples using mothers with premature babies, written in English and published in scientific journals, open-access journals, and exploring the coping strategies. Articles were filtered by reading and focusing on the core content of the articles, paying attention to the topic and appropriateness of the journal content including abstract, keywords, introduction, and conclusion. The exclusion criteria were coping strategies by mothers with non-premature babies and coping strategies by mothers with babies having congenital diseases.

Three reviewers selected the research based on the eligibility of articles to be reviewed, which included the ti-

tle, abstract, and the full text. Four reviewers selected the articles based on their area of expertise. Two reviewers independently assessed the content of the article as a whole, starting from the title to the content of the article according to the set inclusion criteria. After removing inappropriate articles, the complete articles obtained were those eligible for entry into further research. In case the assessment from two reviewers was different, then the other two reviewers would examine the articles.

Data taken were based on the conditions met stated in the Systematic Review Flowchart (Figure 1); the author, the study period, the year of publication, the country, the study design, the study method, the study area, and the mother coping with caring for premature babies. Data synthesis used narrative synthesis. To reduce a risk of bias, four reviewers worked independently. It would be done through discussion and reading all the selected articles if they had different opinions. The eligible articles were then analyzed qualitatively based on the three variables: coping factors, maternal coping strategies, and interventions to enhance maternal coping strategies. The review used the preferred reporting items for systematic review and meta-analyses (PRISMA) guideline; a checklist has been carried out using the 2020 PRISMA Checklist.

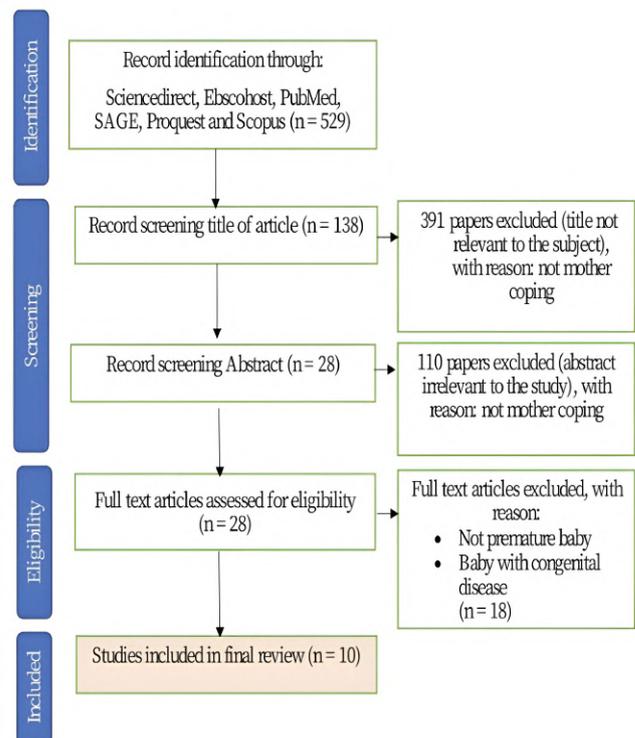


Figure 1. Systematic Review Flowchart

Results

Searching and Screening

From the ScienceDirect, EBSCOhost, PubMed, SAGE, ProQuest, and Scopus databases, all the 529 articles obtained were imported to Mendeley for further processing. Subsequently, a further checking was conducted based on the article’s title. The study found that 391 articles were similar articles. Then re-screening was taken and the study found that some articles were irrelevant as their titles were not about coping. After the first screening stage, of 138 articles’ abstracts read, 110 articles were found irrelevant because they did not discuss mothers dealing with premature babies. After the second screening stage, of 28 articles read for the whole text, 18 articles were found irrelevant because they did not discuss premature babies and discussed infants with congenital diseases, and finally the study selected 10 articles which were relevant and suitable for further review.

Characteristics of Research and Review

This review included 10 articles: three from Iran, two from India, and five from Colombia, Ghana, Indonesia, South Africa, and Spain respectively. The research designs reviewed were five qualitative and five quantitative studies (three cross-sectional studies and two intervention studies). The selected 10 articles reported the study results with quantitative and qualitative designs, consisting of three themes. The first theme was sourced from four articles involving factors related to coping;¹⁸⁻²¹ the second theme was sourced from four articles involving coping strategies and obstacles,¹⁴⁻¹⁷ and the last theme was sourced from two articles involving interventions to enhance coping.^{11,22} The complete review results are presented in Table 1.

Findings Regarding Factors Affecting Maternal Coping with Premature Baby

The four articles examined the influential factors to

Table 1. Review Results: Factors Affecting Maternal Coping with Premature Baby

Author	Year	Country	Sample	Study Design	Result
Delgado Galeano & Villamizar Carvajal	2016	Colombia	144 mothers with premature babies	Prospective, descriptive, correlational study.	The regression results indicated that income variables, information provided at hospital, and preparation for parenthood were related to maternal coping.
Tambunan, Pratomo, Hadi & Rustina	2020	Indonesia	60 mothers with premature babies	Cross-sectional	There was a significant relationship between maternal knowledge of the care for the LBW infants and coping strategies.
Paul, Pais, Kamath, Pai, Lewis	2018	India	61 mothers with premature babies	Cross-sectional descriptive survey.	Most mothers (78%) indicated an average coping category. The mean and standard deviation of self-efficacy was 58.8±8.7. There was a positive relationship (r = 0.318, p-value = 0 .015) between perceptions of self-efficacy and parental coping, which was statistically significant.
Hendricks, Carter, Rao	2020	India	6 mothers with premature babies	Qualitative descriptive design.	Parents were reported to experience fear, anxiety, uncertainty, lack of control, and low self-esteem. Mothers showed coping skills and emotional strength and were confident in caring for the babies.
Sih, Bimerew & Modeste	2019	South Africa	11 mothers with premature babies	Qualitative	Major themes emerging from the data analysis were praying as a coping strategy, the mother’s attachment to the baby, and accepting the situation.
Ochandorena-acha, et al.	2020	Spain	15 mothers and 14 fathers with premature babies	Qualitative phenomenology.	The results of the study contained the three themes: parents’ ability, difficulties during care for premature babies, and coping strategies.
Tabrizi, Alizadeh & Radfar	2017	Iran	8 mothers with preterm babies	Qualitative	Mothers’ experience depicted that they had obstacles while being a mother, thereby implementing several strategies to overcome the situation. The coping strategy applied was building communications.
Akum	2018	Ghana	21 mothers with premature babies	An explorative, descriptive study design using a qualitative approach.	Mothers experienced physical, economic, sociocultural, and spiritual challenges. The support received was mainly from husbands, in-laws, friends, extended family members, and religious groups. The coping strategy was understanding the baby’s needs and belief in God.
Karbandi, Momenizadeh, Heidarzadeh & Mazlom	2018	Iran	70 mothers with premature babies	Clinical trial	The results indicated a significant difference after the intervention was practiced. There was an increase in problem-focused coping strategies and a decrease in emotion-focused coping strategies.
Mirlashari, et al.	2020	Iran	80 mothers with premature babies	Non-randomized, prospective, interventional study.	In the intervention group, there was a significant increase in the value of problem-focused coping strategies and a decrease in emotion-focused coping after the intervention.

Note: LBW = low birth weight

maternal coping with premature babies. The first article reported that the method of giving birth, income, information, and preparation for parenthood were related to maternal coping.¹⁸ The cesarean section method affecting the maternal coping at home was feasible due to the separation from the baby, exacerbated by the mother's incapability to perform her role due to the influence of surgery recovery and the premature baby's condition. In addition, income affected maternal coping because having a premature baby required extra economic resources supporting the required care for premature babies. The last factor included the need of information at the admission time, during the baby's hospitalization, and after discharge.

The second article indicated a correlation between knowledge of infant care and coping strategies after controlling the mother's stress levels (p -value <0.001). The adjusted R-value of 0.453 denoted that the maternal knowledge of infant care and record had an influence by around 45% on maternal coping strategies. Based on the reported results, it was estimated that, for each one-point increase in the knowledge score, the coping strategy score simultaneously increased by 0.630 times after controlling the stress levels. Hence, it concludes that increasing knowledge and reducing stress could improve maternal coping strategies.¹⁹

The third article reported that family support and health workers largely facilitated most mothers' coping strategies. Mothers expressed the necessity for support from their families to help them perform their maternal role. Furthermore, mothers also expect to get professional health care support related to their skills, competencies, and communication skills.²¹

The fourth article reported that maternal self-efficacy in caring for premature babies was related to maternal coping with a p -value of 0.0013. It was also observed that most of the 47 (78%) mothers had an average level of coping, and 14 (22%) mothers had a good level of coping with premature birth. The average coping score was 51.7 ± 8.9 . The mean and standard deviation of the maternal self-efficacy in caring for her baby was 58.7 ± 8.7 .²⁰

Findings Regarding Coping Strategies for Mothers with Premature Baby

The first article discussing maternal coping strategies for premature birth resulted in three themes.¹⁵ The first theme referred to praying, consisting of gratitude and prayer sub-themes. The second theme was closeness or bonding to premature babies, consisting of sub-themes: bonding and interacting with the baby, as well as evidence of life, progress on babies, and feeling of no regrets. The last theme was acceptance of the situation with sub-themes: perseverance in the situation and the mo-

ther's awareness of her responsibility.

The second article reported that maternal coping strategies for premature babies are divided into problem-focused and emotional-focused coping strategies.¹⁶ Strategies applied in the problem-focused coping include closer bonding with the baby and involvement in baby care, support-seeking from family, health workers, and other patients, and the last was to navigate information from the internet and health workers. Emotional-focused coping strategies were regarded as dreams, hopes, and positive thinking, focusing on positive emotions and progressing premature babies' health and daily condition.

The third article, regarding the coping strategy of mothers with premature babies, was to build communications with categories of "interacting with baby" and "support-seeking".¹⁴ Interacting with baby consisted of physical and emotional interactions. At the beginning of physical interaction, mothers often experienced doubts and fears. However, when mothers had learned how to interact with and understand the baby's condition, they gradually became more stable, and with the support and guidance of health workers such as nurses, mothers were more confident to touch and hug their babies. Mothers interacted physically with their babies gradually before they were finally able to participate in baby care activities. The second category was support-seeking, referring to the support needed by mothers, including family, health workers, and mothers of other premature babies.

The fourth article reported the following results: the coping strategy by mothers in performing responsibilities to care for their premature babies was through understanding the baby's needs and having faith in God.¹⁷ Mothers generally observing the baby understood the baby's needs, such as hunger, wet diapers, or needs of attention. The second coping strategy referred to having faith in God was by accepting any God's blessing, thereby receiving strength to live it.

Findings Regarding Coping Interventions for Mothers with Premature Baby

Interventions to enhance maternal coping strategies for premature babies included mother's empowerment programs,¹¹ consisting of four stages of "behavioral training" with the following details: the first stage of 2-4 days after the infant was admitted to the hospital, the second stage of 2-4 days after the first stage, the third stage of 1-3 days before the baby was discharged and the fourth stage of a week after the hospital discharge. The empowerment program called "Creating Opportunities for Parent Empowerment (COPE)" was an educational-behavioral intervention designed based on self-regulation and control theory. This program increased problem-focused coping strategies and decreased emotion-focused coping strategies.

The second intervention involved group discussion with health workers,²² conducted from the third day since the baby was admitted to the Neonatal Intensive Care Unit (NICU). Four sessions of discussion were conducted fortnightly on Monday and Saturday every week, and all mother participated in all four group discussion sessions; each session lasted 60 minutes. The discussion topics were selected based on most common topics related to the needs of mothers and agreed upon by all discussion members. All mothers in the study received a free booklet about caring for premature babies. Each session was attended by a mother, a pediatrician, and a nurse. This intervention significantly increased problem-focused coping scores during and after two weeks of intervention. Mothers in the intervention group implemented a higher level of problem-focused coping strategies. In contrast, there was a significant decrease in emotion-focused coping scores during and after two weeks of intervention. Mothers from the intervention group implemented less emotion-focused coping strategies.²²

Discussion

The discussion is based on the research objectives; the first is the factors influencing the coping, maternal coping with premature babies, and interventions to improve maternal coping.

Factors Affecting Maternal Coping with Premature Babies

Caring for premature babies generates significant stress for mothers.²³ Premature babies need a special care which is different with the full-term babies, leading mothers to experience numerous daunting challenges, such as the baby's minimal bond with the mother, depression, anxiety, and fears about their health, future, and mortality.²⁴ Hence, the mother's assessment of the situation is pivotal because the mother must accept and understand that a premature baby is different from a full-term baby.²⁵ Mothers must adapt to such condition through effective coping strategies to deal with the stressful situations.²⁶ Coping refers to a process of cognitive and behavioral changes to cope with internal and external demands generating stress.²⁷ Proper coping strategies could assist mothers in reducing stress and improving maternal behavior, such as the ability of mothers to take good care of themselves.¹²

Attempts to generate effective and efficient coping strategies involve mothers' and health workers' attention regarding the affected factors, such as the delivery method, income, available information, knowledge, support, and maternal self-efficacy.¹⁸⁻²¹ Providing information and elevating maternal knowledge played a fundamental role in term of maternal coping strategies. Consequently, providing appropriate information on baby

care from admission to the hospital is vital to developing maternal coping when discharged. The type of information and the way the information is provided should be reviewed and considered according to the mother's needs. The need of information typically originates from the need to control the situation and facilitate active information seeking.²⁸ The main factor which elevates maternal knowledge includes information on the condition and education for baby care.

Coping Strategies for Mother with Premature Baby

Based on the review results, the coping strategies of mothers with premature babies referred to this entire article explaining that maternal coping relates solely to a closer bond with premature babies. This closeness is commonly formed by understanding the baby's needs, interacting with the baby, and involving in the care of premature babies.^{14-16,25} The following two articles explained the belief in God as part of maternal coping strategies.^{15,25} Such strategy included the grateful feeling for the premature baby's condition through praying for the health and safety of the premature baby and getting closer to God. In addition to those mentioned above concerning two coping strategies, it is explained that support-seeking was also considered a maternal coping strategy.^{14,16} The support needed by mothers was in the form of support from partners, health workers, extended family, and fellow mothers with premature babies. The last coping strategy focused on the progress of the baby's condition practiced by the mother to deal with the experienced stressful conditions.^{15,16}

Coping Interventions for Mother with Premature Baby

From the review results, the two interventions to improve the coping were navigated, including mother's empowerment program and group discussions with health workers.^{11,22} This review result is in accordance with a study by Karbandi suggesting the effectiveness of empowerment programs in improving coping strategies; thus, it is necessary to implement the program as service standard for enhancing maternal coping strategies.¹¹ While, study by Mirlasari reported limited participation of fathers and other family members in caring for premature babies, leaving the mothers as the primary caregiver for their babies. Numerous efforts had been devoted to improving the quality of care in the neonatal intensive care unit (NICU), yet in most hospitals, the family was reported to be less involved in the decision-making process and baby care. These conditions thus encouraged health services and health workers to facilitate mothers to form discussion groups to improve health care for mothers and babies and promote collaboration between mothers and health care teams. The health care team could support mothers by facilitating their participation

in the caring to express affection for their babies.²²

Limitations, Weaknesses, Strengths, and Recommendation of This Review

This systematic review has several limitations. First, the authors only found 10 articles which met the inclusion criteria. Second, not all articles discussed the three variables for this review. Lastly, the study designs of selected articles in this study are qualitative and quantitative, which unfortunately affects the results of the review. Researchers were trying to expand the applied keywords and published articles to solve these limitations. Also, the authors focused the discussion on the articles obtained. This review is the first to critically review and discuss coping strategies among mothers with premature babies. The results of this review encourage further studies emphasizing the exploration of maternal coping strategies and the interventions to improve maternal coping strategies.

Conclusion

The results of this review state that the influential factors to maternal coping for premature babies are delivery method, income, available information, knowledge, support, and maternal self-efficacy. Coping strategies implemented by mothers with premature babies are solely believing in God, grateful feeling, a closer bond with premature babies, support-seeking, and focusing on the baby's condition progress. Nurses must enhance maternal coping strategies with empowerment programs and group discussions to improve coping strategies.

Abbreviations

PRISMA: Preferred Reporting Items for Systematic Review and Meta-analyses; LBW: Low-Birth-Weight; COPE: Creating Opportunities for Parent Empowerment; NICU: Neonatal Intensive Care Unit.

Ethics Approval and Consent to Participate

Not applicable.

Competing Interest

The authors declare that there are 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

As a source of data and information, ScienceDirect, EBSCOhost, PubMed, SAGE, ProQuest, and Scopus databases are utilized.

Authors' Contribution

REK and YSA contributed substantially to the concept and work design. MT, QIL, LS and NA conducted data analysis, data interpretation, and drafting of the manuscript. REK and YSA revised it critically for the important intellectual content and final approval of the version to

be published.

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The Significance of Trimester-Specific Thyroid Hormones Reference Intervals in Iraqi Pregnant Women

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Abstract

In Iraq, there is no obvious considerable data regarding trimester-specific reference intervals of thyroid hormones despite documented multiple physiological hormonal changes during pregnancy. Thus, this study aimed to determine trimester-specific reference intervals for serum TSH, FT3, and FT4 and assess the incidence of thyroid function test misinterpretation and misdiagnosis among pregnant women using non-pregnant reference intervals. A thyroid function test was performed for 774 enrolled pregnant women. Reference intervals of TSH, FT3, and FT4 were ascertained in each pregnancy trimester. It was then compared to the adult non-pregnant values, and the incidence of misinterpretation was later calculated. TSH and FT4 reference interval values were lower than non-pregnant reference interval values. The application of non-pregnant women references values in pregnant women caused a serious misinterpretation and misdiagnosis in 66 (8.5%) pregnant women regarding TSH, and 34 (4.4%) pregnant women regarding FT4, while no misdiagnosis was noticed regarding FT3. The trimester-specific reference interval values of TSH, FT3, and FT4 in Iraqi pregnant women showed an obvious variation from non-pregnant reference intervals and the urgent advice to use the trimester-specific reference intervals to avoid misclassification of thyroid dysfunction during pregnancy.

Keywords: gestation, iodine, pregnancy, reference interval, thyroid-stimulating hormone

Introduction

The optimal function of the maternal thyroid gland is critical for both the fetus and mother's health. Thyroid hormones are crucial for the development and growth of fetal skeletal and nervous systems, especially during the first trimester of pregnancy.¹ Diagnosis of maternal thyroid gland diseases during early pregnancy is important for timely medical intervention since these diseases are common, with a prevalence ranging from 2% to 5%.^{2,3}

Gestational maternal thyroid gland dysfunctions can be associated with many maternal and adverse fetal outcomes. For example, subclinical hypothyroidism is found in about 2.3% of pregnant women and is characterized by symptomless abnormally high thyroid-stimulating hormone (TSH) and normal free thyroxine (FT4). It can be associated with many obstetric complications like hypertension, repeated abortions, preterm delivery, placental abruption, intra-uterine growth retardation, increased cesarean section, and increased insulin resistance rate.^{4,5} In addition to various impairments of cognitive and neurological development and decreased intelligence quotient in the child.⁶⁻¹⁰ Regarding thyroid autoantibodies, such as thyroid peroxidase antibody (TPO-Ab) and thy-

roglobulin antibody (Tg-Ab), most available research indicates that the high serum level of these antibodies is associated with the increased rate of recurrent abortions and preterm birth.¹¹⁻¹³ At the same time, the prevalence of gestational subclinical hyperthyroidism is around 1.7% and usually not associated with any significant adverse pregnancy outcomes.¹⁴

Profound maternal thyroid physiological changes occur during pregnancy. The purpose is to fulfill both the maternal and fetal demanded amount of thyroid hormones, especially during the early stages of pregnancy. It is because the fetus depends on the maternal thyroid hormones for development and maturation (till approximately the 20th week of gestation) when the fetal thyroid tissue starts to secrete a sufficient amount of thyroid hormones.^{2,15} Most important physiological changes include increased serum level of thyroxine-binding globulin (TBG), which elevates the serum level of total thyroxine (TT4) and total triiodothyronine (TT3) in pregnant women compared to non-pregnant women. In addition, thyroid gland stimulation with increased serum level of human chorionic gonadotrophin (HCG) is caused by its structural similarity to TSH. It stimulates the thyroid

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gland (agonist effect) to secrete more thyroxine (T4) and triiodothyronine (T3) hormones, especially during the first trimester of pregnancy.¹⁶

All these changes during pregnancy can affect the maternal thyroid gland homeostasis and complicate the correct interpretation of thyroid function test results.¹⁷⁻¹⁹ These mentioned gestational facts and variations necessitate the determination of thyroid hormones reference interval values for each trimester of gestation. The purpose is to minimize the chance of misinterpreting thyroid function test results and to diagnose and control gestational thyroid gland dysfunctions with its dangerous maternal and adverse fetal outcomes.²⁰ Therefore, Endocrine Society (ES), European Thyroid Association (ETA), and American Thyroid Association (ATA) guidelines for diagnosis and management of thyroid gland diseases during pregnancy and postpartum 2017 established a presumed geographic and ethnic variation in serum level of TSH throughout the pregnancy. With a decline in its lower value of reference range, trimester-specific reference ranges for TSH should be determined for each different population. Also recommended that each region and center decide on its gestational age-specific reference ranges for thyroid hormones through blood specimens from pregnant women free of any thyroid diseases and negative for thyroid (TPO-Ab, Tg-Ab) autoantibodies.²¹⁻²³

The majority of centers and laboratories in different countries and regions still depend on the thyroid hormone reference ranges in non-pregnant women to evaluate and interpret the thyroid hormone test results during pregnancy. This is because only several studies have been established to define gestational trimester-specific reference intervals for thyroid hormones in different regions worldwide.²⁴⁻²⁶ In Iraq, no thyroid hormones trimester-specific reference range has been set for pregnant women because of the limitation of the available data. Therefore, this study aimed to determine thyroid hormones trimester-specific reference ranges by using routine laboratory analysis methods and applying these new reference intervals to get a precise and correct interpretation of thyroid function test results among Iraqi pregnant women.

Method

This study was performed from February 2019 to October 2021 at Al-Noor University College in Mosul City, Iraq. This study was in collaboration with local obstetrical and gynecological centers, where pregnant women were asked to participate through the kind efforts and help from the medical staff in the obstetrical and gynecological clinics during their recurrent visits to the clinics. Few pregnant women declined to participate in this study due to socioeconomic reasons. The study's protocol and design were approved by the internal scientific re-

view board and ethics committee at Al-Noor University College.

This was a cross-sectional study; apparently, healthy pregnant women with single intrauterine uncomplicated gestations were enrolled following prior written approval. A questionnaire was used to get the complete records of all participants in this study. The questionnaire included details of personal, geographic, clinical, chronic disease, medications, and family history, with special attention to the personal or family's record of thyroid gland dysfunctions or medications. Obstetrical and gynecological history was recorded to determine the parity, gravida, abortions, ectopic pregnancy, stillbirth, and preterm labor. Gestational age was determined by using both the date of the last menstrual period and the ultrasound examination. A detailed general and systemic physical examination are done.

Exclusion criteria included personal and/or family 's record of thyroid gland dysfunctions, thyroid treatments, systemic diseases like hypertension, diabetes mellitus, record of abortions, stillbirth, ectopic pregnancy, hyperemesis gravidarum, preterm delivery, evidence of fetal genetic abnormalities (e.g., trisomy), presence of visible or palpable goiter (diffuse or nodular), overt hypothyroidism or hyperthyroidism, and pregnant women positive for thyroid peroxidase-Ab (>35 IU/mL) and/or thyroglobulin-Ab (>40 IU/mL). For each blood specimen, five parameters were measured, including FT4, free triiodothyronine (FT3), TSH, and antithyroid antibodies, including TPO-Ab and Tg-Ab. All were measured using a COBAS e 601 analyzer (Roche diagnostics), a highly-specialized immunoassay analyzer using Electro-chemiluminescence (ECL) technique (Roche Diagnostics/Germany) by using its specified kits.

All data were analyzed using the Statistical Package for the Social Sciences Version 16.0 (SPSS Inc., Chicago, IL, USA). Mean, median, standard deviation, and 2.5th, 50th, and 97.5th percentiles were calculated for thyroid TSH, FT3, and FT4 during the three trimesters of pregnancy in rapprochement with the manufacturer's non-pregnant reference interval. TSH data were normalized using log transformation and summarized as a geometric mean.²⁷ To compare data between the trimesters, One-Way ANOVA was used. A two-tailed p-value<0.05 was considered statistically significant.

Results

The total participants in this study were 864 pregnant women. After excluding the TPO-Ab and/or Tg-Ab positive pregnant women and the cases of overt hypothyroidism, only 774 pregnant women were enrolled in this study. The primary characteristics of the study population in Table 1 show that 366 women are in the first trimester, 252 women are in the second trimester, and

Table 1. The Primary Characteristics of Study Population

	1 st Trimester	2 nd Trimester	3 rd Trimester	Total
Number (n)	366	252	156	774
Age (year)				
Mean±SD	23.4±2.44	24.6±3.64	26.1±3.89	24.7±3.32
Gestational age (weeks) mean±SD	8.2±1.8	18.6±3.1	32.2±2.4	-
Primigravida	213	136	73	422 (54.5%)
Multigravida	153	116	83	352 (45.5%)

Note: SD = Standard Deviation

Table 2. Thyroid Gland Diseases Incidence in Each Trimester

	1 st Trimester	2 nd Trimester	3 rd Trimester	Total
TPO-Ab	28 (3.2%)	15 (1.7%)	10 (1.2%)	53 (6.1%)
Tg-Ab	18 (2.1%)	10 (1.2%)	3 (0.3%)	31 (3.6%)
TPO-Ab and/or anti Tg-Ab	40 (4.6%)	22 (2.5%)	10 (1.2%)	72 (8.3%)
Overt hypothyroidism	12 (1.4%)	6 (0.7%)	0 (0.0%)	18 (2.1%)
Hyperthyroidism	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Notes: TPO-Ab = Thyroid Peroxidase Antibody, Tg-Ab = Thyroglobulin Antibody.

156 women are in the third trimester.

The mean age of participants in the first, second, and third trimesters was 23.4±2.44 years, 24.6±3.64 years, and 26.1±3.89 years, respectively. While the mean age of all participants was 24.7±3.32 years, the median age was 27.7 years (range = 15 – 40 years). Gestational age during the first, second, and third trimesters was 8.2±1.8 weeks, 18.6±3.1 weeks, and 32.2±2.4 weeks, respectively (Table 1).

Regarding the trimesters' distribution, the first trimester involved 366 pregnant women, with a mean age of 23.4 years and a median gestational age of 8.2 weeks. The second trimester involved 252 pregnant women with a mean age of 24.6 years and a median gestational age of 18.6 weeks. At the same time, the third trimester involved 156 pregnant women, with a mean age of 26.1 years and a median gestational age of 32.2 weeks. Primigravida women were 422 (54.5%), and multigravida women were 352 (45.5%).

Table 2 shows that the TPO-Ab and/or Tg-Ab were positive in 72 (8.3%) pregnant women; 53 (6.1%) were TPO-Ab positive, and 31 (3.6%) were Tg-Ab positive. Depending on the reference interval of the laboratory kit (non-pregnant women), overt hypothyroidism was diagnosed in 18 (2.1%) pregnant women, while no case of hyperthyroidism had been diagnosed. As a result, these 90 pregnant women were excluded, and the study population's total number became 774 pregnant women.

Figures 1, 2, and 3 show the trimester-specific reference range of thyroid hormones TSH, FT3, and FT4, determined by the 2.5th, 50th, and 97.5th percentile of these hormones in each pregnancy trimester. The TSH refer-

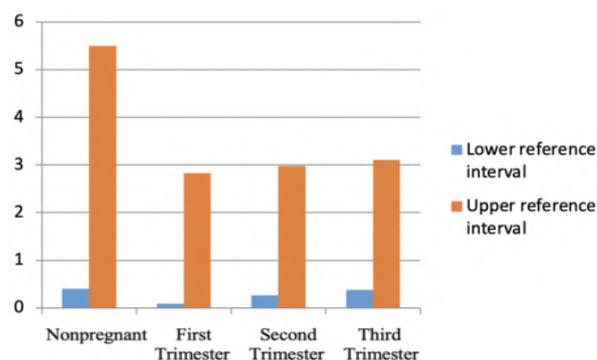


Figure 1. Tthyroid-Stimulating Hormone Reference Intervals

ence interval in the first trimester, second, and third trimester was 0.09 to 2.83 mIU/L, 0.26 to 2.98 mIU/L, and 0.38 to 3.11 mIU/L, respectively, with an obvious increase in both the upper and lower values toward the end of pregnancy. The FT4 reference interval in the first, second, and third trimester was 10.88 to 19.86 pmol/L, 9.82 to 17.44 pmol/L, and 8.92 to 15.22 pmol/L, respectively, with a slight decline in both the upper and lower values toward the end of pregnancy. The FT3 reference range in the first, second, and third was 3.64 to 6.49 pmol/L, 3.32 to 5.66 pmol/L, and 3.11 to 5.39 pmol/L, respectively, with obvious stability in both the upper and lower values toward the end of pregnancy. TSH and FT4 values statistically showed significant differences (p-value<0.05) among different trimesters of pregnancy. These differences were seen between the first, second, and third trimesters, with increasing values toward the third

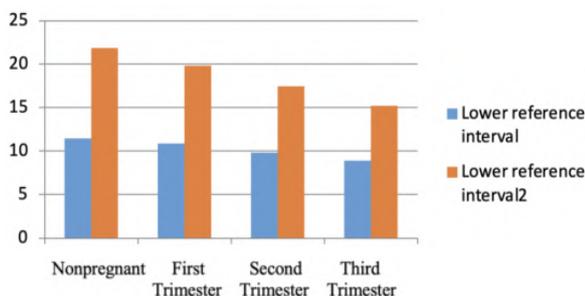


Figure 2. Free Thyroxine (FT4) Reference Intervals

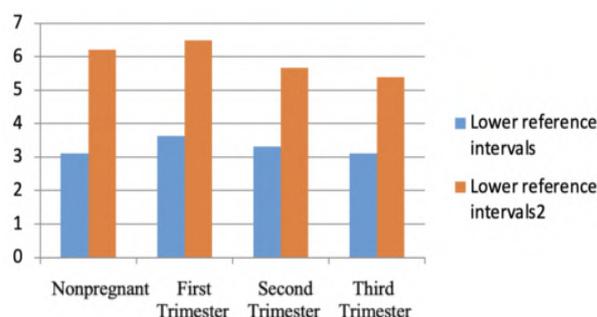


Figure 3. Free Triiodothyronine (FT3) Reference Intervals

Table 3. Hazard of Misidentification When Applying Non-Pregnant Reference Interval Values in Pregnant Women

Hormone	Misclassified / n (%)			
	1 st Trimester (n = 366)	2 nd Trimester (n = 252)	3 rd Trimester (n = 156)	Total (n = 774)
TSH	41 (11.2)	19 (7.5)	6 (3.8)	66 (8.5)
Free T4	14 (3.8)	14 (5.5)	6 (3.8)	34 (4.4)
Free T3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Note: TSH = Thyroid-Stimulating Hormone, T4 = Thyroxine, T3 = Triiodothyronine.

trimester for TSH values while decreasing values are seen toward the third trimester for FT4 values.

In this study, a lower TSH reference interval occurred in the first trimester (0.09 µIU/mL) and was significantly lower than the adult non-pregnant reference interval (0.4 µIU/ml). The upper TSH reference range occurred during the third trimester (3.11 µIU/mL) and was significantly lower than the adult non-pregnant reference interval (5.5 µIU/mL). For FT4, the reference range gradually declined from the first trimester to the second trimester and then to the third trimester. The lower reference limit of FT4 occurred in the third trimester (8.92 pmol/L), whereas the upper reference interval occurred in the first trimester (19.86 pmol/L).

To discover the possibilities of misdiagnosis and misclassification of different thyroid gland diseases during pregnancy, the new trimester-specific reference intervals of thyroid hormones were obtained by this study. It was then compared to the manufacturer's adult non-pregnant reference interval for TSH, FT4, and FT3, and the results are summarized in Table 3. Regarding TSH, 66 (8.5%) pregnant women obtained misidentification of thyroid gland dysfunction, while 31 (4.0%) of enrolled pregnant women would not be identified despite their elevated TSH. In comparison, 35 (4.5%) of enrolled pregnant women would faulty be identified with a decreased TSH level. The first trimester presented the highest incidence of misidentification of TSH results (11.2%). Regarding FT4, 34 (4.4%) pregnant women obtained misidentifica-

tion of thyroid gland dysfunction, and 19 (2.4%) pregnant women with elevated results would not be identified. While, 15 (1.9%) of enrolled pregnant women would faulty be identified with decreased FT4 levels. The second trimester presented the highest incidence of misidentification of FT4 results (5.5%). Regarding FT3, no misidentification or misdiagnosis had been noticed.

Discussion

Gestation gives rise to many physiological and hormonal changes in different body systems. The pituitary-thyroid hormonal axis will be affected during pregnancy due to the activation of TSH receptors by the HCG, so the negative feedback effect of TSH will decline due to the partial structural similarity of these two hormones.²⁸⁻³⁰ At 10-12 weeks of gestation, the TSH reaches maximum serum level. The TBG levels will increase; nevertheless, serum levels of TT4 and TT3 do not rise more than 50%.⁷ So, assessing thyroid gland function is more precise by measuring TSH and FT4.

The status of iodine nutrition was not determined because of the Iraqi community's daily consumption of iodized salt for many years. Therefore, all enrolled pregnant women were assumed to have sufficient amounts of iodine. In this study, the prevalence of thyroid gland autoimmune diseases in pregnant women has been determined, and 8.3% of enrolled pregnant women were positive for TPO-Ab and/or Tg-Ab. In contrast, it was 10.0–12 % in Vanderpump's study,³¹ and 14.8% in Godines-

Enriquez, *et al.*, study.¹⁵

During this study, it was determined that with trimester-specific reference values for TSH, FT4, and FT3 in enrolled pregnant women, there were significant differences between trimesters for both TSH and FT4 values (p -value <0.05). During the first trimester, TSH level significantly declined compared to the non-pregnant controls (p -value <0.05). Also, a significant rising trend in TSH levels was noticed from the first to the third trimester (p -value <0.05). A significant decreasing trend was observed regarding FT4 levels from the first to the third trimester (p -value <0.05).

The thyroid hormone values obtained in pregnant women were interpreted by applying both the obtained gestational age-specific reference intervals for thyroid hormones in pregnant women and the reference intervals for those in non-pregnant women. There was an obvious risk of misdiagnosis and misclassification of different thyroid diseases (Table 3), such as hypothyroidism and hyperthyroidism, if the thyroid hormone function tests were interpreted using the non-pregnant reference intervals, which leads to disease underestimation or overestimation with the subsequent wrong treatment. The interpretation of TSH values was particularly important because TSH is the cornerstone in analyzing the results of thyroid hormone. The cause of its low lower limit value (0.09 mIU/mL) during the first trimester was the mimic effect of HCG. Then TSH would increase gradually toward the end of the third trimester due to fading up of the HCG effect, but this process is still poorly understood.³² This process was responsible for the highest incidence of misidentification of TSH results (11.2%) during the first trimester if non-pregnant intervals references were used. This dangerous misinterpretation of TSH test values would occur, especially in pregnant women with pre-conception hypothyroidism, because they need regular monitoring throughout pregnancy and careful adjustment of treatment dose.³³

The TSH results of this study were in line with two studies in Iraq,^{34,15} a study in Egypt,³⁶ and another study in the United Arab Emirate.³⁷ At the same time, there was partial incompatibility with the result of another Iraqi study.³⁸ A study by Yang, *et al.*, showed that the TSH reference interval has a relatively lower cutoff value compared to previous different studies.³⁹ This difference may be due to the maternal iodine status of pregnant women enrolled in this study,⁴⁰ laboratory methods used, or ethical factors.

Regarding FT4 results, there was a significant difference compared to non-pregnant women's values, so this study agreed with a previous study by Padmakumar, *et al.*,⁴¹ and indicated the necessity of determining the trimester-specific reference values to interpret the results of thyroid hormone assays in pregnant women. In this

study, FT4 significantly declined with the progress of pregnancy from the first to the third trimester. The TSH significantly increased with the progress of pregnancy from the first to the third trimester, while FT3 showed no differences. It was difficult to compare different studies due to various causes and study variations, such as the size of the enrolled study sample, assay methods used, inclusion and exclusion criteria, iodine status, diverse centile range, and ethical and geographical factors.

The results of this study come in partial agreement with the Mehran, *et al.*, study.⁴² Although no significant difference was found in TSH values among the pregnancy trimesters by Azizi, *et al.*, study,⁴³ another study conducted in India by Sekhri *et al.*,⁴⁴ stated that there was a decline in TSH value during the first trimester, followed by an increase during the second and third trimester. In contrast, FT4 values showed a gradual decline throughout the pregnancy trimesters but were significantly lower during the second and third trimesters. While FT3 values started declining during the second trimester and remained stable during the third trimester.⁴⁴

Another study used liquid chromatography-tandem mass spectrometry and immunoassay techniques; FT4 showed significant differences between these techniques during the first trimester, while no significant difference was noticed regarding TSH.⁴⁵ A study from China showed a considerable decline in TSH values during the first trimester compared to non-pregnancy values, while there was an increase in the second trimester, and throughout pregnancy, there was a gradual decrease in FT4 and FT3.⁴⁶ Another study done by Kurioka, *et al.*, in Japan indicated significant changes in TSH and FT4 during the first trimester and showed a substantial decrease of FT4 during the progress of pregnancy.⁴⁷

Lastly, the US national academy of clinical biochemistry recommended that the interpretation of serum thyroid hormone test values must be done using the trimester-specific reference interval values of thyroid hormones.⁴⁸ In summary, this study and most available data from previous studies confirmed the differences in the thyroid hormones reference interval values between pregnant and non-pregnant women and demonstrated the necessity to establish the thyroid hormones trimester-specific reference intervals to avoid serious misdiagnosis of thyroid gland diseases during pregnancy.

Limitation

Interindividual variation cannot be excluded because thyroid hormones could not be measured consecutively in each enrolled pregnant woman. The urinary iodine concentration was not measured to assess the iodine status because of the assumption that all participating pregnant women ingested sufficient iodine quantity through the daily consumption of iodized salt for many years, and

the ultrasound examination of the thyroid gland was not done. Poor methodology standardization is a significant limiting factor.

Conclusion

This study shows a significant difference in thyroid hormone reference intervals in pregnant women compared to nonpregnant. Using the thyroid hormone values of nonpregnant women to interpret thyroid hormone values in pregnant women can cause many misinterpret test results. Hence, it is very important to achieve the trimester-specific reference interval values to get a correct and proper diagnosis of thyroid diseases and dysfunction, such as missing many cases of hypothyroidism which can cause dangerous maternal and fetal complications (such as fetal mental retardation, which can be prevented by thyroxine) or giving unnecessary thyroid treatment to normal pregnant women misdiagnosed as hypothyroidism cases.

For Iraqi pregnant women, this study recommends using the thyroid hormones reference intervals determined for each trimester of pregnancy to interpret the thyroid function test (TFT) values. This study suggests doing more national studies to obtain national gestational age-specific reference interval values of different thyroid hormones in Iraq. It can be done by using larger study samples, with particular attention to the assay methodology, iodine status, statistical method, and inclusion and exclusion criteria of the enrolled pregnant women.

Abbreviations

TSH: Thyroid-Stimulating Hormone; FT4: Free Thyroxine; TPO-Ab: Thyroid Peroxidase Antibody; Tg-Ab: Thyroglobulin Antibody; TBG: Thyroxine-Binding Globulin; TT4: Total Thyroxin; TT3: Total Triiodothyronine; HCG: Human Chorionic Gonadotrophin; T4: Thyroxine; T3: Triiodothyronine; ES: Endocrine Society; ETA: European Thyroid Association; and ATA: American Thyroid Association; FT3: Free Triiodothyronine; ECL: Electro-Chemiluminescence; SPSS: Statistical Package for Social Sciences and Problem Solutions; μ IU/mL: Micro International Unit/Milliliter; pmol/L: Picomol/Liter; SD: Standard Deviation; TFT: Thyroid Function Test.

Ethics Approval and Consent to Participate

Not applicable.

Competing Interest

The authors declare that there are 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

Materials and data of this study are available from the corresponding author for non-commercial goals and upon a reasonable request.

Authors' Contribution

HMA designed and developed this research and directed the overall work. MAA, KMS, and MY were responsible for samples and data collection. All authors shared data analysis and interpretation. Last, they reviewed and approved the final version of the manuscript.

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Review of Different Methods of Abnormal Mass Detection in Digital Mammograms

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Abstract

Various images from massive image databases extract inherent, implanted information or different examples explicitly found in the images. These images may help the community in initial self-screening breast cancer, and primary health care can introduce this method to the community. This study aimed to review the different methods of abnormal mass detection in digital mammograms. One of best methods for the detection of breast malignancy and discovery at a nascent stage is digital mammography. Some of the mammograms with excellent images have a high intensity of resolution that enables preparing images with high computations. The fact that medical images are so common on computers is one of the main things that helps radiologists make diagnoses. Image preprocessing highlights the portion after extraction and arrangement in computerized mammograms. Moreover, the future scope of examination for paving could be the way for a top invention in computer-aided diagnosis (CAD) for mammograms in the coming years. This also distinguished CAD that helped identify strategies for mass widely covered in the study work. However, the identification methods for structural deviation in mammograms are complicated in real-life scenarios. These methods will benefit the public health program if they can be introduced to primary health care's public health screening system. The decision should be made as to which type of technology fits the level of the primary health care system.

Keywords: breast cancer, computer-aided diagnosis, digital mammography, feature extraction

Introduction

One of most feared diseases in today's world is cancer. A widespread cause of cancer affects mortality, posing a problem relating to public health in the modern world, especially in elderly females. One of the most rapidly-emerging diseases in the world is breast cancer, the second most common type of cancer. Approximately, one million females are examined and treated for breast cancer, but over 400,000 die.¹ Early identification and analysis and recognition detect cancer efficiently and minimize mortality. Numerous imaging methods exist that diagnostically and effectively map human anatomy in a non-invasive manner, like X-Ray, MRI, CT, USG, and so forth. Due to its accuracy and cost-effectiveness, computer-aided diagnosis (CAD), a reasonably developed interdisciplinary mechanism for cancer detection, helps detect abnormalities in analyzing medical images following a pattern of the robust segmentation algorithm.²

The grey shades are wide ranges in Computed Radiography (CR) mammogram DICOM images. So that, the intensity of the image is the primary feature to determine the abnormality. The primary characteristics

derived from medical images are utilized to a greater degree by computerized images and decision-making algorithms to analyze medical images.

The fact that medical images are so familiar on computers is one of the main things that helps radiologists make diagnoses. Image preprocessing highlights the portion after extraction and arrangement in computerized mammograms. Moreover, the objective in the near future is to examine and pave the way as a top invention in the CAD for mammograms in the coming years. This also distinguished the CAD that helped identify strategies for mass widely covered in the study. However, the identification methods for structural deviation in mammograms are complex in real-life scenarios.

Literature Review

One of the leading efficient methods for breast cancer detection at a nascent stage is digital mammography, which requires high computational capabilities. There are several techniques for segmentation, feature extraction, and classification, and some of these procedures are discussed in Figure 1.

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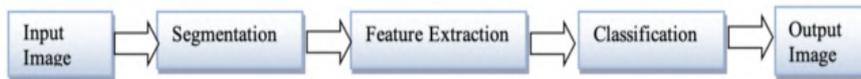
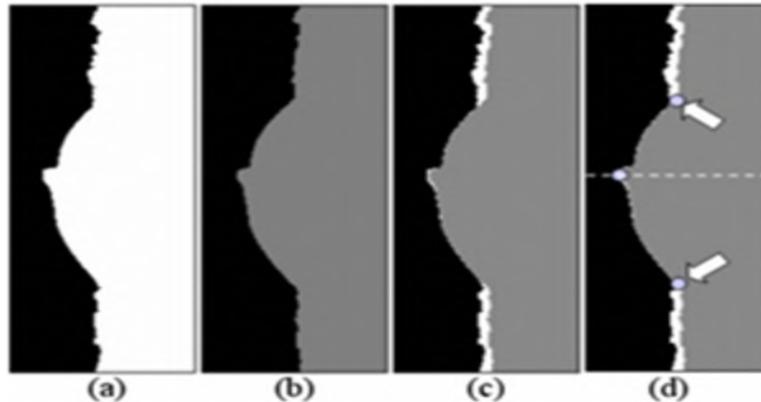


Figure 1. The Major Preprocessing Steps Followed in Mammogram Image



Notes:

- (a) The original greyscale image depicting the breast boundary
- (b) The threshold images in two consecutive threshold levels
- (c) Comparison of the two threshold images by overlapping
- (d) The new breast boundary points are derived by analyzing the differences between the two threshold images.

Figure 2. An Example Illustrating the Breast Boundary Tracking Procedure

Image Segmentation

Medical image data from different sources are combined in the 3D volume due to its growing importance in modern times. Numerous algorithms are planned in the area of image segmentation.

Region Growing

By definition, the region-growing method assumes that the neighboring pixels within one region have similar features. The pixels can be grouped to form a cluster if a similarity exists. Senthilkumar, *et al.*,³ proposed an automated seeded region growing algorithm (SRGA) based on Harri’s detector method.

Statistical Methods

Different mathematical and statistical concepts, formulas, and models are used for medical image segmentation. Gouda, *et al.*, described how segmentation is based on statistical region merging (SRM) and linear discriminant analysis (LDA) for classification.⁴

Thresholding

Thresholding is one of the simplest methods for creating binary images in image segmentation (Figure 2). This proposed method by Maitra, *et al.*,⁵ of Binary Homo-

geneity Enhancement Algorithm (BHEA) for digital mammography is followed by the technique of Edge Detection Algorithm (EDA) and the Breast Border Boundary Enhancement Algorithm (BBEA).

Fuzzy Method

Fuzzy logic is a multi-value function where the variable’s truth value aids the segmentation procedure. Divyadarshini, *et al.*,⁶ describes shape and margin characteristics obtained geometrically of maximum and minimum mass radius that can be utilized for classifying masses.

Information Difference

One valuable and usually-formatted data allowing straightforward human interpretation is preferably known as information difference. Cheng, *et al.*,⁷ has shown how symptom of the abnormal region is essential.

Feature Extractions

The primary pair of estimated data feature extraction methods was calculated by modified resultant standards, proposed as carrying information and not redundant, facilitating the successive learning to improve interpretations.

Gabor

Different filtering models are used to improve the exterior of an image by compressing the intensity. Jangala, et al.,⁸ portrayed mass detection as an edge detection technique that resides upon the segmentation for filtering in mammography.

Laplacian of Gaussian

This method has a filtering technique which is high pass to show faintly principal edges in an image for enhancement of the quality of the image. Cheng, et al.,⁷ has shown that the CAD could offer similar assistance, and they are critical and indispensable for controlling breast cancer.

Gradient Vector Flow Snakes

This method used minimizing energy spline influenced by exterior constrain extraction of lines and edges. Malek, et al.,⁹ is based on active contour methods to locate and isolate the core portion extracted from the image.

Statistical Texture Features

The textural features of region of interests (ROIs) are extracted using gray level co-occurrence matrices (GLCM), constructed in four directions for each ROI (Figure 3).

Morphological

The device used to extract several parts is helpful in the demonstration, along with describing the different regions, sizes, shapes, and boundaries for implementa-

tion. Halkiotis, et al.,¹⁰ considered every piece of a mammogram to represent the topography.

Image Classification

The classification process is performed on the ROI obtained from the image to classify the mass surrounding the suspected region. This classification improves efficiency to minimize the malignant count of false positives. The CAD assists the radiologist’s interpretation of mammograms for performance evaluation.

Markov

This technique involves random transitions in state space from one state to another. The MRF-based classification by Li, et al.,¹¹ uses a binary decision tree that is fuzzy based and possesses radiography features inter-linked with density.

K-nearest Neighbour

The nearest neighborhood method implements every intensity of nearest neighbor pixels found inside the unique image. The K-nearest neighbor is a non-parametric in classifying and finding regression (Figure 4). Akila, et al.,¹² showed the K-means used classification of the tumor degree and number of mammogram pixels.

Linear Discriminant Analysis

The linear discriminate algorithm (LDA) is primarily a traditional classification method. Cheng, et al.,⁷ have proposed that these boundaries set by the decision are built straight by maximizing the error condition to detach the object class.

Discussion

According to Sung, et al.,¹ the extraordinary diversity of cancer continues to offer clues to the underlying caus-

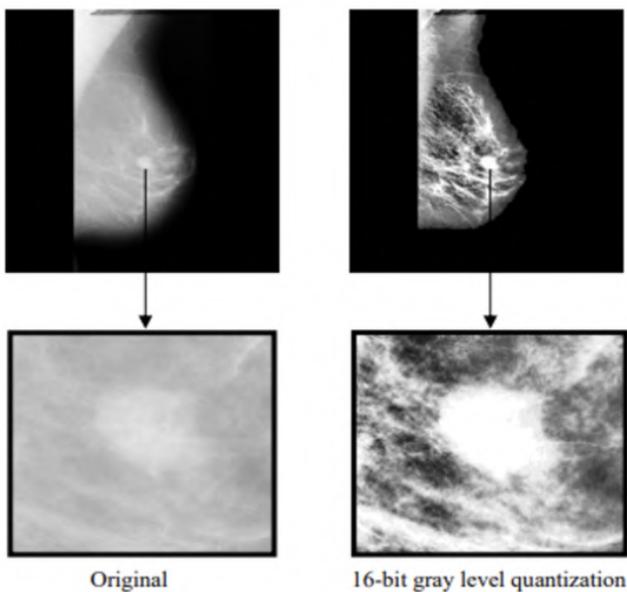


Figure 3. The 16-Bit Gray Level Quantization Produces Better Information than the Original

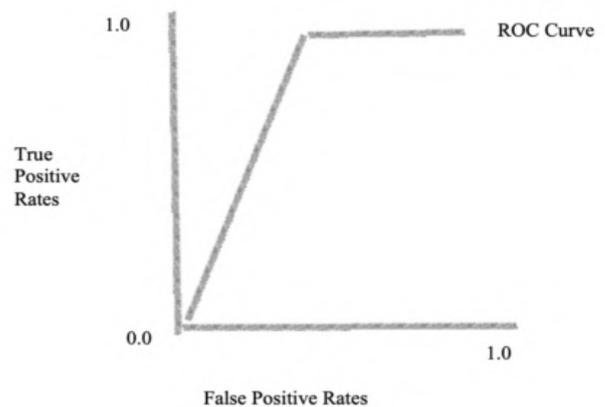


Figure 4. The Empirical Receiver Operating Characteristics Curve for Tumour Identification

es, but also reinforces the need for a global escalation of efforts to control the disease. The packages of effective and resource-sensitive preventative and curative interventions available for cancer and their tailored integration into health planning nationally can only serve to reduce and curb the future burden of cancer. The outcome was also accompanied by low referral rates for additional assessments, resulting in significant reductions in false-positive tests and unnecessary workup procedures.

Jangala, *et al.*,⁹ showed that in the frequency components or the smoothing introduced by most sensing devices, sharp discontinuities had been found to exist in real signals scarcely, which is a unique achievement rarely found in other works. This method also showed the K-means clustered image segmentation for detecting masses, that the method would only find masses when they are still harmless. The results achieved by this methodology will give better results in terms of accuracy using statistical values.

Divyadarshini, *et al.*,⁶ showed that the advantage of this method lied in its simplicity and cost-effectiveness. These geometric features are good at discriminating regular shapes from irregular ones. It is found that the masses, represented using shape and margin properties, possess a certain amount of imprecision. The disadvantage is that it can be deceptive at times. The classification accuracy for different shapes and severeness yields comparatively better results.

Maitra, *et al.*,⁵ showed a fully-automated detection technique of abnormal masses by anatomical segmentation of the breast ROI in a mediolateral oblique (MLO) view of mammograms using different algorithms like binary homogeneity (BHEA), breast boundary detection algorithm (BBDA), and pectoral muscle detection (PMDA) to suppress the breast ROI. Also, the anatomical segmentation of breast (ASB) ROI in various regions within the breast and the SRGA to isolate abnormal regions in a simple and faster method compared to others. The limitation is that these results had been tested only in the mini-MIAS database and detected abnormalities in only those mammograms that contain abnormal masses according to the MIAS database. The percentage of accuracy agreement achieved is approximately 0.9987.

Malek, *et al.*,⁸ obtained a higher classification performance that diagnoses the presented cases accurately and categorizes them as benign or malignant. This system provided a binary diagnosis and an output as a numeric value representing the degree to which the system could confidently respond in achieving placement and routing. This diagnostic system performs similarly to a software solution as a hardware solution, which is sometimes confusing. The malignant textures are distinguished from the benign ones solely based on assumption. This method attained a 97% correct classification over the benign cases,

a 93% correct classification over the malignant cases, and an overall classification rate of 95% of the testing data. At the end of this process, the images in the database were categorized more accurately.⁸

Dong, *et al.*,¹³ showed that the performance of the bilateral image feature subtraction method is better than the single image processing technique. This technique did not reduce false positives and further tested the bilateral image subtraction method on a smaller rather than more extensive data set. The classification accuracy on bilateral image feature extraction is 71.15%, and single image processing is 51.92%.

Eddaoudi, *et al.*,¹⁴ cited normal mammogram images based on statistical feature calculations used to define decision criteria that would allow distinguishing between normal and pathological tissue types. Each value represented the average of the parameters computed over the entire dataset. These preliminary results showed that the statistical features of the mammary gland tissue are insignificant and proved to be different from the statistical features of the fat one. A new method has been described to characterize normal mammograms with a set of parameters calculated to find the variance, the contrast, and the correlation representing the most significant features in characterizing the fat tissue and the mammary gland. The results are in the formation of the tissue for a normal breast. The effectiveness of these features and the computational results shown by processing 30 normal mammograms showed the contrast and the correlation in the directions $dx = 1$ $dy = 1$ and $dx = 1$ $dy = 2$ are found to be more significant in terms of discriminating a normal mammogram.

Hassan, *et al.*,¹⁶ provided a dataset-based quantitative comparison of the most recent techniques and the most commonly-used evaluation metrics for the breast cancer CAD systems. The survey also highlighted challenges and limitations of the current breast cancer detection and classification techniques. The results showed that the segmentation accuracy increased to 73.6% when using samples from the Curated Breast Imaging Subset of the Digital Database for Screening Mammography (CBIS-DDSM) dataset. Furthermore, the classification accuracy improved to 87.2%, with an area under the curve (AUC) of 94%. Due to the insufficient number of mammographic images in the publicly available datasets, data augmentation techniques are required to create synthetic mammographic images. This method has been demonstrated to have promising performance and contribute significantly to the development of CAD systems.

Gouda, *et al.*,⁴ showed that using patient-controlled analgesia (PCA) in selecting features gave good results. This selection could be made by developing a CAD system capable of assisting health professionals in the painstaking task of tracing mammograms and abnormal-

ities. There is a need for methodologies that support the automatic detection of lesions in mammogram images with little or no specialist participation. Such an objective is still a great challenge for the segmentation methods because of the dependability of the characteristics of objects. The testing accuracy of this method is 98.00995, and its sensitivity is 94.87%.

Suliga, *et al.*,¹⁵ showed a new pixel clustering model for analyzing digital mammograms. The clustering represents the first step in a more general method aimed at creating a concise clustered dataset for automatic detection and classification of masses, typically among the first symptoms analyzed in early diagnosis. A probabilistic description of the model, which can be written in any high-level or low-level programming language, makes it possible to run on almost any platform. The MRF-based technique is suitable for clustering in an environment that is limited and described by poor or limited data. Evaluation of the algorithm against the classical K-means clustering routine yielded comparatively superior results to the MRF scheme.

Halkiatos, *et al.*,¹⁰ showed a new algorithm for detecting clustered microcalcifications using mathematical morphology and efficiently combining an artificial neural network approach. The morphological filters are applied in order to only remove (a) noise from the image and (b) regional maxima that do not even correspond to calcifications. The MLP with 10 hidden nodes achieved the best classification score with a true positive detection rate of 94.7% and 0.27 false positives per image.

Akila, *et al.*,¹² showed that the primary step is pre-processing, which removes noise in the images. Then canny edge detection is used to detect the edges of images. After finding the edges, morphological operations are done to get the clearest mass. Then the original image overlapped with the eroded image to get an even more detailed view of the tumor. The K-means algorithm is used as an effective method to classify the tumor level. Thresholding segmentation is performed after edge detection is applied to get a vague or clear border of the mass. The mass morphological filtering is done, including grayscale dilation, hole-filling, and erosion, to obtain a clearer image. Then the original image overlapped with the eroded image to get an even more detailed view of the tumor since it failed to obtain a better view at the first attempt. This method shows that mammography detects about 80–90% of breast cancers in women without symptoms.

Ozha, *et al.*,¹⁷ surveyed the different scientific methodologies and techniques to detect suspicious regions in mammograms, spanning from methods based on low-level image features to the most recent novelties in artificial intelligence (AI)-based approaches. This method proved a considerable success with mammography in

biomedical imaging. Detecting suspicious areas remains challenging due to the manual examination and variations in shape, size, and other mass morphological features. Mammography accuracy changed with the density of the breast. This model was tested on the MIAS dataset and achieved an accuracy rate of 98.5%.

Shen, *et al.*,¹⁸ obtained the AI system achieving radiologist-level accuracy in identifying breast cancer in ultrasound images. The hybrid models of the AI system and the predictions of each of these were computed as an equally weighted average between the AI system and each value reader. This analysis revealed that the performance of all reader values was improved to some extent by incorporating the predictions of the AI system, which was otherwise not possible. The result achieved by the AI was an area under the receiver operating characteristic curve (AUROC) of 0.976 on a test set consisting of 44,755 exams.

Senthilkumar, *et al.*,³ included a new uncertainty theory, namely the Cloud Model, to realize automatic and adaptive threshold selection, which considers the uncertainty of an image and extracts concepts from characteristics of the region to be segmented as efficiently as a human being. Segmentation of medical images using a seeded region growing technique is increasingly becoming popular because of its ability to involve anatomical structures in the seed selection process. In this paper, only the part showing improvements in region-growing image segmentation has been shown. Furthermore, the method had been tested for over 40 sample images, and the results were comparatively better.

Li, *et al.*,¹¹ show that general mammographic parenchymal and ductal patterns could be well modeled by a set of parameters of affine transformations. The present study results are compared with those of the partial wavelet reconstruction and morphological operation approaches, which yield not the best but comparatively better results. The results demonstrated that the fractal modeling method is an even more effective way to yield better results for enhancing microcalcifications.

Lee, *et al.*,² reviewed computer vision techniques adopted in medical image analysis, particularly for cancer detection. This work focused on detecting the most common types of cancer forms. A cloud computing framework in modern days inspired the study to utilize the existing work on image-based cancer study and develop an even more versatile CAD detection technique. The results only gave a general idea of how segmentation was used in these common medical image modalities to find the most common types of cancer, and the results were good.

Cheng, *et al.*,⁷ have shown a significant advantage of the proposed method in detecting microcalcifications at every point in dense breast mammograms. Mostly, the

Table 1. The Different Methods of Segmentation and Feature Extraction

Category	Rational	Method	Reference
Region growing	Homogenous gray level information for detection of the region found as potential.	Region-growing-based algorithm multi-tolerance region-growing.	[3], [4]
Statistical methods	Global and local thresholding. Estimation of model spatial relation by maximizing estimation. The area under receive operating characteristics curve.	Histogram threshold-holding. Markov random field model estimation. This curve and this method determine the sensitivity and specificity.	[5] [6] [16]
Thresholding	Used to create binary images.	Binary homogeneity enhancement algorithm.	[5]
Fuzzy method	Using fuzzy rules and properties to separate	Fuzzy logic	[7]
Information difference	The difference between a pair of mammograms to detect the ROI.	Bilateral image subtraction.	[13]
LOG	Filtering technique which is high pass to show faintly principal edges which is critical and indispensable.	Transformation of an image to different scale space, Laplacian of Gaussian.	[7]
GVF Snakes	Active contour and Snakes.	Energy minimizing spline, which is guided by external constraint forces to extract features like lines and edges.	[8]
Statistical texture	Gray level histogram moments and gray level co-occurrence (matrix). Texture descriptor analysis.	4 features: energy measure, correlation, skewness, kurtosis, 1 inertia, entropy, inverse difference moment, sum average, sum, variance, correlation. This method helps indicate visual patterns in medical images and feed into the classification system that enables decision-making.	[14] [17]
Morphological	Morphological operations: dilation and erosion.	Measurement by mathematical morphology in case suspicious such as shape.	[10]

Notes: LOG = Laplacian of Gaussian; ROI = Region of Interests; GVF = Gradient Vector Flow.

Table 2. The Different Methods of Classification

Category	Detail	Reference
Markov	Statistical classification model by the use of statistical and contextual information for masses, based on K-means cluster scheme.	[15]
KNN	Co-occurrence features, wavelet features, and shape features Convolution Neural Network (CNN) showed an improved technique over CAD.	[12]
LDA	Texture features and morphological features.	[7]

Notes: KNN = K-Nearest Neighbor; LDA = Linear Discriminant Analysis, CAD = Computer Aided Diagnosis.

clusters in the mammogram detected are almost invisible, making it exceedingly difficult to distinguish them for the radiologist. This kind of error is because microcalcifications are superimposed on curve-like tissues and are removed when the curve detector for removing irrelevant breast structures is applied. The Free-response Receiver Operating Characteristics (FROC) curve proved that the proposed method achieved a greater than 96% TP rate with an FP rate of four clusters per image. The work discussed has been summarised in Tables 1 and 2. Table 1 shows the different methods of segmentation and feature extraction and Table 2 shows the different methods of classification.

Conclusion

The present study on the CAD mammography is a key point for detecting breast abnormalities as benign, malignant, or normal. Several techniques of segmentation, feature extraction, and classification have been developed,

as different scholars propose. Numerous study have been carried out, but selecting an accurate segmentation, detection, and classification method to detect the abnormality in the breast ROI remains a major challenge.

The objective is to examine and pave the way as a top invention in the CAD for mammograms in the coming years. This also distinguishes the CAD that helped identify strategies for mass widely covered in this study work. However, the identification methods for structural deviation in mammograms are complex in real-life scenarios and remain a significant challenge.

Further discussion should be made among Information Technology personnel and statisticians and the primary health care team management in the Ministry of Health to decide which method suits the primary health care system. The mechanism can help the decision process to refer the suspect directly to the higher-level health institution to be treated accordingly and at the very early stage.

Abbreviations

CAD: Computer Aided Diagnosis; CR: Computed Radiography; DICOM: Digital Imaging and Communications in medicine; 3D: Three-Dimensional; SRGA: Seeded Region Growing Algorithm; SRM: Statistical Region Merging; LDA: Linear Discriminate Analysis; BHEA: Binary Homogeneity Enhancement Algorithm; EDA: Edge Detection Algorithm; BBEA: Breast Border Boundary Enhancement Algorithm; ROIs: Region of Interest; GLCM: Gray Level Co-occurrence Matrices; MLO: Mediolateral oblique (MLO); PMDA: Pectoral Muscle Detection; ASB: Anatomical Segmentation of Breast; MIAS: Malnutrition, Inflammation, Atherosclerosis Syndrome; CBIS-DDSM: Curated Breast Imaging Subset of the Digital Database for Screening Mammography; AUC: Area Under the Curve; PCA: Patient-Controlled Analgesia; MRF: Markov Random field; AI: Artificial Intelligence; AUROC: Area Under the Receiver Operating Characteristic Curve; FROC: Free-response Receiver Operating Characteristics; LOG: Laplacian of Gaussian; GVF: Gradient Vector Flow; KNN: K-Nearest Neighbor; LDA: Linear Discriminant Analysis.

Ethics Approval and Consent to Participate

Not applicable.

Competing Interest

The authors declare that there are 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 dataset used and analyzed are available in published documents and on the internet.

Authors' Contribution

SB and IKM have contributed to developing the algorithms, detailed investigation and analysis of the methods, implementation of the methods, and writing the manuscript. SP helped verify, guide, and supervise this work's findings. AB has also helped in guiding and supervising this work. DS and AW both helped review and edit and provided valuable feedback that helped shape the research work.

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