

Kesmas

Jurnal Kesehatan Masyarakat Nasional
(National Public Health Journal)

Quarterly Journal

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A Qualitative Exploration of Exclusive Breastfeeding Practices Among Karen Ethnicity Mothers in Northern Thailand Remote Rural Area
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Research Articles:

Healthy Lifestyle Behaviors and Sociodemographic Characteristics Among Medical Students in Indonesia During New Normal Era: A Cross-Sectional Study (pp. 160-167)

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A Qualitative Exploration of Exclusive Breastfeeding Practices Among Karen Ethnicity Mothers in Northern Thailand Remote Rural Areas

Wanchalerm Ritthimon¹, Aksara Thongprachum², Jukkrit Wungrath^{2*}

¹Health Center for Ethnic Group, Marginal People, and Migrant Workers, Lampang, Thailand, ²Faculty of Public Health, Chiang Mai University, Chiang Mai, Thailand

Abstract

Low exclusive breastfeeding rates among the Karen ethnic group in Northern Thailand's remote rural areas underscore the need to understand knowledge, attitudes, and social support to develop targeted interventions. This qualitative study examined exclusive breastfeeding practices and the factors influencing breastfeeding behavior among 14 Karen ethnicity mothers in Northern Thailand. A structured interview was used to collect the data, a triangular method to determine the data's validity, and a content analysis method to examine the data revealed seven themes and 14 subthemes. This study identified three key factors for successful breastfeeding: self-motivation, social support, and effective problem management, which included overcoming the family's anti-breastfeeding beliefs. Conversely, unsuccessful breastfeeding stemmed from four issues: inadequate maternal knowledge and misconceptions, family beliefs and culture, maternal health problems, and economic constraints. Therefore, the success of breastfeeding was heavily influenced by both personal and environmental factors. As a result, every Karen ethnicity mothers should be encouraged to recognize the importance of breastfeeding and to exclusively breastfeed for at least six months, especially those living in remote rural areas and have a different way of life than the natives.

Keywords: exclusive breastfeeding, Karen ethnicity, remote rural area, Thailand

Introduction

Exclusive breastfeeding (EBF), providing only breast-milk to infants for the first six months, contributes significantly to infant health, nutrition, cognitive development, and mortality reduction.^{1,2} The World Health Organization recommends initiating breastfeeding within an hour of birth and continuing EBF for six months, supplemented by age-appropriate foods beyond that.^{3,4} Optimal breastfeeding has the potential to reduce infant deaths and public health costs significantly.⁵ EBF rates are monitored globally, with the World Health Assembly aiming for a 50% rate by 2025.⁶ Thailand, however, lags behind in EBF practices, ranking lowest in the Asia/Pacific region with only 34.0% initiating breastfeeding within the first hour and a mere 14.0% practicing EBF for six months in 2019.^{7,8} This disparity underscores the need for resources and strategies to boost EBF in Thailand to meet global targets and improve infant health outcomes.¹

Omkoï District in Chiang Mai Province, Thailand, home to the Karen ethnic group, is a remote, mountain-

ous region. The Na Kian Subdistrict has a particularly low breastfeeding rate of 13.17% in the first six months, significantly below the provincial average of 44.06%.^{9,10} Up to 95% of lactating mothers in this area have reported using alternatives to breast milk from birth. In 2020, three cases of acute respiratory failure were reported in infants under 6 months, all of whom were fed solid foods before this age.¹¹ The Thai Ministry of Public Health has tried various strategies, such as training health workers, promoting the Baby-Friendly Hospital Initiative, deploying mobile clinics, community outreach, and local support groups. However, continuous support is needed to improve breastfeeding rates.

No qualitative studies on breastfeeding behavior have been conducted among Karen ethnic hill communities in Northern Thailand. To fill this study lacuna, knowledge, attitudes, and impact of social support on the breastfeeding behavior of Karen ethnicity mothers (KEMs) in Na Kian Subdistrict, Omkoï District, Chiang Mai Province were investigated. The findings can be used as a guideline to encourage KEMs to breastfeed their babies and as a

Correspondence*: Jukkrit Wungrath, Faculty of Public Health, Chiang Mai University, Chiang Mai, Thailand, E-mail: jukkrit.w@cmu.ac.th, Phone: +66 81-595-9638

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model to encourage breastfeeding practices in other remote areas to promote the health of both mothers and babies. Results may guide tailored interventions to promote breastfeeding and enhance global child nutrition efforts using culturally sensitive approaches to achieve the United Nations’ Sustainable Development Goals and benefit communities worldwide facing similar challenges.

Method

An ethnographic qualitative study was conducted from September 2021 to May 2022 on the Karen ethnic community living in the remote rural area of Na Kian Subdistrict, Omkoi District, Chiang Mai Province, Northern Thailand. Due to the outbreak of COVID-19 at that time, preventive measures were implemented to ensure safety during data collection. These measures included adopting remote methods when possible, maintaining social distancing, wearing face masks, sanitizing shared surfaces, screening participants for symptoms, limiting the number of participants, choosing outdoor venues for necessary in-person meetings, and securing informed consent.

Purposive methods were used to recruit an information-rich sample, with selection criteria specifying that participants must be KEMs aged between 18 and 40 years and having at least one child who was either breastfeeding at the time of the study or had been breastfed within the preceding five years. KEMs who were ill or pregnant were excluded from the study. A total of 14 KEMs were recruited from primary health care (PHC) in the study area. The interviews ranged from 45 minutes to 1.5 hours and were conducted at the participants’ houses. The semi-structured interviews were conducted in the Lanna language, the local language in Northern Thailand, using a translator to communicate with the participants.

A semi-structured guide utilized to facilitate the interview sessions was independently developed and as-

sessed for quality by three subject matter experts, achieving an Item-Objective-Congruence (IOC) value of greater than 0.5 for all items. The interview guide was also pilot tested by 10 individuals with characteristics similar to the sample group before application in this study. The key questions covered the participants’ beliefs, culture, and social support affecting the adoption of EBF, the acceptability of EBF, and their experiences with practicing EBF until their infants reached six months of age. The discussions were not limited to the items in the interview guide, and each participant was allowed to express their opinions freely. Audio recorders were used to record the interviews.

The process was repeated for subsequent interviews. Similar coding and interview themes were collected, and the differences were recorded. Interviews with new participants continued until data saturation was achieved, and no new themes were identified. To ensure validity, the interview transcripts and emergent themes were shown to some of the participants for comments and confirmation. The transcripts and themes were accepted by all the participants.^{12,13}

The interviews were transcribed in the Lanna language before translation into Thai with the support of the translator. All data were analyzed manually using thematic content analysis. Each transcript was coded by reading it several times and attaching words or phrases to form a code to describe each statement or new issue raised by each participant. Following this initial coding, each transcript was compared against other transcripts noting patterns of similarities and differences. The final codes were formed by merging or dividing the initial codes and renaming them, if necessary. Subthemes were formed by grouping related codes with similarly related subthemes to form major themes. The analysis was a continuous process until the final codes, themes, and subthemes fully captured the participants’ accounts. Therefore, the themes and subthemes were not predetermined

Table 1. Participants’ Sociodemographic Information

Variable	Category	Exclusive Breastfeeding Group	
		Complete	Not Complete
Number of participant		7	7
Average age (years)		24.7	25.2
Education level	Primary school	2	1
	Secondary school	4	5
	No education	1	1
Average household’s monthly income (Bath)	<5,000	7	7
Occupation	Housewife	2	1
	Farmer	5	6
Number of children	1	3	1
	2	3	4
	3	1	2

but were derived inductively during the data analysis.¹³⁻¹⁷

The interviews and subsequent transcriptions were conducted in Thai, presenting the potential for inaccuracies in conveying intended meanings. To mitigate such risk, scrutinized translations and edited renditions of the quotes were cross verified and rechecked against the original transcripts to ensure semantic consistency. The methodology and contextual background were delineated to facilitate the reader's evaluation of their applicability. A meticulous audit trail was established through comprehensive memos and extensive field notes, with data collection pursued until data saturation, as per established study protocols. Triangulation of data was accomplished by integrating interviews from various individuals situated in diverse locales and supplemented using field notes and memos.

Results

The results were presented in two sections. The first section encompassed data from KEMs who followed EBF for an initial period of six months and was categorized into three themes. The second section included data from the group that could not maintain EBF, which was categorized into four themes.

Group 1: KEMs who completed EBF for the first six months

Three significant concerns were: 1) self-motivation; 2) social support; and 3) management of EBF problems during the first six months of EBF.

1) Self-motivation

The motivation for breastfeeding stems from two main sources: seeing the benefits of breastfeeding and the KEM's own breastfeeding experiences.

a. Seeing the Benefits of Breastfeeding

EBF was recognized as beneficial and valuable by the participants. They were aware of the risks or negative effects of feeding children foods other than breast milk before aged six months, as detailed below.

"I breastfed my baby until he was almost seven months old without giving him any other food because I wanted him to benefit from the nutrition and benefits of breast milk. I also breastfed my last child until he was six months old." (KEM-1)

"From the moment I found out I was pregnant. I decided that I would breastfeed my baby for six months before introducing other foods. My next-door neighbor has been feeding her baby other foods since she was one month old, and her baby became ill. The doctor diagnosed an intestinal problem. So, I don't want my child to be like that." (KEM-3)

"I could see the advantages of breastfeeding my baby.

He excretes easily. His stomach is not constricted, with only occasional crying. My son is in good health and does not require frequent doctor visits." (KEM-9)

b. Breastfeeding Experiences of KEMs

Findings revealed that the success of EBF during the first six months was shown by the direct experiences of KEMs, including previous parenting experiences as well as observations of other breastfeeding mothers, such as the following comment.

"In the village, I saw that my friend breastfed her baby. Her children are rarely sick and always look healthy. I want my children to be the same. So, I intend to continue breastfeeding for another six months." (KEM-9)

2) Social Support

Factors contributing to successful EBF were as follows.

a. Obtaining Breastfeeding Knowledge and Information from Health Professionals

"Someone told me you can start feeding the baby when the child is two months old. The child will mature rapidly. However, I continue to believe that doctors recommend breastfeeding for at least six months before starting solids." (KEM-4)

"I learned about breastfeeding from the health workers at the PHC. The staff educated me. They had reading materials that helped me to understand breastfeeding better. They also taught me about postnatal care, how to breastfeed, how to position the baby at the breast, managing lactation, dealing with engorgement and breast pain, and instructions on how to massage the breast to facilitate milk flow." (KEM-12)

b. Breastfeeding Support from Family Members and Neighbors

"I had to deal with some problems of breastfeeding my child. My baby was unable to suck, and the milk did not flow. My breasts became engorged, which made me very stressed and worried. My baby cried and was deprived of milk. So, I spoke with the PHC staff, who encouraged me and told me to relax. They taught me the proper techniques and allowed me to practice until I felt more confident." (KEM-8)

"I considered stopping breastfeeding several times due to a lack of milk and thought of feeding my baby other foods at four months like other mothers. However, I did not do that because my neighbors and relatives encouraged and advised me to increase my milk supply. My child is nine months old today and still has enough milk to eat, along with rice and bananas." (KEM-9)

"The early stages of childbirth were extremely stressful. I had to combine breastfeeding with household chores and cooking for family members. Fortunately, I had a mother-in-law who assisted me to fully breastfeed without concern." (KEM-4)

3) Management of EBF Problems

Many KEMs faced difficulties and obstacles while breastfeeding, but they managed to overcome them. Here are some specific comments.

a. Overcoming Breastfeeding Challenges Through Experienced Guidance

KEMs experienced difficulties while breastfeeding during the first six months but managed to overcome these problems by asking people with direct experience and knowledge about breastfeeding.

"I have no problems with milk supply because it is plentiful. My issue is that the baby will not suckle. He cries every time I breastfeed him. However, my mother, who has breastfed at least five children, taught me how to help my baby suckle more effectively." (KEM-4)

"I had a very limited supply of insufficient milk to feed my baby. I was worried and had no idea how to solve the problem. However, in my village, a local sage who is knowledgeable and experienced in breastfeeding suggested some foods and herbs to stimulate milk production, which worked extremely well." (KEM-9)

b. Dealing with Problems Arising from Family Factors, Beliefs, and Culture

Na Kian Subdistrict, Omkoi District, Chiang Mai Province, is a rural area with a majority of ethnic people following old beliefs and culture about feeding newborn babies or children under the age of six months. Members of the older generation believe that children should be fed the same way as adults and do not need to breastfeed for up to six months. Participants addressed this issue by relying on their knowledge and convincing their families of the benefits of breast milk.

"My elders insisted that I should start feeding the baby when he is two months old to grow quickly; but, I still believed the doctor who said that I should breastfeed my baby for six months before starting to eat. I tried very hard to explain this to my family members." (KEM-4)

"The elders in my community believe that newborn children must eat rice from the first day because rice contains a sacred thing. They believe that if the baby does not eat at birth, the child will have difficulty eating and chewing when they grow up; but, I don't think so. Health professionals say young children cannot chew and digest their food. Feeding them could be hazardous."

Babies should be breastfed for at least six months. I have tried to explain this accurate knowledge to others." (KEM-12)

Group 2: KEMs who did not complete EBF for the first six months

These KEMs fed their babies food other than breast milk before they were six months old. Four significant findings from the study are presented below.

1) Lack of Knowledge

Some KEMs did not truly understand the benefits of breastfeeding and could not deal with the limitations or problems that arose. Many myths exist about breastfeeding, such as the belief that giving the baby something other than breast milk during the first six months of life will cause them to feel full, stop whining, sleep longer, and grow faster.

"When I had a new baby, I only fed him breast milk for the first month, but he cried frequently. I was concerned he was not getting enough nutrients, so I bought a baby supplement to mix with water and occasionally gave him rice, boiled eggs, and ripe bananas." (KEM-5)

"I'm worried about my child's intelligence. I want him to eat healthy foods. So, I let him eat whatever he wanted: rice, bananas, steamed pumpkin, and boiled eggs. I believe that breastfeeding alone is insufficient for brain development." (KEM-6)

2) Family Influence on Beliefs and Cultures

The family influence had a significant impact on EBF. KEMs who cannot exclusively breastfeed their babies for at least six months are frequently pressured to introduce other foods. The family members argue that feeding children has been a traditional ritual practiced since ancient times. Furthermore, Karen people, particularly the elderly, believe that newborn Karen children must eat rice and other foods from birth. They believe that when the children grow, they will not forget how to chew rice and food in the future.

"My family started feeding my baby from the first day after birth, putting cooked rice in my child's mouth. In some families, if there is no cooked rice, the parents will chew raw rice and put it in the mouth of the child. The elderly believe that if the child does not eat rice from the first day of birth, the child will forget to eat when growing up and have a disfigured body." (KEM-2)

"My parents believe that humans must consume rice from birth. If the baby does not consume rice, he or she will be considered a ghost child." (KEM-7)

3) Maternal Health Issues

Some KEMs could not successfully breastfeed their

babies up to 6 months because of maternal health issues such as having underlying diseases that are not conducive to breastfeeding, poor nutrition, cracked nipples, and insufficient milk supply.

"I'm having a milk supply issue. I tried several methods to increase the amount of milk, but none of them worked, so I decided not to breastfeed my baby." (KEM-7)

"After about a month of breastfeeding, my nipples started cracking and bleeding. I was in so much pain and suffering that I decided to stop breastfeeding from then on." (KEM-10)

4) Financial Difficulties

Another factor influencing EBF for the first six months is family economic problems. The majority of KEMs come from low-income families. Agriculture provides household income once a year, but it is insufficient for subsistence. As a result, some KEMs commute to the city for work, leaving grandparents to care for their children. Instead of breast milk, babies are fed infant formula or other instant foods.

"I had to return to work in Chiang Mai with my husband three months after giving birth. If I do not work, there will be no money for family expenses. As a result, I had to leave my baby with my mother and feed him infant formula instead. The grandmother also fed my children other foods such as rice with boiled egg or mashed banana." (KEM-6)

"I had planned to breastfeed my child, but due to the high cost of living, my parents forced me to work in the capital with my husband when the child was about four months old. My husband's parents look after my children. Breastfeeding had to be discontinued, and my husband's family began feeding my baby regular foods such as steamed rice, mashed eggs, mashed boiled chicken, mashed vegetables, and mashed fruit." (KEM-11)

Discussion

In-depth interviews were conducted with key participants among KEMs who completed EBF for six months or more and the group of KEMs who were unsuccessful with EBF. Conditions for success, as well as problems and obstacles, are discussed below.

Cultural Beliefs About Breastfeeding

The Karen ethnic group in remote areas of Thailand has cultural beliefs hindering EBF, including feeding other foods from birth based on ancestral practices.^{18,19} These cultural barriers included the belief that breastfeeding could sicken the baby and offend ancestral spirits.¹⁹ However, several KEMs in this study successfully breastfeed by leveraging knowledge from health profes-

sionals to persuade their families about breastfeeding benefits. Although challenging, these mothers persisted because they believed in the health benefits for their children.¹⁹ A study by Paparwarin, *et al.*, stated that KEMs accessing medical services received valuable information leading to positive attitudes toward breastfeeding.²⁰ Despite initial resistance, family members eventually understood and accepted the advantages of EBF for the health and growth of their children.²⁰

Self-Motivation and Maternal Experience

Breastfeeding self-motivation is a maternal condition. KEMs must understand the benefits of EBF and the risks of feeding their babies other foods before they are six months old. Furthermore, having their direct breastfeeding experiences as a result of raising a previous child, as well as seeing others breastfeeding, was a driving force behind the intention to breastfeed successfully. Kestler-Peleg, *et al.*, reported the same results, that mothers with good experiences and success with EBF with a previous child, as well as those seeing another mother's successful EBF experience, were motivated to continue breastfeeding.²¹ Thomas, *et al.*, suggested that seeing examples or good experiences from other breastfeeding mothers caused a re-evaluation of their abilities. Seeing other mothers successfully breastfeed gave them the confidence to succeed.²²

Social Support

Social support is key for KEMs in Thailand to successfully practice EBF for six months. This support includes EBF knowledge and psychological backing from family, health workers, and friends.^{23,24} However, family pressure can deter EBF, especially without husbands, mothers, or mothers-in-law support in the early postpartum months.^{25,26} Timely assistance from health professionals and EBF skill-building opportunities can lessen maternal anxiety and enhance breastfeeding success.²⁷ Crucially, husbands, mothers, and grandmothers can provide vital support, drawing from their own experiences, setting positive examples, and helping with child-rearing and household tasks.²⁸

This study showed that KEMs who could not continue EBF for at least six months did not receive support from society, particularly family members. They bowed down to advice from family members or relatives, who frequently pressured them to feed other foods before their baby was six months old. A study in the Northwestern Nigeria found that families strongly influenced rural breastfeeding mothers.¹⁵ Older people in rural areas still have strong cultural beliefs about feeding their children foods other than breast milk because they believe that breastfeeding alone will cause the child to be weak, slow to grow, and have poor intelligence.¹⁵ The elderly living

under the same roof will be very strict about giving children food other than breast milk, and KEMs cannot refuse, especially mothers with the status of daughter-in-law.¹⁵

Physical Problems and Obstacles

Physical challenges like low milk supply, sore and cracked nipples, and nipple inflammation are common obstacles to EBF among KEMs.^{26,29} Despite these difficulties, successful KEMs persisted with EBF, knowing its benefits for their infants. They sought advice from experienced individuals like health workers, family, relatives, and neighbors.²⁰ Some KEMs used traditional medicines, such as herbal compresses, to manage issues like nipple inflammation.^{24,30} Even when facing excruciating pain from cracked nipples, these KEMs continued breastfeeding for their babies' health.²⁹

The KEMs in the unsuccessful EBF group with less frequency at first when experiencing nipple inflammation or cracked nipples. They gave their baby additional food, such as mashed bananas and rice. When the breastfeeding symptoms did not improve, they switched to using prefabricated milk powder with other foods to raise their children. Once breastfeeding ended, it was difficult to return to breastfeeding again.^{12,31-33} Most KEMs who had problems and stopped breastfeeding before six months were inexperienced teenage mothers or mothers with their first child who lacked proper family support, resulting in a lack of breastfeeding skills. No one was available to provide proper advice to deal with the problem. When experiencing nipple pain, KEMs are at risk of becoming mentally weakened, especially in the early postpartum period. This condition can exacerbate the inability to manage breastfeeding and lead to cessation.³⁴

Family Economic Situation

Another factor influencing EBF success is family economic problems. Most respondents came from low-income households. As a result, some KEMs have to work to support their families. The household socioeconomic survey found that Omkoi was the poorest district in Chiang Mai Province and the top ten in Thailand.^{35,36} Na Kian Subdistrict is a remote area with mountainous terrain and difficult to travel. The majority of the population are ethnic people living in the mountains and on the foothill plains, with scant access to government services and utilities.

These people work in agriculture, including animal husbandry and crop cultivation, such as rice, corn, and peanuts. Their agricultural products are sold in cities or through middlemen, and the people are poor due to capitalist exploitation. Regardless of sex, both men and women in Karen culture are responsible for working to fulfill the family income. However, the women in the

family have additional responsibilities as mothers of their children. Most villagers rely on an irregular primary source of income from rice sales that exceed annual household consumption, combined with a small income from selling forest products such as bamboo shoots, mushrooms, and honey. Some work in coffee plantations, longan harvesting, weaving, and satchel bag production.³⁷

Another interesting finding was young people in the Na Kian Subdistrict and many areas in Omkoi District prefer to work in big cities and send money back to their families. A previous study also found that the migration of ethnic groups of working-age people to the plains in search of work occurs continuously, and this trend is increasing.³⁸ They seek jobs in industrial factories, restaurants, and various service places.³⁸ Because of poverty, many KEMs cannot successfully breastfeed their children because they have to work either in the neighborhood or migrate outside the area to support their families. Children are raised by grandparents and fed infant formula along with other food. In some cases, families are impoverished and unable to purchase infant formula for their children.

Conclusion

KEMs are divided into two groups based on EBF success. Those who successfully managed EBF identify three success factors: 1) self-motivation, such as seeing the benefits of EBF and having their own breastfeeding experiences; 2) social support, such as obtaining knowledge and information; and 3) management of EBF problems such as milk supply shortages, pain or inflamed nipples and problems concerning beliefs and culture that hinder EBF. Those who belonged to the unsuccessful EBF group have four failure factors: 1) the KEMs' lack of knowledge and understanding, as well as incorrect beliefs about EBF; 2) the influence of families who do not support EBF and Karen ethnic culture about EBF; 3) maternal health problems; and 4) financial difficulties.

Recommendation

This study underscores the crucial need for tailored interventions to promote EBF among KEMs in the Chiang Mai Province, taking into account their unique socio-cultural and economic circumstances. It highlights the importance of incorporating social support networks, including family members and community leaders, into breastfeeding education programs to influence cultural practices. Policymakers and healthcare providers must engage in culturally sensitive dialogues with these communities. The study also suggests the need for further study on the complex factors influencing breastfeeding behavior, particularly in marginalized communities, to formulate more effective and context-specific health in-

terventions.

Abbreviations

EBF: Exclusive Breastfeeding; KEM: Karen Ethnicity Mother; PHC: Primary Health Care.

Ethics Approval and Consent to Participate

Participation in this study was voluntary and provided informed written consent. Ethical approval was obtained from the Research Ethics Committee of the Faculty of Public Health, Chiang Mai University, with reference number: ET029/2564, on 16 August 2021.

Competing Interest

The authors declared that there are no significant competing financial, professional, or personal interests that might have affected the performance.

Availability of Data and Materials

Data used in this study are available from the corresponding author upon reasonable request.

Authors' Contribution

WR and JW were responsible for conceptualization and methodology. WR collected data and investigated. JW wrote the original draft. JW and AT critically reviewed the manuscript. JW supervised this study. All authors read and approved the final manuscript.

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Healthy Lifestyle Behaviors and Sociodemographic Characteristics Among Medical Students in Indonesia During the New Normal Era: A Cross-Sectional Study

Sharren Shera Vionnetta¹, Tommy Nugroho Tanumihardja^{2*}, Kevin Kristian³

¹School of Medicine and Health Sciences, Universitas Katolik Indonesia Atma Jaya, North Jakarta, Indonesia, ²Department of Anesthesiology, School of Medicine and Health Sciences, Universitas Katolik Indonesia Atma Jaya, North Jakarta, Indonesia, ³Department of Public Health and Nutrition, Faculty of Public Health, Universitas Katolik Indonesia Atma Jaya, North Jakarta, Indonesia

Abstract

This study aimed to identify medical students' healthy lifestyle behaviors during the new normal era and to determine its relationship with sociodemographic factors, bearing in mind that, as future physicians and health role models, medical students play an important role in adopting and promoting healthy lifestyle behaviors to reduce the risk of future health problems as well as optimize communities' health status. This cross-sectional study was conducted at the School of Medicine and Health Sciences of a university in North Jakarta, with 111 medical students selected through stratified random sampling. Data were collected using sociodemographic characteristics (sex, residence, year of study, and participation in health promotion training) and the Health-Promoting Lifestyle Profile-II (HPLP-II) questionnaire and analyzed using descriptive and bivariate analyses. The results showed a moderate total HPLP-II score (2.46 ± 0.37). Interpersonal relations had the highest mean score, and health responsibility had the lowest. A significant difference in the total HPLP-II scores was identified between students participating in health promotion training and those who did not (p -value = 0.049). Further study is needed to explore other factors influencing healthy lifestyle behaviors among medical students.

Keywords: healthy lifestyle behavior, health-promoting behavior, HPLP-II, medical student, sociodemographic factor

Introduction

Health is not exclusively defined by the absence of a disease, illness, or weakness. It encompasses a holistic state of well-being that includes physical, mental, and social aspects.¹ Pender's Health promotion Model, used in this study as the theoretical framework, states that this health-promoting behavior represents the desired outcome of health decision-making and preparatory actions involving actions that enhance well-being and improve overall health.² A way to achieve a healthy life is to adopt a healthy lifestyle behavior, which is described as activities or behaviors believed and practiced by individuals to be healthy, enabling them to maintain their well-being and prevent diseases.³ Consistent with the definition of Pender's Health Promotion Model, health-promoting behavior comprises six health dimensions: health responsibility, physical activity, nutrition, spiritual growth, interpersonal relations, and stress management.² Components which collectively influence these health behaviors are individual characteristics and experiences, behavior-specific cognitions and affect, commitment to a plan of ac-

tion, demands, and preferences.² Individual factors include biological, psychological, and sociocultural aspects, as well as prior related behaviors. The behavior-specific cognitions and affect component encompasses factors such as perceived benefits of action, perceived barriers to action, perceived self-efficacy, and interpersonal and situational influences.²

Studies show that adopting a healthy lifestyle can help sustain or enhance an individual's health and reduce morbidity and mortality rates.^{4,5} Inversely, engaging in negative health behaviors raises the risks and likelihood of poor health outcomes.⁶ Unhealthy lifestyles and risky behaviors, including unhealthy diet, inadequate physical activity, smoking, and harmful alcohol consumption, contribute to metabolic changes such as obesity, elevated blood pressure, and increased blood glucose and cholesterol levels.⁶ At the same time, according to the World Health Organization, 60% of the morbidity and mortality associated with noncommunicable diseases (NCDs) are influenced by these behavioral and lifestyle factors.⁶ Adopting healthy behaviors in adolescence and youth is

Correspondence*: Tommy Nugroho Tanumihardja, Department of Anesthesiology, School of Medicine and Health Sciences, Universitas Katolik Indonesia Atma Jaya, Pluit Raya 2 Street, North Jakarta, Indonesia 14440, Email: tommy.tanumihardja@atmajaya.ac.id, Phone: +62 81519252584

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crucial as these habits persist into later stages of life,⁶ where if these conditions are not properly controlled, managed, or treated, they can eventually lead to the development of NCDs.⁷ A healthier lifestyle change from an early age is expected to prevent health concerns, as well as the number of NCDs still a burden in Indonesia.

As future physicians and health role models, medical students play an important role in implementing and promoting healthy lifestyle behaviors to reduce the risk of future health problems,⁶ as well as in optimizing society's overall health status, especially in situations such as the COVID-19 pandemic. A previous study revealed that medical students did not develop healthy lifestyle behaviors positively despite receiving health education,⁸ and maintaining this healthy lifestyle behavior continues to pose a challenge for medical students. Multiple studies have shown relatively poor health behaviors among nursing students in Indonesia.^{9,10} This failure to develop healthy lifestyles may be due to the mounting academic workload that students must face during their medical school studies. The COVID-19 pandemic has drastically changed various aspects of societies' daily lives, including lifestyle and health habits.¹¹ The lockdown measures implemented during the early stage of the pandemic, resulting in increased sedentary behavior, changes in sleep patterns, dietary habits, physical activity, and a decline in mental health, have thus also affected the health behaviors of students.¹² On the one hand, there is a lack of available data regarding Indonesian medical students in this particular context. Further findings on the health behaviors during the new normal phase remain scarce.

Medical schools generally provide training, activities, and experiences that enable students to participate in health promotion. Through these sessions, medical students will be able to enhance their knowledge and abilities to promote healthy behavior, positively influencing and enabling society to be more self-reliant in achieving a healthy lifestyle. By doing so, it can eventually raise students' self-awareness to implement healthy behaviors in themselves.¹³ Despite the importance of knowledge and abilities in promoting healthy behavior, studies exploring how this specific factor is related to healthy behavior have not yet emerged. Therefore, the primary focus of this study was to identify healthy lifestyle behaviors among medical students in Indonesia during the new normal era and to investigate the relationship between individual sociodemographic factors, including sex, residence, year of study, participation in health promotion training, and health behaviors.

Method

This descriptive cross-sectional study was conducted from February to June 2023 among medical students at the School of Medicine and Health Sciences of a univer-

sity in North Jakarta, Indonesia. Samples were selected using proportionate stratified random sampling. The inclusion criteria were preclinical medical students in their first, second, and third-years who agreed to participate in the study, excluding students taking a temporary break or period of absence from their studies and those who did not complete the questionnaire.

Data were obtained using a self-administered questionnaire consisting of two sections. The first part of the questionnaire contained questions about respondents' sociodemographic characteristics (sex, residence, year of study, and participation in health promotion training) as independent variables. The second section used the Indonesian version of the Health-Promoting Lifestyle Profile-II (HPLP-II) questionnaire that has been validated (Cronbach $\alpha = 0.934$) to measure respondents' healthy lifestyle behavior as the dependent variable in this study.

The HPLP-II questionnaire, developed by Walker, *et al.*,¹⁴ consisted of 52 items under six subscales (health responsibility, physical activity, nutrition, spiritual growth, interpersonal relations, and stress management). Each subscale's score was measured by the frequency of behavior using a Likert scale, ranging from never (1) to regularly (4). The total HPLP-II score was determined by calculating the mean score of the responses to all 52 items. It was further classified into four categories: poor (1–1.73), moderate (1.74–2.48), good (2.49–3.23), and excellent (3.24–4).¹⁵ Data were analyzed using the STATA statistical software (under license of the School of Medicine and Health Sciences of Atma Jaya Catholic University), utilizing parametric tests (independent t-test and one-way ANOVA) for normally distributed data and non-parametric tests (Mann–Whitney and Kruskal–Wallis) for non-normally distributed data to determine the differences and compare the total HPLP-II along with each of the subscales' scores among respondent's sociodemographic factors.

Results

This study included 111 of the 617 medical students. Figure 1 illustrates the distribution of the respondents' sociodemographic characteristics. Regarding sex, most students were female (65.8%). The proportion of students living with their families (49.5%) was nearly equal to that of students who did not live with their families (50.5%). This study comprised 39.5% of first-year students, 29.7% of second-year students, and the remaining were third-year students. Most students participated in health promotion training (71.2%).

Table 1 shows that most students in this study had moderate to good levels of healthy lifestyle behaviors (46.8% and 48.6%, respectively). According to Table 2, the mean \pm SD score of the students' total HPLP-II was 2.46 \pm 0.37, indicating a moderate level of healthy lifestyle

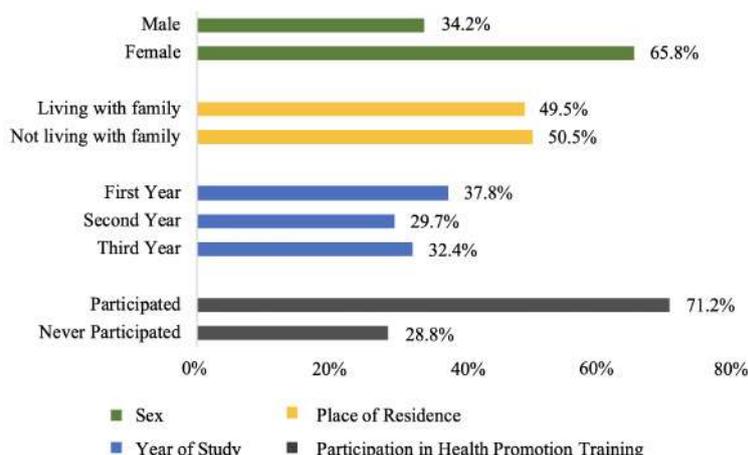


Figure 1. Distribution of Respondents' Sociodemographic Characteristics (n = 111)

Table 1. Distribution of Respondents' Profile-II and Each Subscale's Category During the New Normal Era (n = 111)

Students' HPLP-II	n	%
Poor	5	2.7
Moderate	52	46.8
Good	54	48.6
Excellent	2	1.8

Note: HPLP-II = Health-Promoting Lifestyle Profile-II

Table 2. Distribution of Respondents' Total Health-Promoting Lifestyle Profile-II and Each Subscale's Mean Score (n = 111)

HPLP-II Subscale	Mean±SD
Health responsibility	2.04±0.55
Physical activity	2.23±0.56
Nutrition	2.39±0.41
Spiritual growth	2.79±0.54
Interpersonal relation	2.87±0.47
Stress management	2.40±0.41
Overall/total HPLP-II	2.46±0.37

Notes: HPLP-II = Health-Promoting Lifestyle Profile-II, SD = Standard Deviation

Table 5. Sociodemographic Factors Differences in Overall Health-Promoting Lifestyle Profile-II

Variable	Category	Students' HPLP-II				p-value
		Poor	Moderate	Good	Excellent	
		n (%)	n (%)	n (%)	n (%)	
Sex	Male	0 (0.0)	20 (52.6)	18 (47.4)	0 (0.0)	0.710
	Female	3 (4.1)	32 (43.8)	36 (49.3)	2 (2.7)	
Residence	Living with family	1 (1.8)	25 (45.5)	28 (50.9)	1 (1.8)	0.594
	Not living with family	2 (3.6)	27 (48.2)	26 (46.4)	1 (1.8)	
Year of study	First-year	1 (2.4)	23 (54.8)	16 (38.1)	2 (4.8)	0.114
	Second-year	1 (3.0)	18 (54.5)	14 (42.4)	0 (0.0)	
	Third-year	1 (2.8)	11 (30.6)	24 (66.7)	0 (0.0)	
Participation in health promotion training	Participated	1 (1.3)	34 (43.0)	42 (37.8)	2 (53.2)	0.049*
	Never participated	2 (6.3)	18 (56.3)	12 (37.5)	0 (0.0)	

Notes: HPLP-II = Health-Promoting Lifestyle Profile-II, *Correlation is significant at the 0.05 level

behaviors. This study assessed six subscales of the HPLP-II. All the subscales of the students' HPLP-II fell within the moderate and good categories. Among the HPLP-II subscale, interpersonal relations had the highest mean

score (Mean = 2.87, SD = 0.47), followed by spiritual growth subscale (Mean = 2.79, SD = 0.54). At the same time, health responsibility appeared the lowest (Mean = 2.04, SD = 0.55).

Table 4. Sociodemographic Factors Differences in Health-Promoting Lifestyle Profile-II Subscales

Variable	Category	Health-Promoting Lifestyle Profile-II Subscale (Mean±SD)					
		Health Responsibility	Physical Activity	Nutrition	Spiritual Growth	Interpersonal Relation	Stress Management
Sex	Male	1.85±0.50	2.40±0.54	2.38±0.37	2.82±0.58	2.81±0.50	2.39±0.41
	Female	2.14±0.54	2.14±0.55	2.39±0.45	2.76±0.51	2.91±0.46	2.41±0.41
	p-value	0.015*	0.019*	0.810	0.614	0.501	0.675
Residence	Living with family	2.01±0.53	2.25±0.56	2.46±0.44	2.78±0.48	2.86±0.45	2.41±0.34
	Not living with family	2.08±0.57	2.25±0.57	2.32±0.37	2.79±0.59	2.88±0.50	2.39±0.47
	p-value	0.420	0.927	0.046*	0.939	0.731	0.432
Year of study	First-year	2.10±0.65	2.20±0.56	2.35±0.42	2.76±0.64	2.92±0.53	2.39±0.49
	Second-year	1.86±0.37	2.16±0.53	2.34±0.40	2.69±0.42	2.71±0.45	2.32±0.36
	Third-year	2.15±0.53	2.35±0.60	2.48±0.40	2.91±0.50	2.97±0.39	2.49±0.34
	p-value	0.033*	0.471	0.258	0.205	0.042*	0.105
Participation in health promotion	Participated	2.12±0.56	2.25±0.55	2.44±0.40	2.84±0.52	2.90±0.49	2.46±0.41
	Never participated	1.86±0.47	2.19±0.59	2.25±0.41	2.66±0.56	2.80±0.44	2.25±0.39
	p-value	0.049*	0.526	0.055	0.116	0.307	0.022*

Notes: *correlation is significant at the 0.05 level, SD = Standard Deviation

Table 5. Post Hoc Comparisons with Mann–Whitney U-Test

Health-Promoting Lifestyle Profile-II Subscale	Year of Study	Mann–Whitney U		
		U	Z	Asymp Sig.
Health responsibility	First-year	526.0	-1.788	0.074
	Second-year			
	First-year	691.0	-0.655	0.514
	Third-year			
	Second-year	375.0	-2.639	0.008*
	Third-year			
Interpersonal relation	First-year	551.5	-1.730	0.084
	Second-year			
	First-year	703.0	-0.534	0.594
	Third-year			
	Second-year	380.0	-2.577	0.010*
	Third-year			

Notes: Asymp Sig. = Asymptotic Significance, *Correlation is significant at the 0.05 level

The analyses of sociodemographic factors (sex, place of residence, year of study, and participation in health promotion training) on the total HPLP-II and its subscales are presented in Tables 3, 4, and 5. Among medical students, there was a significant difference in the total HPLP-II scores between individuals who participated in health promotion training and those who did not (p-value = 0.049). Notably, students who participated in health promotion training displayed significantly higher total HPLP-II scores. In contrast, no significant differences were observed between sociodemographic factors, including sex, residence, and year of study, concerning the total HPLP-II (p-value>0.05). Regarding the HPLP-II subscale comparison, health responsibility scores were significantly higher in female students than in male students (p-value = 0.015).

In contrast, physical activity scores were significantly higher among male and female students (p-value = 0.019). Students living with their families scored significantly

higher on the nutrition subscale (p-value = 0.046) than those who not living with their families. Significant differences were also identified between students' health responsibility (p-value = 0.033) and interpersonal relations (p-value = 0.042) based on their year of study. The pairwise comparison between the second and third-years revealed a statistically significant difference (p-value<0.05), where further analysis showed that second-year students had significantly higher scores in health responsibility (p-value = 0.008) and interpersonal relations (p-value = 0.010) compared to the third-year students. In addition, health responsibility (p-value = 0.049) and stress management (p-value = 0.022) scores were significantly higher in students who did participate in health promotion training than in those who did not.

Discussion

In this study, medical students demonstrated a moderate level of healthy lifestyle behaviors according to their

total HPLP-II average score. Healthy lifestyle behaviors were specifically examined by assessing the subscales of the HPLP-II, with similar results to those found in studies of medical students in Turkey,⁸ and dental medicine students in Indonesia.¹⁶ The spiritual development and interpersonal relations among the students were classified in a good category; while, the other four subscales, including health responsibility, physical activity, nutrition, and stress management, were categorized as moderate. Consistent with this study's findings, previous studies also indicated interpersonal relations and spiritual development as two subscales that showed higher scores than other subscales among medical students.^{16,17} With interpersonal relations being taught to medical students during their education to ensure effective and efficient communication with their patients,¹⁸ these skills play a crucial role in their ability to communicate and build rapport. This skill teaching is likely a contributing factor to the high score in interpersonal relations among medical students.

Moreover, spiritual development was also a prominent component among the medical students in this study, which may be due to the nurturing of religious and spiritual values within the university environment. Because of the high academic workload in medical education,¹⁷ there is a tendency for medical students to spend more time on academic activities compared to non-academic activities such as physical activity, health responsibility, and physical activity, which were reported as two of the lowest HPLP-II subscale scores in this study. Additionally, academic workload is associated with low awareness of maintaining health and decreasing health responsibility.¹⁹ Nevertheless, the health responsibility subscale in the HPLP-II emphasizes the need for health consultation with medical professionals. While the total HPLP-II scores did not show a significant difference between sex, health responsibility was reported to be significantly higher in female students, whereas, since respondents were medical students, they may perceive themselves as part of the healthcare personnel and therefore felt less inclined to seek consultation regarding their health.

In contrast, male students demonstrated higher scores in physical activity, with females tending to have higher curiosity and motivation regarding health information and self-care than males.^{21,22} Similar to the findings of these studies, previous studies presented the same result.^{8,20} The higher physical activity observed in males was related to their self-efficacy. Moreover, males commonly spend more time participating in sports activities, a characteristic of the masculine domain; while, females tend to spend time with family and are more likely to have a sedentary lifestyle.^{4,24,25} With this in mind, males tend to have higher motivation and confidence in their

ability to engage in physical activity consistently.²³

This study, which compared students' residences, was similar to previous studies conducted by Tapare, *et al.*,²⁰ and Ardiç, *et al.*,²⁶ who reported that students living with their families had significantly better nutrition scores. Intensive learning systems in medical schools may disrupt students' eating patterns. However, the nutritional needs of students living with their families could be better fulfilled by family supervision. Living independently puts students at a higher risk of developing poor eating habits, such as relying on unhealthy or fast-food options for time efficiency, which can negatively impact their nutritional status.²⁷ This study's findings demonstrated slight differences from other studies. While, differences in respondents' characteristics and family factors, such as backgrounds, cultures, parenting styles, and any other such factors may contribute to different health behavior outcomes among students, a study by Tampubolon, *et al.*¹⁶ reported that students not living with their families tended to take responsibility for their health even without parental supervision, as they believed that their declining health would affect their academic progress.

Based on the students' years of study, significant differences were identified between the students' health responsibility and interpersonal relations subscales, although the total HPLP-II did not differ significantly. Unlike what was expected, first-year students who were initially presumed to have lesser knowledge regarding healthy lifestyle behaviors obtained higher HPLP-II scores across all subscales compared to second-year students, where it was shown that the analysis revealed statistically significant differences between the second- and third-year students. However, as time progresses, the increasing academic workload could lead to a decline in healthy lifestyle behaviors, especially among second-year students; similar results were found in a study by Tapare, *et al.*²⁰

One potential explanation was that students recently entering university would still carry healthy behaviors or habits instilled by their families since childhood and continue to be supervised by their families to maintain those behaviors. For instance, a decline in supervision due to living away from their families may contribute to a change in this lifestyle, particularly in nutrition. Subsequently, upon entering the third year of education, they may raise their self-awareness to maintain a healthy lifestyle as their knowledge of health increases. This condition could account for improving HPLP-II scores across various subscales upon entering the third year of education.²⁰ Nonetheless, further study is needed to explore the reasons behind the fluctuations in healthy living habits observed in the findings of this study.

A significant difference was observed in the total HPLP-II scores between medical students participating

in health promotion training and those who did not (p -value = 0.049), where higher total HPLP-II scores were observed in students participating in health promotion training. This study was the first to determine the relationship between participation in health promotion training and healthy lifestyle behaviors based on HPLP-II scores among medical students in Indonesia. The findings of this study provided evidence that participation in health promotion training played an important role in enhancing healthy lifestyle behaviors among medical students. Throughout their studies, medical students generally have received early exposure to health promotion training aimed at preventive and promotive healthcare practices, in addition to curative and rehabilitative strategies.²⁸ This condition portrayed that they have acquired more relevant health information or knowledge for health promotion activities. Consequently, students with this experience are more likely to possess better health-related information and understanding.¹³

This situation may eventually increase students' self-awareness in maintaining their personal health, as evidenced by the results presented in Table 4, which highlighted significantly higher scores on the health responsibility subscale among students who had participated in health promotion training than those who had not. In addition, regarding the HPLP-II subscales, stress management scores were significantly higher among the group of students who received health promotion training. Additionally, the ability to analyze problem causes of stress was also a contributing factor toward coping abilities in individuals, where it was seen that stress management was related to coping mechanisms.²⁹⁻³⁰

Referring to the findings of this study, better stress management in students with a history of health promotion training could be associated with the health information received through the training, which would lead them to be more aware of the negative impacts of unmanaged stress. In line with similar studies, Askarian, *et al.*,³¹ reported a significant positive correlation between health knowledge and healthy lifestyle behaviors among medical students. Tunc, *et al.*,³² also identified a significant relationship between healthy lifestyle behavior based on the HPLP-II and students' perception of health, encompassing self-awareness of health's importance. These findings showed the importance of targeting the knowledge and attitudes of medical students to adopt healthy lifestyle behaviors and implementing related intervention programs to enhance those behaviors and well-being.³¹

This study had several limitations, including its cross-sectional design, which restricted the ability to determine causality and the long-term effects of the relationships between variables. This study was conducted at only one university in Indonesia. At the same time, it is important to note that the data collected relied on self-administered

questionnaires, which introduced the possibility of response bias. Therefore, these results do not represent the entire population of medical students in the country. Despite these limitations, this study provided valuable insights into the relationship between participation in health promotion training and healthy behaviors among medical students. Further assessment and study on the association between these variables are needed to gain a more accurate understanding. Alternative research methods and the use of additional parameters of healthy lifestyle behaviors beyond the scope of the HPLP-II may be considered.

Conclusion

In summary, a moderate level of health-promoting lifestyle is observed among medical students in Jakarta, Indonesia. Notably, experience in health promotion training is a significant factor in healthy lifestyle behaviors. Medical schools should proactively establish a supportive environment that encourages and facilitates healthy living. Additionally, this study's findings suggest the importance of prioritizing, developing, and implementing promotive and preventive health programs to enhance the overall lifestyles of medical students. Further assessment and exploration of other factors influencing healthy lifestyle behaviors among medical students are necessary.

Abbreviations

NCDs: Noncommunicable Diseases; HPLP-II: Health-Promoting Lifestyle Profile-II.

Ethics Approval and Consent to Participate

The study protocol was approved by the Research Ethics Committee of the Faculty of Medicine and Health Sciences of the Atma Jaya Catholic University of Indonesia (number: 20/30/KEP-FKIKUJ/2023).

Competing Interest

The authors affirm that no notable conflicts of interest, including financial, professional, or personal aspects, could have influenced the execution of the study.

Availability of Data and Materials

The raw data and STATA outputs obtained from the study are available and kept by the corresponding author.

Authors' Contribution

SSV and TNT conceptualized theories and frameworks related to healthy lifestyle behaviors among medical students. SSV analyzed the data using statistical computation software and interpreted the results. SSV and KK contributed to the design and preparation of this manuscript. All authors reviewed and approved the final version of the manuscript and agreed to be responsible for all aspects of this work.

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Comparison of Prevalence and Associated Factors of Multi-system Health Symptoms Among Workers in the Gas Station Area, Thailand

Chan Pattama Polyong¹, Anamai Thetkathuek^{2*}

¹Occupational Health and Safety Program, Faculty of Science and Technology, Bansomdejchaopraya Rajabhat University, Bangkok, Thailand,

²Department of Industrial Hygiene and Safety, Faculty of Public Health, Burapha University, Chon Buri, Thailand

Abstract

This cross-sectional study aimed to compare the prevalence of multisystem health symptoms (MHS) of workers in gas station areas before and after their employment and examine the factors affecting the MHS of workers. Data were collected by an interview questionnaire from 200 workers inside and outside refueling areas at eight gas stations in Rayong Province, Thailand. This study found that employees had a statistically significant increase in the prevalence of current MHS in comparison to before starting work (p -value <0.05), with 31.5%. Working overtime for more than 6 hours per week led to respiratory symptoms (OR = 2.63, 95% CI = 1.14–6.07) and psychological symptoms (OR = 2.69, 95% CI = 1.12–6.49). Wearing respiratory protective equipment for less than three hours affected ear/throat/nose systems (OR = 4.26, 95% CI = 1.43–12.65). Petrol refueling resulted in liver (OR = 2.32, 95% CI = 1.4–12.65) and eye symptoms (OR = 2.57, 95% CI = 1.10–5.39). Therefore, gas station owners should set up enclosed rooms to reduce the duration of fuel exposure, and workers should wear personal protective equipment when refueling or near the dispenser.

Keywords: BTEX, gas stations, multisystem health symptoms, prevalence, risk factors

Introduction

The global gasoline and diesel fuel vehicle fleets substantially impact human health.¹ Therefore, individuals working at gas stations (GS) are at the highest risk of exposure and experiencing multisystem health symptoms (MHS), which refers to the occupational awareness of individuals who can perceive their symptoms across various systems of the body, such as the respiratory system, visual system, integumentary system, and mental state, among others.² In a study conducted by Al-Harbi, dominant symptoms reported by gasoline station workers were headache, depression, fatigue, and throat irritation at 50, 40, 25, and 20%, respectively.³ Furthermore, studies conducted in Thailand have confirmed the occurrence of neurotoxic symptoms. There have been reports of individuals encountering chemicals associated with fuel oil and experiencing symptoms related to headache, dizziness, and stress/irritability at 49, 42.5, and 38.5%, respectively.⁴ A recent study has provided clear evidence of neurotoxicity; however, when it comes to other symptoms, various studies have documented a range of different manifestations, such as sore throat, drowsiness, mus-

cle weakness, and unconsciousness.⁵

The Benzene, Toluene, Ethylbenzene, and Xylenes (BTEX) will impact the human body, especially for workers at the GS, because 50% of the BTEX inhaled throughout their lifetimes will be absorbed into the body.⁶ Moreover, workers had a low level of safe behavior while working; for example, clothes wet with fuel, not wearing a respiratory protection mask, and putting their faces close to the tank were 62.7, 62.2, and 25.5%, respectively.⁷ Therefore, exposure to such substances can affect workers' multisystem health, resulting in acute and chronic damage to the target organs. In terms of acute damage, poisoning affects the nervous system, thereby causing headaches and dizziness,^{4,6,8} skin symptoms such as eye irritation and allergic skin rash,⁹ respiratory symptoms such as coughing,¹⁰ and psychological symptoms such as irritability, insomnia, inattentiveness, and lack of concentration, which were significantly higher than those in the non-exposed group.¹¹ Additionally, renal symptoms, such as difficulty urinating and less output,¹² have been found. If workers are continuously exposed, significant chronic effects can occur. Importantly,

Correspondence*: Anamai Thetkathuek, Faculty of Public Health, Burapha University, Chonburi Province 20131, Thailand, E-mail: anamai@buu.ac.th, Phone: +66-16-921013

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benzene is a human carcinogen. It was reported that exposure to benzene at an airborne concentration of 1 $\mu\text{g}/\text{m}^3$ causes approximately six cases of leukemia per million inhabitants.¹³

Prevention of exposure to BTEX aims to reduce the adverse health effects on workers. It is important to take occupational health precautions to avoid exposure to vapors while providing fuel services.¹⁴ For example, protection at the source can be implemented by installing a vapor recovery system (VRS), which can reduce the level of BTEX in the atmosphere by 60.9–76.5%.¹⁵ In Thailand, however, there are still obstacles to preventing exposure to BTEX; for instance, the general lack of VRS systems in use in stations, inadequate personal protection against fuel such as not using personal protective equipment (PPE), or using the equipment incorrectly.^{7,16,17} In addition, individual behavioral factors such as smoking,¹⁸ as well as demographic characteristics like sex,^{10,19} and age,²⁰ are risk factors for exposure to BTEX.

Workers in GS are regarded as an important force in the economic development of the service sector in the Eastern Economic Corridor area of Thailand; however, this group of workers still lacks equality in health care,²¹ and there is concern regarding their health conditions. Therefore, early health prevention should be sought by evaluating exposure and health effects. The impact assessment by abnormal symptom interviews is a simple tool for self-assessing unusual health-related sensations. Therefore, this study's inquiry revolves around identifying the prevalence of health symptoms arising from employment at the GS and understanding the associated factors. The aim was to study the MHS of workers in the refueling area by comparing the symptoms before and after their employment. Additionally, this study aimed to determine which factors affected the employees' health symptoms at the GS. In the past, it was mainly confirmed by neurological symptoms.^{4,6,8} In this study, however, the knowledge of other systemic symptoms, such as respiratory, skin, psychological, liver, and kidney disorders, was added. The benefits of this study can be used for comprehensive health screening against acute toxicity of BTEX in the future.

Method

A sample of 200 workers was calculated based on the proportion from a previous study.²² It was found that 83.7% of the workers at the GS had adverse reactions (p -value = 0.837). Error was 5% ($e = 0.05$), with 95% confidence ($Z = 1.96$), using cluster sampling until all numbers were reached. This was done because each GS' job position and environment were similar. There were two sample groups—with the first consisting of 100 inside fuel dispenser areas (I-FDA), including those filling and

cashiers, and the second consisting of 100 outside fuel dispenser areas (O-FDA), including those working in offices, convenience stores, coffee shops, and food vendors in GS—working for over three months and voluntarily agreeing to join the project. The exclusion criteria were illness on the day of the sample collection or exacerbation due to existing underlying diseases, such as migraines, allergies, asthma, and so forth, and being absent from work on the data collection date.

This study had a data collection period from October to November 2020, and laboratory analyses and results were reported from November 2020 to March 2021. This study complied with the Declaration of Helsinki; protecting the rights of the individuals in the sample was an important concern. Consequently, this study's objectives were explained to all participants, who were free to choose whether or not to participate voluntarily. No coercion was applied, and participants could withdraw from the trial at anytime.

This study used two research tools: an interview questionnaire and a urinary collection device. The details of each tool are as follows.

1. The interview questionnaire was divided into general information, work records, and health symptoms. General information included six items: sex, age, weight, height, smoking, and drinking alcohol. Work records included eight items: job positions, duration of work, working overtime, personal hygiene, behavior of wearing PPE, types of vehicles that were serviced each day, and number of vehicles that were serviced each day. Health symptoms in eight systems, with 36 items related to eyes, ears/throat/nose, respiratory tract, skin, psychological, liver, kidney, and anemia symptoms.

The MHS were identified from the literature review,² and previous studies involving symptoms of BTEX poisoning.^{9–12} The questionnaire was found to have an Item Objective Congruence value greater than 0.5 for all questions. For the interview questionnaire collection, the authors coordinated with GS managers. Sample group participants interested in being volunteers were invited through public relations. The data were collected after the end of work. The interview took about 20 minutes per person within the GS area.

2. The equipment for collecting urine included plastic cups, polyethylene jars (50 ml), temperature-insulating foam boxes, and ice packs. For analytical instruments, such as high-performance liquid chromatography, the laboratory has passed international quality control standards (ISO 15189: 2012) and the Thai Ministry of Public Health standards. The laboratory reported the analysis results in the metabolized form of BTEX. The quantity was analyzed using column type C18, mobile phase, containing water/acetonitrile at a ratio of 50:50 by volume (50:50v/v), flow rate of 1.0 mL/min at 37.0°C, sample

solvent by methanol, and ultraviolet detection at 254 nm wavelength.²³ This study’s results used the intersection of the ACGIH standard.²⁴

For the urine samples, a sample collection device was provided to the workers during their work. They clarified that the urine samples should be collected at the end of the work shift and that the mid-stream urine should be collected into a polyethylene jar of at least 25 milligrams and immediately packed in a cool box. After that, the samples were sent for laboratory analysis.

The data were analyzed by descriptive and inferential statistics, such as discrete variables, with analysis by frequency and percentage. A depiction with mean and standard deviation (SD) was used for the continuous variables for normally distributed data. If the distribution was abnormal, the depiction with median and interquartile range (IQR) was applied. The proportion of symptoms in the non-independent data was compared using the McNemar test. The analysis of factors affecting MHS classified by health system was performed with logistic regression statistics showing the crude odds ratio (OR) and 95% CI (confidence interval) were statistically significant (p-value<0.05).

Result

The results of the demographic description of 200 workers showed that approximately 2 in 3 (68.5%) were females, and mostly over 30 years old (56%) and had an income of more than 305 USD per month (56.5%) (1 USD = 32.8 THB at the time of the study). In respect to the health behaviors, there was smoking or smelling cigarettes from another person (34%), drinking alcohol (45.5%), and having rest of less than or equal to eight hours (54%). The workers had work experience of one year or more (73.5%), workers worked every day a week (55.5%), more than eight hours of work per day (56%), and additional overtime of six hours per week (86.5%). The workers followed proper hygiene practices (79%) and wore PPE for more than three hours a day (69.5%).

The interviews with 100 I-FDA employees on Table 1 found that those wear personal protective equipment (PPE), which was classified as wearing trousers covering the ankles (98%) and masks (95%). Moreover, those who refueled provided the information that diesel was the fuel filled the most (72%), followed by gasohol (20%). On average, 4-wheel pickup trucks were filled at 32.65±24.80 vehicles per day, and motorcycles account-

Table 1. Work Records of Inside Fuel Dispenser Areas Workers (n = 100)

Variable	Category	n	%	Mean±SD (Car/Day)
Types of PPE	Long pants covering the ankles	98	98.0	
	Mask	95	95.0	
	Closed-toe shoes	58	58.0	
	Long-sleeved shirt	38	38.0	
	Gloves	12	12.0	
	Glasses	5	5.0	
Types of oil refueled	Diesel	72	72.0	
	Gasohol 91, 95	20	20.0	
	Petrol	14	14.0	
	Gasohol E20	5	5.0	
Types of cars refueled	Bus			4.16±4.68
	Truck with more than 4 wheels			9.68±8.67
	Van			10.62±8.90
	Pickup truck with 4 wheels			32.65±24.80
	Personal car with 4 wheels			28.52±20.27
	Motorcycle			31.51±30.43

Notes: PPE = Personal Protective Equipment, SD = Standard Deviaton

Table 2. Comparison of Total Health Symptoms Before and After the Employment (n = 200)

Health Symptom	Symptoms Presently Occurring in the Past Three Months	Symptoms Before Working at the Gas Station	χ ²	p-value
No	42 (21.0)	105 (52.5)	41.14	<0.001**
Yes (more than one symptom)	158 (79.0)	95 (47.5)		
1–5 symptoms	80 (40.0)	66 (33.0)		
6–10 symptoms	34 (17.2)	16 (8.0)		
>10 symptoms	44 (22.0)	13 (6.5)		

Note: **p-value<0.001

Table 3. Comparison of Multisystem Health Classified by Symptoms Before and After the Employment (n = 200)

Health Symptom		Symptoms Presently Occurring in the Past Three Months	Symptoms Before Working at the Gas Station	Change in Past and Present Symptom	p-value
Eye system	Blurred vision	53 (26.5)	24 (12.0)	+29 (14.5)	<0.001**
	Dry/itchy/irritated eyes	43 (21.5)	17 (8.5)	+26 (13.0)	<0.001**
Ear, nose, and throat system	Sore throat/dry throat/irritated throat	75 (37.5)	41 (20.5)	+34 (17.0)	<0.001**
	Stuffy nose	70 (35.0)	38 (19.0)	+32 (16.0)	<0.001**
	Runny nose	68 (34.0)	40 (20.0)	+28 (14.0)	<0.001**
	Tinnitus	30 (15.0)	8 (4.0)	+22 (11.0)	<0.001**
	Ear pain	12 (6.0)	5 (2.5)	+7 (3.5)	<0.001**
Respiratory system	Ringling in the ears	6 (3.0)	3 (1.5)	+3 (1.5)	0.375
	Cough with mucus	58 (29.0)	32 (16.0)	+26 (13.0)	<0.001**
	Chest tightness	31 (15.5)	13 (6.5)	+18 (9.0)	<0.001**
	Panting	25 (12.5)	10 (5.0)	+15 (7.5)	0.001**
	Wheezing	25 (12.5)	9 (4.5)	+16 (8.0)	<0.001**
	Chest pain when breathing	20 (10.0)	9 (4.5)	+11 (5.5)	0.003*
Skin system	A red rash that appears on various parts of the skin	30 (15.0)	14 (7.0)	+16 (8.0)	0.002*
	A red rash on the hands and arms	12 (6.0)	4 (2.0)	+8 (4.0)	0.021*
Psychological symptom	Insomnia, difficulty sleeping	69 (34.5)	31 (15.5)	+38 (19.0)	<0.001**
	Loss of appetite	50 (25.0)	18 (9.0)	+32 (16.0)	<0.001**
	Mood swings	50 (25.0)	21 (10.5)	+29 (14.5)	<0.001**
	Heart palpitations	33 (16.5)	11 (5.5)	+22 (11.0)	<0.001**
	Feel depressed	30 (15.0)	11 (5.5)	+19 (9.5)	<0.001**
	Restless	22 (11.0)	10 (5.0)	+12 (6.0)	<0.001**
	Sweating without a known cause	21 (10.5)	9 (4.5)	+12 (6.0)	<0.001**
	Panting without exertion	10 (5.0)	3 (1.5)	+7 (3.5)	0.016*
	Being in a happy mood without drinking alcohol	7 (3.5)	2 (1.0)	+5 (2.5)	0.063
	Liver symptom	Nausea, vomiting	20 (10.0)	11 (5.5)	+9 (4.5)
Abdominal pain under the ribcage		16 (8.0)	9 (4.5)	+7 (3.5)	0.016*
Yellow eyes, jaundice		14 (7.0)	6 (3.0)	+8 (4.0)	0.008*
Kidney symptom	Back pain	91 (45.5)	36 (18.0)	+55 (27.5)	<0.001**
	Profuse urination	25 (12.5)	10 (5.0)	+15 (7.5)	<0.001**
	Infrequent urination	19 (9.5)	9 (4.5)	+10 (5.0)	0.002*
	Pain when urinating	17 (8.5)	5 (2.5)	+12 (6.0)	<0.001**
	Swelling of the eyelids, face, feet, and legs	10 (5.0)	4 (2.0)	+6 (3.0)	0.109
	Blood in the urine	3 (1.5)	1 (0.5)	+2 (1.0)	0.500
Anemia symptom	Eyes/body yellow	8 (4.0)	5 (2.5)	+3 (1.5)	0.250
	Bleeding easily throughout the body	7 (3.5)	4 (2.0)	+3 (1.5)	0.250
	Enlarged liver with hemorrhage	0 (0.0)	0 (0.0)	-	-

Notes: *p-value<0.05, **p-value<0.001

ed for 31.51±30.43 vehicles per day.

The results of the measurement of urinary metabolites of BTEX showed that employees had t,t-MA higher than the standard (29.5%), with the highest t,t-MA exceeding the standard almost 3 times (1,482.46 µg/g Cr) (Median = 393.40, IQR = 244.59). The levels of HA, MA, and MHA were detected as being lower than the standard (HA; Median = 0.31, IQR = 0.14: MA; Median = 0.06, IQR = 0.02: and MHA; Median = 0.4, IQR = 0.2, respectively).

When comparing health symptoms occurring within the past three months to those before starting work at the gas station, the results of the total MHS of the interviews with workers revealed that prior to working at this GS, they had experienced at least one health symptom (out of 36) (47.5%), with an increase in overall health symptoms of 31.5%. The largest segment of employees

had 1–5 symptoms (40.0%) (Table 2).

The results of MHS classified 36 symptoms revealed that employees had the highest prevalence of back pain at 45.5%, followed by sore throat/dry throat/irritated throat, and stuffy nose at 37.5 and 35.0%, respectively, in the past three months. The workers had a statistically significant increase in health symptoms (p-value<0.05), with 29 symptoms after employment. The top three symptoms that changed the most were back pain, insomnia/difficulty sleeping, and sore throat/dry throat/irritated throat (Table 3).

The factors affecting the current health symptoms were statistically significant (p-value<0.05), according to the factors as health behaviors, amount of work and wearing PPE, and refueling service (Table 4A and B). For health behaviors, sleeping less than or equal to eight hours per day affects the symptoms of the ear/throat/

nose system (OR = 2.21, 95% CI = 1.02–4.80), psychological symptoms (OR = 2.08, 95% CI = 1.18–3.66), and liver symptoms (OR = 1.80, 95% CI = 1.03–3.17).

For the amount of work and wearing PPE, working for more than eight hours per day affected the psychological symptoms (OR = 1.93, 95% CI = 1.09–3.39); working overtime more than six hours per week affected respiratory symptoms (OR = 2.63, 95% CI = 1.14–6.07) and psychological symptoms (OR = 2.69, 95% CI = 1.12–6.49); wearing a respiratory protective device for less than three hours had an effect on ear/ throat/nose symptoms (OR = 4.26, 95% CI = 1.43–12.65); and wearing closed-toe shoes affected the eye symptoms (OR = 2.36, 95% CI = 1.04–5.35), ear/throat/nose symptoms (OR = 8.12, 95% CI = 3.00–21.93), respiratory symp-

toms (OR = 2.81, 95% CI = 1.57–5.02), liver symptoms (OR = 2.70, 95% CI = 1.25–5.83) and kidney symptoms (OR = 1.98, 95% CI = 1.12–3.48).

Regarding the refueling service, most of the refueling employees were affected by liver symptoms (OR = 2.32, 95% CI = 1.43,12.65); refueling more than 10 trucks affected the eye symptoms (OR = 2.57, 95% CI = 1.10–5.39), and refueling more than 33 pickup trucks per day affected the respiratory symptoms (OR = 2.36, 95% CI = 1.04–5.35) (Table 4B).

Discussion

The factors affecting MHS found that regarding health behaviors, sleeping less than or equal to eight hours per day affected the symptoms of the ear/throat/

Table 4A. Factors Affecting Multisystem Health Symptoms (n = 200)

Variable	Multisystem Health Symptoms ^a							
	Eye	Ear/Throat/Nose	Respiratory	Skin	Psychological	Liver	Kidney	Anemia
Sex								
Female	4.92 (0.25–9.54)	0.86 (0.36–1.79)	0.63 (0.34–1.16)	3.39 (1.25–9.19)	1.14 (0.63–2.08)	1.10 (0.50–2.41)	1.46 (0.80–2.65)	1.01 (0.03–3.04)
Age (years)								
>30	1.42 (0.79–2.55)	0.81 (0.38–1.70)	0.96 (0.54–1.69)	0.93 (0.45–1.94)	0.84 (0.48–1.48)	0.49 (0.23–1.07)	0.71 (0.40–1.24)	1.03 (0.36–2.89)
BMI (kg/m ²)								
Overweight-obese	1.01 (0.57–1.02)	1.10 (0.49–2.09)	1.24 (0.46–1.41)	2.26 (0.21–3.95)	1.04 (0.59–1.81)	1.87 (0.89–3.92)	1.70 (0.62–1.87)	0.11 (0.70–6.30)
Income per month (USD)								
305	0.74 (0.41–1.33)	0.91 (0.43–1.89)	0.65 (0.37–1.16)	0.59 (0.27–1.26)	0.69 (0.39–1.21)	0.86 (0.41–1.78)	0.62 (0.35–1.10)	1.32 (0.47–3.69)
Currently smoking								
Yes	1.41 (0.76–2.63)	0.77 (0.37–1.63)	0.69 (0.38–1.27)	1.69 (0.74–3.82)	0.77 (0.43–1.38)	0.94 (0.44–1.38)	0.81 (0.45–1.47)	0.85 (0.29–2.43)
Currently drinking alcohol								
Yes	1.39 (0.78–2.50)	0.53 (0.26–1.11)	0.57 (0.32–1.02)	2.17 (1.00–4.68)	0.89 (0.51–1.55)	0.75 (0.37–1.53)	1.15 (0.66–2.02)	0.82 (0.29–2.29)
Sleep time per day (hours)								
<8	1.57 (0.87–2.82)	2.21* (1.02–4.80)	0.91 (0.52–1.60)	1.08 (0.52–2.23)	2.08* (1.18–3.66)	1.80* (1.03–3.17)	1.46 (0.51–4.19)	0.55 (0.15–2.01)
Work experience (year)								
1 or more	0.70 (0.36–1.38)	0.62 (0.25–1.52)	0.77 (0.41–0.45)	0.91 (0.39–2.08)	0.41 (0.21–0.79)	0.59 (0.24–1.45)	0.65 (0.36–1.27)	1.75 (0.60–5.07)
Working time per day (hours)								
>8	1.59 (0.89–2.86)	1.17 (0.57–2.42)	1.22 (0.69–2.77)	1.34 (0.65–2.77)	1.93* (1.09–3.39)	1.64 (0.80–3.37)	1.26 (0.72–2.20)	2.27 (0.79–6.50)
Working period per week (days)								
Every day	0.92 (0.51–1.64)	0.58 (0.28–1.20)	0.86 (0.45–1.51)	1.00 (0.49–2.07)	0.75 (0.43–1.32)	1.22 (0.59–2.52)	0.90 (0.52–1.58)	1.85 (0.62–5.53)
Working overtime per week (hours)								
>6	1.39 (0.58–3.34)	1.89 (0.54–6.64)	2.63* (1.14–6.07)	0.96 (0.34–2.73)	2.69* (1.12–6.49)	0.99 (0.35–2.83)	1.45 (0.64–3.29)	0.65 (0.17–2.45)
Personal hygiene								
No	0.91 (0.41–2.03)	1.34 (0.53–3.39)	1.28 (0.58–2.78)	1.66 (0.68–4.08)	1.57 (0.72–3.38)	1.95 (0.81–4.67)	2.25* (1.01–5.04)	2.64 (0.85–8.20)
Wearing respiratory protection equipment (hours/day)								
≤3	1.89 (0.97–3.68)	4.26* (1.43–12.65)	0.82 (0.44–1.53)	1.17 (0.52–2.61)	0.65 (0.35–1.19)	1.45 (0.64,3.31)	0.68 (0.37–1.25)	3.30 (0.72–1.51)

Notes: ^a = Crude Odd Ratio (95% Confidence Interval), *p-value<0.05, BMI = Body Mass Index

Table 4B. Factors Affecting Multisystem Health Symptoms (n = 200)

Variable	Multisystem Health Symptoms ^a							
	Eye	Ear/Throat/Nose	Respiratory	Skin	Psychological	Liver	Kidney	Anemia
Type of fuel refilled								
Diesel	0.52 (0.29–0.95)	0.60 (0.29–1.39)	0.79 (0.45–1.39)	0.79 (0.38–1.63)	0.66 (0.38–1.16)	0.96 (0.47–1.97)	0.81 (0.46–1.41)	0.91 (0.33–2.54)
Petrol	0.50 (0.24–1.02)	0.65 (0.26–1.56)	0.90 (0.20–1.31)	0.51 (0.20–1.31)	0.90 (0.47–1.69)	2.32* (1.01–4.92)	0.96 (0.51–1.82)	1.32 (0.43–4.01)
Gasohol 91,95	0.59 (0.33–1.06)	0.57 (0.27–1.20)	1.04 (0.59–1.82)	1.00 (0.48–2.05)	0.85 (0.48–1.48)	0.93 (0.45–1.91)	1.04 (0.59–1.81)	1.31 (0.47–3.67)
Gasohol E20	0.90 (0.50–1.64)	0.94 (0.47–2.08)	1.10 (0.62–1.96)	0.86 (0.40–1.82)	0.91 (0.52–1.62)	1.24 (0.60–2.55)	1.04 (0.56–1.77)	1.23 (0.44–3.47)
Type of cars refueled								
Trucks >10	2.57* (1.10–5.39)	1.62 (0.59–4.40)	1.56 (0.77–3.14)	2.17 (0.71–6.55)	1.38 (0.68–2.79)	1.05 (0.42–2.60)	1.56 (0.77–3.16)	0.71 (0.21–2.32)
Vans >11	1.78 (0.62–5.12)	0.87 (0.27–2.76)	1.12 (0.44–2.84)	1.27 (0.35–4.59)	1.57 (0.61–4.02)	0.65 (0.22–1.91)	1.39 (0.55–3.53)	0.76 (0.16–3.61)
Pickup trucks >33	1.82 (0.73–4.52)	0.78 (0.29–2.07)	2.36* (1.04–5.35)	0.78 (0.29–2.07)	1.18 (0.53–2.63)	0.81 (0.30–2.15)	1.23 (0.51–2.50)	0.45 (0.13–1.51)
Motorcycles >31	0.89 (0.38–2.07)	0.91 (0.32–2.60)	0.68 (0.29–1.62)	0.85 (0.34–2.14)	0.70 (0.31–1.61)	0.45 (0.18–1.13)	0.94 (0.41–2.15)	1.05 (0.23–4.91)
Types of PPE worn								
Glasses (no)	0.54 (0.15–1.94)	2.03 (0.24–16.56)	0.56 (0.14–2.25)	0.87 (0.17–4.28)	0.41 (0.10–1.63)	2.10 (0.25–17.14)	0.26 (0.05–1.26)	0.44 (0.05–3.92)
Mask (no)	1.47 (0.68–3.17)	2.48 (1.05–5.84)	0.60 (0.28–1.28)	0.42 (0.12–1.47)	1.00 (0.47–2.13)	1.02 (0.47–2.13)	0.76 (0.35–1.63)	0.73 (0.15–3.39)
Gloves (no)	0.78 (0.39–1.57)	1.12 (0.45–2.78)	1.01 (0.51–2.02)	1.12 (0.45–2.78)	0.61 (0.30–1.22)	1.17 (0.47–2.89)	1.00 (0.50–1.98)	1.94 (0.42–8.91)
Closed shoes (no)	2.27* (1.25–4.12)	8.12* (3.00–21.93)	2.81* (1.57–5.02)	1.25 (0.60–2.58)	1.49 (0.85–2.60)	2.70* (1.25–5.83)	1.98* (1.12–3.48)	3.133 (0.97–10.07)
Long-sleeved shirt (no)	1.36 (0.71–2.61)	2.32 (0.91–5.92)	0.40 (0.20–0.78)	0.91 (0.41–2.00)	0.82 (0.44–1.51)	0.52 (0.25–1.10)	0.65 (0.34–1.18)	0.65 (0.22–1.89)
Long pants that cover the ankles (no)	1.48 (0.73–3.05)	3.53 (1.60–7.82)	1.61 (0.77–3.37)	0.99 (0.40–2.47)	1.06 (0.52–2.14)	1.17 (0.49–2.81)	1.21 (0.60–2.46)	0.56 (0.12–2.60)
t,t-MA >500	0.79 (0.41–1.56)	0.76 (0.33–1.73)	0.75 (0.41–1.39)	1.68 (0.79–3.57)	0.71 (0.39–1.31)	0.61 (0.26–1.42)	0.83 (0.45–1.52)	0.83 (0.45–1.52)

Notes: ^a = Crude Odd Ratio (95% Confidence Interval), *p-value<0.05, PPE = Personal Protective Equipment

nose, psychological, and liver symptoms by 2.21, 2.08, and 1.80 times, respectively. These findings aligned with a study in New York City that investigated sleep and psychological symptoms and found that the subjects had an average sleep duration of 5.8±1.2 hours per night, with a prevalence of short-term sleep duration (<6 hours/day), which was 38.8%.²⁵ The sample group had psychological symptoms that occurred as follows: insomnia, acute stress, depression, and anxiety, which were 72.8, 57.9, 33.8, and 48.2%, respectively.²⁵

Concerning the amount of work and wearing PPE, it was found that the workers who worked more than eight hours per day were affected by their psychological symptoms 1.93 times. Overtime work of more than six hours per week affected respiratory and psychological symptoms at 2.63 and 2.69 times, respectively. Workers may have a common exposure to various chemicals in fuel, particularly those working long hours or overtime. These findings were consistent with the Agency for Toxic

Substances and Disease Registry report stating that exposure to very high levels of benzene in the air (10,000–20,000 ppm) in a short period (5–10 minutes) can cause death. At low concentrations (700–3,000 ppm), however, it can cause drowsiness, nausea, hallucinations, and depression.²⁶

Wearing respiratory protective equipment for less than three hours affected ear/throat/nose symptoms 4.26 times. Wearing closed-toe shoes affects the eyes, ear/throat/nose, respiratory, liver, and kidneys at 2.36, 8.12, 2.81, 2.70, and 1.98 times, respectively. These findings were consistent with a previous study that found significant exposure in GS, in which the workers exposed to low concentrations were associated with a prevalence of hearing impairment or loss.²⁷ There are more studies conducted on ototoxicity from exposure to various organic solvents, such as toluene and styrene, leading to effects on hearing.²⁴ This study's results provided more supporting evidence in the form of an interview on ear

abnormality in workers who work around the fuel dispenser, which found that the highest number of ear-related symptoms were tinnitus, ear pain, and ringing in the ears at 12, 4, and 2%, respectively.

Another important finding from this study was that the health symptoms of the employees who did not wear closed-toe shoes could be affected. It can also be caused by spills or splashes of fuel on their feet while refueling. A previous study found that in 1 week of work, 64.1% of fuel filler workers suffered skin accidents.²⁸ The spill can cause the evaporation of oil into the air, resulting in the presence of vapors in the vicinity,²⁹ because the organic solvents in the fuel easily evaporate into the air. Therefore, evaporation has the potential for employees to touch their eyes and affect their respiratory and ear/nose/throat systems, which will increase the symptoms that can occur even more.

During the interviews, participants were asked about the type of fuel added, which is important regarding health symptoms linked with the various fuel categories. In the past, no studies have been focused on this factor. This study indicated that petrol refueling affected liver symptoms 2.32 times, as the chemicals in the fuel can affect liver function. There is further evidence supporting an effect on increased liver function enzymes, as it was found that the exposure to benzene among fuel workers was $0.79 \pm 0.26 \mu\text{g}/\text{m}^3$ and significantly correlated with AST and ALT statistically.¹²

It is generally known that the process of metabolites of oils and compounds in fuels forms 1,2,4-benzene triol and j-benzoquinone, which interacts with adipose tissue in hepatocytes to form lipid peroxide and ROS consisting of hydroxyl and superoxide radicals, wherein reactive oxygen and lipid peroxidation cause the destruction of biomembranes.³⁰ This process causes the leakage of various components in the liver cells.¹² Therefore, liver dysfunction should be assessed with the liver function enzyme level, as mentioned above, since the evidence shows prolonged exposure to BTEX compounds in the fuel. In this study, however, the sample group only had a working period of approximately 1 year.

Refueling more than 10 trucks had effects on eye symptoms 2.57 times, and refueling more than 33 trucks per day had effects on respiratory symptoms 2.36 times; however, the study area is an economic province of Thailand with investment in the country's heavy industry.²¹ It links sea transportation from a deep-sea port to road and rail transportation. In addition, the way of life of the local community is linked with agriculture and fruit plantations. Therefore, the trucks and pickup trucks are the vehicles that use many service stations, and both vehicles have larger fuel tanks than personal vehicles. Therefore, it takes a long time to add fuel to each vehicle, which may also affect the oil's evaporation.²¹ This study

found that refueling these two types of vehicles leads to eye and respiratory symptoms. The most common eye symptoms were dry/itchy/irritated eyes and blurred vision at 18.0% and 17.0%, respectively. These findings were consistent with a study by Sirdah, *et al.*, that found a statistically significant increase in eye itches, redness, and pain among employees working at liquefied petroleum GS in the Gaza Territory.³¹ Hence, GS workers may be at a higher risk of visual impairment in the future, so they should be cautious about their health regarding regular visual abnormalities.

Adding gas to pickup trucks can result in respiratory symptoms due to the composition of the fuel, causing significant damage to the respiratory system. This can occur in both the upper and lower respiratory tracts, thereby causing mucosal irritation, inflammation, swelling, and acute bronchitis.³² In this study, occupational workers had the most productive cough, at 29%. It has previously been reported that exposure to fuel vapor at a concentration of 900 ppm for an hour caused symptoms of irritation of the eyes, nose, and throat. Fuel exposure at 10,000 ppm causes nose and throat irritation within 2 minutes and dizziness within 4 minutes.² Employees' exposure to fuel vapors through direct inhalation can lead to respiratory function impairment.³³ Therefore, continuous health surveillance should be emphasized.

The highlight of this study was that the interviews about the health symptoms retrospectively before and after employment which was considered to control various confounding factors. As a result, there was reliability of the outcomes in the occurrence of symptoms. In addition, the sample size was sufficient to answer the study objectives more effectively than many previous studies on the same issue. The weakness of this study was that the assessment of health symptoms was done using an interview form for the evaluation of the symptoms without a medical examination; however, the interview forms had been evaluated for validity in terms of content by occupational medicine physicians, and the validity is following the measurement and evaluation criteria.

Conclusion

The factors affecting MHS with statistical significance include working for more than eight hours per day, working overtime more than six hours per week, wearing respiratory protection equipment for less than three hours, refueling mostly petrol, refueling more than 10 trucks, and refueling more than 33 pickup trucks per day. Therefore, the results show that these risk factors are preventable. This study recommends the GS workers to stay away from the dispensers or stay in an enclosed room to reduce exposure time. Additionally, PPE should be worn while refueling or standing near the dispenser, and those who refuel should be careful when refueling vehi-

cles with large fuel tanks, such as trucks and pickups, by not standing near the fuel dispenser for an extended period.

Abbreviations

GS: Gas Stations; MHS: Multisystem Health Symptoms; BTEX: Benzene Toluene Ethylbenzene Xylenes; VRS: Vapor Recovery System; PPE: Personal Protective Equipment; I-FDA: Inside Fuel Dispenser Area; O-FDA: Outside Fuel Dispenser Area; SD: Standard Deviation; IQR: Interquartile Range; OR: Odds Ratio.

Ethics Approval and Consent to Participate

This study was conducted with the approval of the Burapha University Institutional Review Board for Protection of Human Subjects in Research (BUU-IRB) (certificate no. 019/2020). Before beginning the survey, informed consent was obtained from all the study participants.

Competing Interest

The authors declared 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 study data are available upon reasonable request to the corresponding author. The identities of the participants remain classified.

Authors' Contribution

CPP and AT led the design of the work. CPP analyzed and interpreted the data and is a major contributor to writing the manuscript. AT conducted review and editing, project administration, and funding acquisition. All authors read and approved the final manuscript.

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Development of a Medication Compliance Determinant Instrument for Low-Middle Literate Patients with Type 2 Diabetes Mellitus

Ivans Panduwiguna¹, Rani Sauriasari^{1*}, Ratu Ayu D Sartika², Woro Riyadina³, Fransiskus Samuel Renaldi⁴

¹Faculty of Pharmacy, Universitas Indonesia, Depok, Indonesia, ²Department of Nutrition, Faculty of Public Health, Universitas Indonesia, Depok, Indonesia, ³National Research and Innovation Agency, Jakarta, Indonesia, ⁴Royal Progress Hospital, Jakarta, Indonesia

Abstract

Diabetes, a leading cause of 6.7 million deaths in 2021, poses a significant challenge despite existing interventions. Non-adherence to treatment remains a barrier to diabetes management. However, a comprehensive instrument to assess medication adherence determinants in diabetes patients' population in Indonesia with low-medium literacy levels and following the sociocultural characteristics of Indonesian society has been lacking. This study aimed to develop and evaluate a valid and reliable instrument for measuring medication adherence in type 2 diabetes mellitus patients based on the Borg and Gall model. Through the input of an expert panel, a valid and reliable instrument was developed, which comprised 21 questions and encompassed all medication adherence determinants, with a CVR and CVI value of 1 and a final Cronbach's alpha value of 0.731. This instrument is still being tested and needs to be implemented in the right and wider population to obtain more accurate results.

Keywords: compliance, determinants, development, type 2 diabetes mellitus, questionnaire

Introduction

Southeast Asia ranks second highest in diabetes-related deaths among adults aged 20–79 years, with 1.2 million deaths in 2019 (14.1% of all causes of death).¹ Indonesia ranks seventh among the ten countries with the highest number of diabetes patients, with 10.7 million sufferers.² Complications and adherence to therapy in individuals with diabetes impose an economic burden as they necessitate hospitalization and treatment for comorbidities.² Concerning hospitalization, the average direct medical cost for total treatment in people with diabetes is IDR4,127,180 (USD368.49).³⁻⁴

According to the 2018 Indonesian Basic Health Research data regarding adherence to drinking or injecting antidiabetic drugs in people of all ages, Bali Province has the lowest compliance, at 86.98%.⁵ West Java Province's compliance average is even lower than Indonesia's (89.94%).⁵ Bogor City, West Java Province, is a city with a lower adherence rate (85.22%) compared to the provincial and national averages, despite patient adherence to treatment being a major factor in the successful treatment of diabetes.⁵⁻⁶

A cohort qualitative study in Bogor City identified various factors influencing patient adherence to diabetes

mellitus (DM) treatment, including intrapersonal factors (motivation, experience, knowledge, trauma, forgetfulness, laziness, busyness, conditions); interpersonal factors (medical check-ups, health workers, consultations, services, diagnosis, misinformation, social media, family, health cadres, relatives); treatment and disease characteristics (prescription and herbal drug use, side effects, organoleptic properties, form, taste, type, inappropriate use, complications, diet, physical activity, sports); and environmental factors (economy, culture, queues, distance, service satisfaction, policies, and the health system).⁷

Compliance assessment using a questionnaire is an indirect method of measuring compliance.⁷ Adherence to Refill and Medication Scale (ARMS) is a reliable and valid questionnaire to determine the level of adherence in the Indonesian geriatric population with diabetes.⁸ ARMS and ARMS-7 are comprehensive instruments supported by moderate to high-quality evidence for three measurement properties: structural validity, reliability, and construct validity. Moreover, an Indonesian version of ARMS has demonstrated good reliability, as evidenced by a Cronbach's alpha value of 0.815.⁸⁻¹⁰

Despite the advances that have been made in develop-

Correspondence*: Rani Sauriasari, Faculty of Pharmacy, Universitas Indonesia, Prof. DR. Mahar Mardjono Street, Pondok Cina, Beji, Depok City 16424, Indonesia, Email: rani@farmasi.ui.ac.id, Phone: +62 821-1425-2811

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ing instruments to observe adherence, no instrument has been established through an expert panel that was able to simultaneously assess clinical outcomes and questions in the form of perceptions. This study aimed to develop an instrument to identify the determinants of medication adherence in patients with type 2 diabetes mellitus (T2DM) based on qualitative study and an expert panel and to examine its relationship to clinical outcomes of HbA1C. By this instrument, researchers from other countries can discover the determinants of adherence to taking medication for patients with DM.

Method

This study was conducted in several urban villages in Central Bogor Subdistricts, Bogor City, including Babakan, Panaragan, Ciwaringin, Babakan Pasar, and Kebon Kalapa, from September to December 2022. Expert panel interviews were conducted through Zoom meetings on 29 September 2022. The Borg and Gall model, consisting of 10 stages (Figure 1), was utilized in this study.¹¹ The stages were initiated with information col-

lecting, during which keywords were searched, and the results of existing systematic reviews related to the determinants of adherence to the treatment of diabetic patients were examined. The second stage, planning, was then undertaken. At this stage, the variables to be identified and assessed were planned. The third stage, developing a preliminary product form, involved conducting an expert panel comprising six experts for the initial development. Subsequently, preliminary testing was performed to conduct the initial validation of the instrument, which was created based on the input from the expert panel. To facilitate the assessment, a determinant instrument assessment form to the field panelists, including doctors, pharmacists, nutritionists, and nurses were provided.^{12,13}

To obtain content validity index (CVI) values and content validity ratio (CVR) from the instruments that have been created, requires assessment.¹⁴ In the fifth stage, the main product was revised based on expert team suggestions. This stage was followed by field trials conducted on 30 patients with DM in the Central Bogor Subdistrict, wherein quantitative data were collected. The instru-

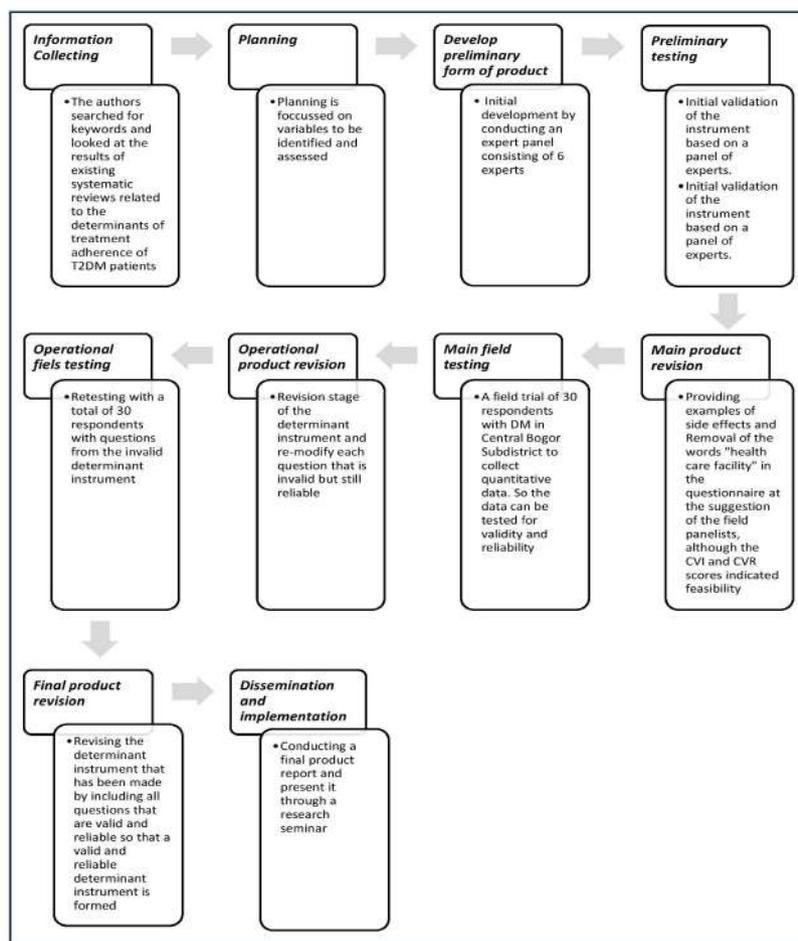


Figure 1. Steps for Build Product

ment's validity and reliability were then tested. Next, the practical product was tested in actual operational circumstances after it had undergone alterations, including modifications to the determinant instrument. This stage involved retesting 30 respondents using questions from the invalid determinant instrument. The next stage was the final product revision, where the determinant instrument was revised to include all valid and reliable questions. Finally, the dissemination and implementation stage entailed creating and presenting a final product report through research results seminars.

The ten stages were selected due to their advantages despite requiring a significant amount of time. These advantages included addressing real and urgent needs (real needs in the here and now) by developing solutions to a problem and generating knowledge for future use; producing a product/model with a high validation value as it undergoes a series of field trials and receiving validation from experts; promoting a continuous process of product/model innovation, aiming to ensure that the products/models are always up-to-date with current demands, and serving as a connection between theoretical and field studies.¹³ This study involved six experts, including professors and Master's students in pharmacy, nutrition, and public health, who each assessed the questions and statements based on their knowledge and experience.

The subject selection was conducted to obtain a review and validation from a panel of health practitioners in the Central Bogor Subdistrict, comprising doctors, pharmacists, nurses, and nutritionists. Data collection involved verbatim transcripts, first-cycle coding, second-cycle coding, and CVI and CVR tests to assess the validity and reliability of the instruments. Validity and reliability tests were performed by administering the instruments to 30 T2DM patients in the Central Bogor Subdistrict, who were part of the Bogor Health Research and Development cohort research data. The respondents' names used in the study were obtained from the Health Development Policy Agency, accessible through <https://www.badankebijakan.kemkes.go.id/>, following specific requirements and procedures.

Results

This study involved seven stages: variable identification, expert panel discussion and review, assessment by field panelists (CVI and CVR), question revision, initial validity and reliability testing, instrument revision, final validity and reliability testing, and instrument completion. Factors influencing treatment adherence in T2DM patients were obtained through a literature search, theory, and verbatim review by six experts. First- and second-cycle coding and validation by a field panelist team were conducted to identify keywords. The results of the coding

cycles are as follows.

Regarding the patients' perceptions of benefits and knowledge, an expert stated, *"Their understanding is that once they have seen the doctor, that's sufficient."* Another expert highlighted the barriers in the environment, stating, *"Access problems persist, especially for those in remote areas, making it challenging to reach health services."*

The patients' perceptions of treatment benefits and knowledge were influenced by their understanding and treatment experience. Good knowledge positively impacted perception, and when patients perceived treatment benefits, they tended to adhere to their treatment. Access to health services, availability, and fear of side effects remained obstacles for patients, affecting their adherence to DM treatment in Indonesia.

An expert said that family support is quite important other than education. *"In fact, we usually work..... Prof. So, of course, this must also come from both the sufferer, meaning the client with diabetes, and must also receive support from the family. So, support from family is quite important."*

Family support was essential in treating patients with diabetes as it provided motivation and positive influence. It was crucial to introduce gradual changes with the support of all family members to overcome potential difficulties. Family involvement included measuring food portions, ensuring consistency in food choices, considering the patient's eating schedule, and providing medication reminders. The patient's family played a pivotal role in the treatment process by acting as companions, promoting healthy habits, and motivating patients to enhance their quality of life.

An expert said medication adherence was related to obstacles, unpleasant experiences, and side effects. *"Well, the biggest obstacle experienced by patients is that they are worried about the side effects of the antidiabetic medicines they are taking, so they stop taking them without consulting a doctor and pharmacists."*

Some patients discontinued antidiabetic medicines without consulting health professionals due to concerns about side effects. Side effects are a common reason for non-compliance with medication. While not all patients experience side effects, those who do may stop taking the medication out of worry.

Another expert cited herbal medicines as related to compliance. *"Because he has a chronic disease, he must have tried all sorts of things, including herbal medicines. It's still better if he doesn't stop taking herbal medicine, but often he takes herbal medicine instead of modern medicine, so he comes with uncontrolled or new complications."*

As a population of a culturally rich country, Indonesians are inseparable from tradition. One such tra-

dition is the consumption of herbal medicines. The use of herbal medicines was carried out as an effort to treat DM. Still, people often do not follow the doctor’s advice and stop modern medicine, which is dangerous.

One expert said the following regarding the frequency of taking medication. *"The frequency of taking medication is often more than once, so if the medication can be taken on a schedule once, the results will be better than if you take it twice."*

The frequency of medication intake directly impacted adherence. To assess adherence among DM patients, 21 questions covered behavior perceptions, intrapersonal and interpersonal factors, disease and treatment characteristics, and environmental factors. Determinants of adherence in T2DM treatment included vulnerability, severity, benefits, self-efficacy, barriers, motivation, knowledge, experience, health services, health workers, family and relatives, drug side effects, herbal medicine use, diet, exercise, medication details, health service system, distance to health facilities, Healthcare Security membership, and education.

To ensure content validity in developing new measurement instruments, this study employed the CVI and CVR methods. Content validity was essential to creating instruments based on theoretical foundations. Initially, a large number of question items were generated to represent a concept or dimension, which were then refined in-

to a smaller set. For instance, in developing a Patient-Centered Communication instrument, the CVI is utilized to evaluate the relevance, clarity, and importance of question items assessed by experts. From the results of the CVI and CVR, the instrument in the form of a questionnaire was built as on Table 1.

Content validity was assessed, resulting in a CVR value of >0.75 and a CVI value of 1 for the overall instrument, indicating excellent content validity. Minor revisions were made based on the panelists’ feedback. A field trial involving 30 DM patients in the Central Bogor Subdistrict evaluated validity and reliability. Preliminary results of the tests are as follows:

- The Determinant Instrument: 4 invalid questions, Cronbach’s Alpha = 0.893
- DKQ-24 Instruments: 10 invalid questions, Cronbach’s Alpha = 0.668
- TSRQ Motivation Instruments: 2 invalid questions, Cronbach’s Alpha = 0.844
- ARMS compliance instrument: 1 invalid question, Cronbach’s Alpha = 0.742

The instrument was revised based on the invalid question, and retesting was conducted with the 30 respondents using the revised determinant instrument. The results of the revision were carried out with the results of the following instruments on Table 2.

Based on feedback from experts and the validity re-

Table 1. Content Validity Index and Content Validity Ratio Assessment

Question	Ne	CVR	Result	CVI	Result
Do you agree that people with diabetes can experience complications from other diseases like kidneys, heart, and eyes?	7	1	Valid	1	Valid
Do you agree that diabetes is a disease that can cause death?	7	1	Valid	1	Valid
Do you agree that taking diabetes medication regularly according to the doctor’s instructions will help to maintain blood sugar levels?	7	1	Valid	1	Valid
Do you agree that people with diabetes find it difficult to get treatment?	7	1	Valid	1	Valid
Are you sure you have been regularly treated at the primary health care (PHC)?	7	1	Valid	1	Valid
Filling out the TSRQ (value calculated)	7	1	Valid	1	Valid
Do you have complaints about diabetes treatment, such as side effects, taste, forgetting to take medication, or other personal things such as what others say, costs, and so on?	7	1	Valid	1	Valid
Filling out the DKQ-24 (value calculated)	7	1	Valid	1	Valid
Are you satisfied with the services provided by PHC?	7	1	Valid	1	Valid
Are you satisfied with the answers from the health workers regarding the questions you asked?	7	1	Valid	1	Valid
Were you not given information (education) about taking medication by health workers?	7	1	Valid	1	Valid
Have you received direct attention from your family regarding your treatment so far?	7	1	Valid	1	Valid
Have you received direct attention from relatives regarding your treatment so far?	7	1	Valid	1	Valid
How much medication are you currently taking?	7	1	Valid	1	Valid
How many times a day do you take the drug?	7	1	Valid	1	Valid
Do you have any complaints after taking the drug?	7	1	Valid	1	Valid
Do you use herbal medicine?	7	1	Valid	1	Valid
During the last three months, have you maintained your diet according to the doctor’s or nutritionist’s instructions?	7	1	Valid	1	Valid
Do you exercise regularly, 30 minutes a day, 5 days a week?	7	1	Valid	1	Valid
Do you experience problems related to the distance to the treatment center?	7	1	Valid	1	Valid
Amount	140	20		20	

Notes: CVR = Content Validity Ratio, CVI = Content Validity Index, TSRQ = Treatment Self-Regulation Questionnaire, DKQ-24 = Diabetes Knowledge Questionnaire-24, PHC = Primary Health Care.

Table 2. Revision of Statement on the Instrument

Before	After
I experienced many obstacles in getting treatment, such as long distances, lack of information from health workers, and not being supported by my family. During treatment, did you have any unpleasant experiences, such as not being served properly by officers, experiencing side effects, being kept away from family/friends, or other experiences?	I feel the obstacles that come from family support in doing the treatment.
In 1 (one) day, do you take 5 (five) different types/types of drugs, including herbal medicine, to treat the disease you are experiencing, such as diabetes or other diseases?	During treatment, did you have any unpleasant experiences, such as: a. Not being served well by officers b. Drug side effects c. Being kept away from friends and family
Do you experience anything unpleasant after taking medication, such as nausea, vomiting, diarrhea, or other uncomfortable feelings, after taking medication?	In 1 (one) day, do you take 5 (five) different kinds of medicine? Do you experience anything unpleasant after taking medication, such as: a. Weakness b. Nausea c. Headache

sults, revisions were made to the instrument (Table 2). Ambiguous questions with the potential for multiple answers were clarified to ensure a definitive “Yes” or “No” response. Modifications were made to the TSRQ motivational instrument by removing two invalid statements (Statement 2: “I am challenged to do this” and Statement 18: “Exercise regularly and paying attention to food is my choice”). The DKQ-24 questionnaire had 10 invalid questions, but no modifications were made due to its simplicity and purpose of assessing knowledge. One question was modified from “Shaking and sweating are a sign of high blood sugar levels” to “Shaking is a sign of high blood sugar levels” to address the possibility of either symptom. The validity and reliability testing yielded a Cronbach’s alpha value of 0.731, indicating the instrument’s validity and reliability as all questions had a higher r count than the r table value (Table 3).

The complete instrument consisted of 10 questions related to patient demographics, 21 questions related to determinants of medication adherence, 7 questions related to motivation, and 24 related to respondents’ knowledge. In measuring adherence, this study used 11 medication adherence questions from the Indonesian version of ARMS. This study was a first step; further testing will be conducted on an appropriate and larger population.

Discussion

The stages of identifying the determinants of adherence to treatment among T2DM patients were derived from a previous study titled “Designing a Model for Handling Factors Causing Non-Adherence to Treatment in Patients with Diabetes Mellitus Type 2.”⁷ Through the analysis of the conducted problems, four factors contribute to non-adherence.⁷ These factors comprise intrapersonal factors, interpersonal factors, drug and disease factors, as well as environmental factors.^{14,15} The results of an existing systematic review titled “Determinants of

Table 3. Validity and Reliability Results of the Instrument Revision

Corrected Item Value	Sig.	r table	Criteria
0.444	0.014	0.361	Valid
0.687	<0.001	0.361	Valid
0.852	<0.001	0.361	Valid
0.444	0.014	0.361	Valid
0.687	<0.001	0.361	Valid
0.687	<0.001	0.361	Valid
0.498	0.005	0.361	Valid
0.498	0.005	0.361	Valid

Factors That Influence Adherence to Treatment of Type 2 Diabetes Patients in Indonesia” revealed the factors influencing treatment adherence among T2DM patients.¹⁶ These factors can be categorized into two groups: factors that can be modified and those that cannot.^{17,18}

Concerning medication adherence, behavior plays a crucial role. One of the behavioral theories widely used in cases of DM patients is the Health Belief Model (HBM).¹⁹⁻²¹ The main concept of HBM consists of five components: perceived susceptibility due to side effects if not adherent to using insulin properly (perceived susceptibility), perceived severity due to disease complications (perceived severity), perceived benefits from using insulin properly (perceived benefit), perceived self-confidence (perceived self-efficacy), and perceived barriers (perceived barrier). Therefore, there is a need for an approach to this.¹⁹

Based on several theories related to instrument development from Borg and Gall,¹¹ this study underwent several stages in this study. The expert panel review served as a reference for determining the determinants as variables in the instrument. This was followed by transcribing the expert panel recordings and providing detailed information through first-and second-cycle coding. Experts emphasized the alignment between theory and

practice, stressing the need to bridge the knowledge–application gap. However, the comprehensive analysis revealed limited progress in perception, behavior, motivation, knowledge, family support, and treatment access. Addressing these challenges required further efforts, strategies, and interventions to advance healthcare.

Determinants of adherence in diabetic patients include susceptibility, severity, benefits, self-efficacy, barriers, motivation, knowledge, experience, health services, health workers, family, relatives, drug side effects, use of herbs, diet, exercise, drug details, health care system, distance to health services, Healthcare Security membership, and education. The panel discussion revealed that these determinant variables, with the support of related studies, have a significant relationship and strong impact on adherence.

While, sex did not significantly affect T2DM patients at health services in Banjarmasin City.²² Moreover, the importance of age, knowledge, and motivation was highlighted in medication adherence.²² Adherence to taking medication can be influenced by the total amount of medication received by T2DM patients at a hospital in Bogor City.²¹ The use of herbal medicines in diabetic patients affects medication adherence.^{23,24} The use of herbal medicines can complicate the treatment regimen received by diabetic patients and lead to low medication adherence. Patients may miss taking prescribed diabetes medication because they already take traditional medicine.^{24,25}

In this study, no significant correlation was found between herbal medicine consumption and adherence to prescribed medications from PHC staff. This result implied that herbal remedies did not affect or predict adherence to conventional medical treatments recommended by health professionals. Patients who used herbal medicines in this study still took their prescribed diabetes medication, but there may have been a delay in the timing of medication intake.^{23,26}

Other studies have also found a relationship between family and health worker support with adherence to anti-diabetic drugs in Jakarta,²⁷ and that education through home pharmaceutical care can improve adherence in Yogyakarta.²⁸ Family support is a vital component that must be included in managing diabetes. Family support can affect medication adherence and facilitate the control of HbA1c levels.²⁹ Families need to realize the importance of providing support and active participation when patients are receiving treatment.²⁹ The assessment instrument was formed and contains all the determinants of medication adherence that have been established based on expert panel discussions, with the aim that each statement or question formed can reflect the determinants of medication adherence that occur in Indonesian society.^{20,30}

The instrument covered various aspects: Perception of Behavior (HBM theory) in statements 1–5, intrapersonal factors (motivation and knowledge) in questions 6–10, interpersonal factors (family support) in questions 11–13, disease and treatment characteristics in questions 14–20, and environmental factors (treatment access) in question 21. It incorporated inputs from keyword searches, expert and field panels, trials, and revisions to effectively represent all factors influencing medication adherence. Preliminary testing involved initial validation by experts, who assessed the instrument using a determinant assessment form.

The assessment yielded the values of CVI and CVR. The content validity was determined by its relevance to T2DM patient characteristics. The CVR values exceeded 0.75 for each criterion, and the CVI value was 1 for the entire instrument. While indicating instrument feasibility, field panelists suggest adding side effect examples and removing “health care facility.”^{9,31} The next stage in developing this instrument was the main field testing. The field trials were conducted on 30 DM patients in the Central Bogor Subdistrict, collecting quantitative data. The next step was to test the validity and reliability of the instrument. This stage entailed the revision of the determinant instrument because some question items were invalid but still reliable, the invalid questions were then re-modified.

Based on the results of the validity and reliability tests as well as the justification from the authors as an instrument, there were several modifications to the TSRQ motivational instrument, which was removing two invalid statements, statement number 2, “*I am challenged to do this,*” and statement number 18 “*Exercise regularly and paying attention to food is my choice.*” In the DKQ-24, there were ten invalid questions. However, because this questionnaire assessed the respondents' knowledge and the questions looked simply, no modifications were made. Except for “Shaking and sweating are a sign of high blood sugar levels,” it was modified to “Shaking is a sign of high blood sugar levels” because one or both symptoms may arise.³¹⁻³⁴

The operational field testing involved retesting the invalid determinant instrument with 30 respondents. The validity and reliability testing showed that all questions had a higher r count value than the r table value, indicating their validity and reliability. The Cronbach's alpha value was found to be 0.731, further confirming its reliability. The final instrument was published after revisions, incorporating all valid and reliable questions, resulting in a comprehensive determinant instrument. This instrument demonstrated validity and reliability, as confirmed through expert panel activities, with a CVR and CVI value of 1 and a final Cronbach alpha value of 0.731. It consisted of 21 questions covering all determinant as-

pects of medication adherence, surpassing previous questionnaires in motivation and knowledge assessment.^{35,36}

Further development is required for this study. The results of the instrument are still in the pilot stage and need to be further assessed for implementation into the population, particularly in streamlining the determinant instrument for medication adherence. The instrument consists of 73 questions alongside the ARMS medication adherence assessment. To enhance respondent convenience requires simplification. Implementing medication adherence determinants independently without the ARMS instrument is challenging, a combined instrument is essential. Additionally, the completion time for the instrument for a single patient range from 30 to 60 minutes, emphasizing the need for practical guidelines and digital design to align with technological advancements and facilitate ease of use.^{37,38}

Conclusion

A breakthrough—a trustworthy instrument for assessing medication adherence in T2DM—has been made as a result of meticulous study and teamwork. Its credibility is ensured by the fact that it was developed by specialists and based on study insights. The right demographic must be targeted while using precision to get maximum effectiveness. Increasing the sample size and participation can improve accuracy and produce robust, representative results that reflect adherence practices.

Abbreviations

DM: Diabetes Mellitus; ARMS: Adherence to Refill and Medication Scale; T2DM: Type 2 Diabetes Mellitus; CVI: Content Validity Index; CVR: Content Validity Ratio; TSRQ: Treatment Self-Regulation Questionnaire; DKQ-24: Diabetes Knowledge Questionnaire-24; PHC: Primary Health Care; HBM: Health Belief Model.

Ethics Approval and Consent to Participate

The development of this determinant instrument has received approval and passed an ethical review from the ethical commission of the Faculty of Medicine, Universitas Indonesia, No. KET-379/UN2.F1/ETIK/PPM.00.02/2022.

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 and materials in this study are available and may be requested from the corresponding author.

Authors' Contribution

IP: Assisted with developing the research question, conducted a litera-

ture review, designed the survey tool, led the data collection, and assisted in interpreting the findings, as well as took the lead role in writing the final written report. RS: Reviewed and assisted with the design of the survey tool, reviewed the Ethics Application, assisted with data entry, led the data analysis, facilitated the research team in an interpretation of the findings, and reviewed the draft of the written report.

RADS: Statistician, assisted in developing the research question, reviewed and contributed to the survey design, assisted in interpreting the survey findings relevant to the clinical community, reviewed and contributed to drafts of the written report. WR: Assisted in the research process throughout the Health Development and Research Agency of the Indonesian Ministry of Health for data research and in developing the survey tool. FSR: Provided writing assistance, set up tables and references, made format adjustments, and edited the content of each section.

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Workload and Stress Level in Non-COVID-19 Zoning Nurses at National Central Public Hospital Jakarta

Zakiah¹, Ulfah Nuraini Karim¹, Aliana Dewi¹, Siti Nuraini², Aan Sutandi¹, Rony Darmawansyah Alnur^{3*}

¹Department of Nursing, Universitas Binawan, Jakarta, Indonesia, ²Cipto Mangunkusumo National Central General Hospital, Jakarta, Indonesia, ³Department of Public Health, Faculty of Health Science, Universitas Muhammadiyah Prof DR. Hamka (UHAMKA) Jakarta, Indonesia

Abstract

The COVID-19 pandemic has increased the workload for nurses directly handling COVID-19 patients and those working in non-COVID-19 zones. As the number of COVID-19 cases rises, nurses face psychological problems, including stress. This study aimed to determine the relationship between workload and stress levels in a non-COVID-19 zoning ward using a cross-sectional approach and Spearman's correlation test conducted on 94 nurses at one hospital in Jakarta, Indonesia, selected through simple random sampling. The workload questionnaire with 15 items and the DASS 42 questionnaire were used to measure stress levels. The results indicated that most nurses (73.4%) experienced a heavy workload. Regarding stress levels, most nurses (66%) reported severe stress, while a small number experienced mild (2.1%) and moderate stress (2.1%). The Spearman's test revealed a significant relationship between workload and stress levels in the non-COVID-19 zoning ward (p -value = 0.001). Based on these findings, hospitals are urged to effectively manage nurses' workload during the COVID-19 pandemic and implement specific interventions for nurses experiencing occupational stress.

Keywords: COVID-19, nurse, occupational stress, workload

Introduction

Stress is the response of both the body and mind to the pressures imposed by the surrounding environment on an individual. In a work setting, individuals may experience feelings of inadequacy, pressure, and boredom, which can lead to reduced productivity and adverse effects on their work unit or company.¹ Extended periods of stress can affect various aspects and systems within a person's body, resulting in emotional, cognitive, physiological, and behavioral consequences.² These emotional impacts may manifest as anxiety, depression, physical tension, and psychological strain.³

The results of a survey conducted by PricewaterhouseCoopers (PwC) among several employees during the coronavirus disease 2019 (COVID-19) pandemic in 2020 explained that in the United States, the decline in work productivity ranked third among the concerns, following financial impacts and the potential for a global recession.⁴ Frontline workers' jobs required them to be close and frequently interact with the general public, which increased their risk of getting infected with the COVID-19 virus.⁵

In a survey by the Indonesian National Nurses Association, 51% of nurses reported experiencing occupational stress, which manifested in exhaustion, unfriendliness, frequent headaches, and insufficient rest due to heavy workloads and inadequate income.⁶ If left unaddressed, this situation may lead to more severe consequences. Based on data from the Indonesian Ministry of Health in 2019, there were approximately 345,508 nurses in the country, meaning there is a high potential for a prevalence of nurse stress.⁷ These data highlight the importance of occupational stress as a significant issue in the working world, affecting both work productivity and personal life.

Although all professional staff are at risk of experiencing occupational stress, those in the health care sector have a particularly high prevalence, with nurses experiencing among the highest levels.⁸ Nurse occupational stress is a condition that results from an individual's subjective appreciation, involving interactions between individuals and their work environments that may threaten and pressure nurses psychologically, physiologically, and behaviorally.⁹ This issue is due to nurses' direct interact-

Correspondence*: Rony Darmawansyah Alnur, Department of Public Health, Faculty of Health Science, Universitas Muhammadiyah Prof DR. Hamka (UHAMKA) Jakarta, Indonesia, Email: ronyalnur@uhamka.ac.id, Phone: +62 853-9954-4788

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ions with patients with various diagnoses and responses. The high stress experienced by nurses at work leads to feelings of saturation and boredom, ultimately affecting work productivity and decreasing both nurses' performance and patient care.¹⁰

However, work-life balance is the most significant factor contributing to nurse stress.¹¹ The increasing number of COVID-19 cases can also add to the nurses' workload, both physically and mentally, leading to occupational stress among nurses. Nurses' roles and responsibilities become challenging when protecting themselves, their colleagues, and their families from this deadly infectious disease.¹²

The impact of occupational stress can be either beneficial or detrimental. Although some stress may motivate employees to work with enthusiasm, unresolved stress may have negative consequences, including physical issues such as increased cholesterol and coronary heart disease; psychological factors, such as moodiness, low trust, and irritability; and organizational factors, such as tardiness, low work achievements, sabotage, and absenteeism.¹³ In general, occupational stress has a negative impact on both employees and companies or organizations. Employees may experience decreased enthusiasm for work, heightened anxiety, frustration, and other adverse consequences. These consequences affect work activities and may extend to other areas outside of work, such as sleep disturbances, reduced appetite, difficulty concentrating, and more.¹⁴

As the number of COVID-19 cases in Indonesia, especially Jakarta, continues to rise, several hospitals have transformed into COVID-19 referral hospitals.¹⁵⁻¹⁷ Every patient admitted to the wards must undergo a polymerase chain reaction (PCR) swab test with a negative result before admission.¹⁸ After a few days of treatment, many patients often begin to exhibit COVID-19 symptoms and test positive in a follow-up PCR swab test. This condition leads health workers in non-COVID-19 zones who frequently care for patients to be confirmed positive without symptoms.¹⁹

From the above explanation, COVID-19 cases significantly impact those on the frontline of handling this disease, especially nurses who have direct and indirect contacts with patients and may experience stress and depression, which they may not even realize. If this issue persists, it can lead to a decrease in work performance. For these reasons, this study aimed to examine the relationship between workload and stress levels among nurses in the non-COVID-19 zoning ward.

Method

This study employed a quantitative approach with a cross-sectional design. This design investigated the correlation between independent variables (exposure or risk

factors) and dependent variables (outcomes or effects) by collecting data simultaneously at a single point in time. This study was conducted from October to December 2021. The target population consisted of all zoning nurses, totaling 558 individuals who were currently active in their roles. The sample size comprised 94 nurses selected using the simple random sampling method based on predetermined inclusion and exclusion criteria.

The data-collection technique involved distributing online questionnaires to the respondents. The collected data were tabulated, and univariate analysis was performed to describe the demographic characteristic variables (age, sex, education, marital status, and length of service), workload, stress level, anxiety, and depression. Furthermore, bivariate analysis was conducted using Spearman's correlation test to establish the relationship between workload and stress levels among non-COVID-19 zoning nurses.

Results

In the univariate analysis conducted on the respondents' characteristics, it indicated that most nurses were female and married (80.9%) and between 26 and 35 years old (68.1%). Regarding the education variable, most held a Diploma III of Nurse qualification and worked for over six years (Table 1). Moreover, Table 2 shows most nurses in this study experienced a heavy

Table 1. Distribution Based on the Respondents' Characteristics (n = 94)

Variable	Category	n	%
Age (years)	≤25	3	3.2
	26-35	64	68.1
	36-45	18	19.1
	46-55	9	9.6
Sex	Male	18	19.1
	Female	76	80.9
Education	Diploma III of Nursing	73	77.7
	Bachelor of Nursing	21	22.3
Marital status	Married	76	80.9
	Single	18	19.1
Length of service	<6 years	23	24.4
	6-10 years	37	39.4
	>10 years	34	36.2

Table 2. Distribution Based on the Workload and Stress Level of the Respondents

Variable	Category	n	%
Workload	Light	6	6.4
	Moderate	19	20.2
	Heavy	69	73.4
Stress level	Normal	3	3.2
	Mild	2	2.1
	Moderate	2	2.1
	Severe	25	26.6
	Very severe	62	66

Table 3. Correlation Between Workload and Stress Level

Workload	Stress Level												p-value
	Normal		Mild		Moderate		Severe		Very Severe		Total		
	n	%	n	%	n	%	n	%	n	%	n	%	
Light	3	3.2	2	2.1	1	1.1	0	0	0	0	6	6.4	0.001
Moderate	0	0	0	0	1	1.1	11	11.7	7	7.4	19	20.2	
Heavy	0	0	0	0	0	0	14	14.9	55	58.5	69	73.4	

workload (73.4%). On the other hand, fewer nurses had light and moderate workloads (6.4% and 20.2%, respectively). Finally, most nurses in this study experienced very severe stress (66%), and only 3.2% experienced normal stress.

Based on the cross-tabulation results (Table 3), it was observed that most nurses had a heavy workload (73.4%). Among them, 55 nurses (58.5%) experienced very severe stress, while 14 nurses (14.9%) reported severe stress. This study also revealed that 19 nurses (20.2%) had moderate workloads, of whom 11 (11.7%) experienced severe stress, seven (7.4%) experienced very severe stress, and one (1.1%) experienced moderate stress.

Moreover, the results indicated that a smaller proportion of nurses had a light workload (6.4%). Within this group, three nurses (3.2%) experienced normal stress, two (2.1%) reported mild stress, and one (1.1%) experienced moderate stress. The results obtained from Spearman’s test revealed a value of 0.001, with p-value = 0.001, which was smaller than the α value of 0.05. These results indicated a significant relationship between workload and stress levels, with a coefficient of 0.563, signifying a strong correlation between workload and stress levels.

Discussion

The heavy workload of nurses can be caused by several factors: age, sex, education, duties, and environmental differences.²⁰ This excessive workload significantly impacts the productivity of health workers and, of course, affects the productivity of nurses.²¹ The heavy workload experienced by nurses in the non-COVID-19 zoning ward was related to work demands amid the COVID-19 pandemic, during which nurses had to provide optimal service related to infection prevention and control measures for the safety of themselves and the community. The heavy workload caused stress for most nurses due to several factors, including that most nurses were 26–30 years old. Another influencing factor was the length of service, which, in this study, was mainly 6–10 years. Various events that workers experience may often help them ad-

just and improve their work quality.²²

Workload is the number of activities an individual or a group must complete within a specific period under normal circumstances.²³ This study revealed that most respondents faced a heavy workload while few experienced light and moderate workloads. The difference in workload was influenced by several factors, including internal factors such as age, sex, education, weight, height, nutrition, physical health, motivation, trust, job satisfaction, and aspirations.²⁰ External factors, however, include work organization, activities, tasks, and environmental differences.²⁰ According to a previous study, workload can be quantified when calculated based on the number of nursing actions performed to meet patient needs.²⁴ On the other hand, workload is qualitative when nursing work is regarded as a responsibility that must be executed optimally or professionally.^{25,26}

The Spearman’s test on the workload variable with stress levels showed a significant relationship between workload and stress levels. This result indicated that the heavier the workload, the more severe the stress level the nurses experienced. This finding was consistent with a study conducted in Semarang City that demonstrated a relationship between workload and occupational stress among nurses.²⁷ Another study in Jember District also found that workload impacted occupational stress among nurses.²⁰

The heavy workload experienced by nurses in the non-COVID-19 zoning ward was closely related to the work demands arising during the COVID-19 pandemic. Nurses were required to provide optimal service regarding infection prevention and control measures to ensure their safety and that of the community. The heavy workload contributed to stress among most nurses, which could be attributed to several factors, including the age and service experience of most of the nurses. The various experiences encountered while working can serve as valuable lessons for adjusting and enhancing the quality of work.²²

Conclusion

There was a significant relationship between work-

load and stress levels in the non-COVID-19 zoning ward. Therefore, nurses are expected to adhere to health protocols consistently, and hospitals are encouraged to manage nurses' workloads effectively during the COVID-19 pandemic. Additionally, special interventions should be provided for nurses who experience occupational stress.

Abbreviations

COVID-19: coronavirus disease 2019; PCR: Polymerase Chain Reaction.

Ethics Approval and Consent to Participate

This study has received approval and passed an ethical review from the ethical commission of the Faculty of Medicine, Universitas Indonesia, No. KET-972/UN2.F1/ETIK/PPM/00.02/2021.

Competing Interest

The authors declared 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 used in this study are available from the corresponding author upon reasonable request.

Authors' Contribution

Z led the study, contributed to the methodology and study design, and wrote the first manuscript draft. UNK, AD, SN, and AS provided resources, supervision, and study design and administration. RDA was involved in visualization, writing the substantial inputs, and editing the manuscript. All authors have approved the final version of the manuscript.

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Effects of Early Hospital-Based Palliative Care Consultation on Length of Stay and Costs of Care at Indonesian Tertiary Hospital

Rudi Putranto,^{1*}, Hamzah Shatri¹, Wulyo Rajabto², Sumariyono³, Edward Faisal¹, Sihwastuti⁴

¹Division of Psychosomatic and Palliative Medicine, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia – Cipto Mangunkusumo National Central General Hospital, Jakarta, Indonesia, ²Division of Hematology and Medical Oncology, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia – Cipto Mangunkusumo National Central General Hospital, Jakarta, Indonesia, ³Director of Medical Service and Nursing, Cipto Mangunkusumo National Central General Hospital, Jakarta, Indonesia, ⁴Nurse Manager of Palliative Care Team, Cipto Mangunkusumo National Central General Hospital, Jakarta, Indonesia

Abstract

Despite the numerous benefits of palliative care for cancer patients, there have been few studies on palliative care services for terminal cancer patients, particularly near the end of life. This study aimed to evaluate whether there were differences in length of stay and cost of care associated with how early or late a patient received palliative care intervention. Another objective was to compare the length of stay and cost of care of those who received palliative care intervention and those who did not. This study used a cohort retrospective design at Hospital A, Jakarta, Indonesia, from January to December 2019. The diagnosis of terminal cancer was based on medical records. Data on length of stay and costs of care were based on medical records and finance billing. The hospitalized terminal cancer patients (392) were recruited by consecutive sampling. The length of stay and costs of care for patients with advanced cancer who received palliative care consultations were longer and higher than for patients who did not receive them. However, if palliative care consultation is provided early, the increase in length of stay and costs are less.

Keywords: costs of care, early consultation, hospital-based palliative care, length of stay

Introduction

Palliative care (PC) is the active, holistic care of people of all ages suffering from disease or injury. Health-related suffering is substantial when it cannot be eased without medical intervention and interferes with physical, social, spiritual, and/or emotional functioning.¹ The PC is an interdisciplinary medical service to reduce the pain and suffering of patients with life-threatening illnesses and limited life expectancy. According to the World Health Organization (WHO), PC is appropriate for both cancer and non-cancer patients.²

The PC arose with the formation of the contemporary medical paradigm as a blossoming specialty of clinical medicine that garnered widespread attention in many nations. Unlike traditional anticancer treatment, which focuses on killing and inhibiting cancer cell reproduction and metastasis through chemotherapy, radiotherapy, surgery, and/or hormone therapy, PC aims to anticipate, prevent, and reduce suffering through patient- and family-centered health care. An interdisciplinary PC team typically designs hospital-based interventions to help patients and their families better understand the

prognosis and treatment options, clarify care goals, and assist in disease progression planning.^{3,4}

The increasing number of cancer patients will increase palliative and end-of-life care needs.⁵ This health service is burdensome for hospitalized cancer patients because it costs more and prolongs their stay. A study on several Southeast Asian countries found an increasing number of cancer patients who required assistance from their respective governments due to their health-related and economic burdens.⁶ A study in the United States reported that implementing PC in hospitals will reduce the length of stay and cost for patients, prevent excessive or unnecessary examinations and procedure costs, and improve physical and psychological complaints.⁷

While, a study in China evaluating the quality of life of patients with advanced lung cancer showed improved quality of life compared to patients who received only standard treatment for their cancer.⁸ Another study in the Netherlands, which evaluated the impact of direct costs on hospitalized patients with advanced illnesses such as terminal cancer, chronic obstructive pulmonary disease, congestive heart failure, and HIV/AIDS, showed

Correspondence*: Rudi Putranto. Division of Psychosomatic and Palliative Medicine, Department of Internal Medicine, Universitas Indonesia – Cipto Mangunkusumo Hospital, Diponegoro Street No. 71, Jakarta 10450, Indonesia, Email: putranto.rudi09@gmail.com, Phone: +62 812-8532-3254

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benefits from implementing PC.⁹ Although many studies reported benefits in cost-effectiveness, one study reported the opposite.¹⁰

Several studies have shown that early palliative care consultation (PCC) in patients with terminal cancer in hospitals and communities may reduce costs of care and length of stay.^{8,9} There was very little data on early PCC in Indonesia by the time this study was conducted. Therefore, the main objective of this study was to evaluate whether there were differences in length of stay and cost of care in the early PC intervention group versus those who received palliative care intervention later (non-intervention group). Another objective was to compare the length of stay and cost of care in the intervention and non-intervention groups.

Method

This study used a cohort retrospective method, conducted in the inpatient unit of Hospital A, Jakarta, Indonesia, from January to December 2019. Several inclusion criteria included terminal cancer patients in stage IV with a life expectancy of 6–12 months, were aged ≥18 years, and, in the intervention group, had received at least one consultation with the palliative team. In a retrospective cohort study, data were gathered from records. This means the results had already happened; however, the fundamental study design remained largely the same. It started with the exposure and other factors at baseline and follow-up, then assessed the outcome during the course of the follow-up period.^{11,12}

The sampling method was consecutive sampling. Each patient with suitable criteria was included in this study until the required number of patients was fulfilled. The sample size used a significance level of 95% or $\alpha = 0.05$ and a power level of 90% or $\beta = 0.10$, and the observed outcome was the difference in hospitalization costs determined to have SD = 0.50 assumed value. The estimated difference between the mean outcome of the non-intervention group and the intervention group to palliative care (U0-U1) was 0.8 (referring to the study results by Johnston, *et al.*,¹³ and Pourhoseingholi, *et al.*,¹⁴); hence, the estimated minimum number of samples needed was 196 in each group. Patients were divided into intervention and non-intervention groups. Intervention patients had received at least one palliative team consultation, while non-intervention patients did not receive consultation.

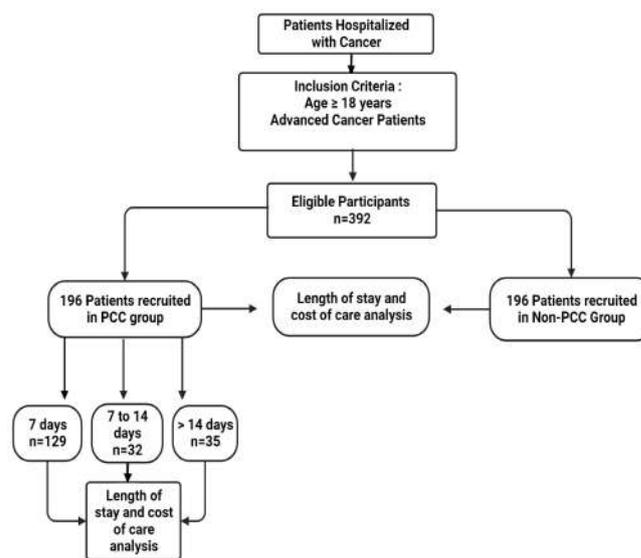
The intervention was a PCC with an interdisciplinary team of palliative care physicians assisting in the treatment of seriously ill patients through the identification and treatment of pain and other symptoms, clarifying treatment options, establishing goals of care and advance plans, and helping patients and family members select treatments that match their goals. The consultations were

initiated at the request of the attending physician. The variable or observed factors in this study consisted of the independent and dependent variables. The independent variable is a variable that affects or causes the change or emergence of the dependent variable.¹² In contrast, the dependent variable is a variable influenced or becomes the result of the independent variable.¹⁴ In this study, the independent variable observed was a PCC, and the dependent variables were the length of stay and costs of care for patients with terminal cancer at Hospital A, Jakarta, Indonesia.

The study instruments were patient medical records, finance billing, and questionnaires. One USD was equivalent to IDR 14,200 at the time of the study. Data were analyzed by univariate, bivariate, and multivariate analysis to obtain baseline data on respondent characteristics. To evaluate the differences between the length of stay and costs of care in terminal cancer patients based on consultation with the palliative team, the Mann-Whitney Test was used. The ANOVA and non-parametric post-hoc tests were used to evaluate the differences in the cost of care and length of stay. Consultation times were divided into three groups: less than seven days, 7–14 days, and more than 14 days. Data were analyzed using SPSS 20.0 software by IBM under the licensed of the Faculty of Medicine, Universitas Indonesia.

Results

Table 1 shows the subject characteristics of the study, and Figure 1 shows a total of 392 hospitalized patients



Note: PCC = Palliative Care Consultation

Figure 1. Study Recruitment and Sampling Technique

with terminal cancer recruited by consecutive sampling. One hundred and ninety-six participants were recruited for the intervention and non-intervention groups: 61.7% were female in the intervention group, and 51.6% were male in the non-intervention group. The mean age of both groups was 53 years. The most common types of cancer were cervical in the intervention group and nasopharynx in the non-intervention group.

Table 2 shows the length of stay for the PCC group was longer (12 days versus 6 days) and the cost of care for all services (doctor visits, accommodation, medication, radiology, laboratory, and procedure) was higher than in the group that did not receive PCC (USD 2,008.07 versus 725.42). Stepwise multivariate linear regression analysis revealed that length of stay was independently associated with doctor visits ($\beta = 0.125$, p -value = 0.031) and radiology examinations ($\beta = 0.132$, p -value<0.001). At the same time, the cost of care was independently associated with doctor visits ($\beta = 0.069$, p -value<0.001), accommodation ($\beta = 0.167$, p -value<0.001), medication ($\beta = 0.386$, p -value<0.001), radiology ($\beta = 0.083$, p -value<0.001), laboratory ($\beta = 0.115$, p -value<0.001), and procedure ($\beta = 0.337$, p -value<0.001).

Table 3 shows the distribution of consultation time concerning the cost of care and length of stay of the

patients who received PCC. Consultation times of less than seven days were most common, followed by more than 14 days, and finally 7–14 days. The analysis found that the longer the patients were consulted, the more the cost of care and length of stay were affected.

After conducting a subgroup analysis in the PCC group, the length of stay and cost of care for the early

Table 1. Characteristic of Respondent

Variable	Category	Palliative Care Consultation	
		Yes (n = 196)	No (n = 196)
Sex	Male	75 (38.3)	110 (56.1)
	Female	121 (61.7)	86 (43.9)
Age (years)	Min-max	53 (21–85)	53 (19–84)
Type of cancer	Nasopharynx	16 (8.2)	60 (30.6)
	Breast	25 (12.5)	12 (6.1)
	Lung	16 (8.2)	5 (2.6)
	Hepatic cancer	17 (8.7)	9 (4.6)
	Cervical	32 (16.2)	12 (6.1)
	Colon	15 (7.7)	9 (4.6)
	Sarcoma	7 (3.6)	12 (6.1)
	Bladder	2 (1.0)	3 (1.5)
	Prostate	3 (1.5)	1 (0.5)
	Kidney	1 (0.5)	0 (0)
	Ovary	9 (4.6)	5 (2.6)
	Blood	15 (7.7)	36 (18.4)
	Other cancers not listed above	38 (19.4)	32 (16.3)

Table 2. Length of Stay and Costs of Care

Variable	Palliative Care Consultation*		p-value
	Intervention	Non-Intervention	
Length of stay (days)	12 (1–91)	6 (1–31)	<0.001
Doctor visit cost (SD)	82.51 (0–1,261.55)	32.96 (0.99–531.85)	<0.001
Accommodation cost	232.40 (25.21–3,461.82)	112.17 (0–3,155.37)	<0.001
Medication cost	571.14 (19.22–8,394.82)	278.28 (2.54–3,182.38)	<0.001
Radiology cost	69.42 (0–1,537.39)	00 (0–817.59)	<0.001
Laboratory cost	260.55 (32.40 – 2,105.12)	60.83 (0 – 1,209.82)	<0.001
Procedure cost	4,035.76 (7.31–5,721.09)	147.47 (0–4,735.47)	<0.001
Total cost	2,008.07 (264.56–17,910.59)	725.42 (109.37–10,807.05)	<0.001

Notes: *Median (Minimum-Maximum), SD = Standard Deviation, All the cost is in USD

Table 5. Distribution of Consultation Time Concerning Costs of Care and Length of Stay in Patients with Palliative Care Consultation (n = 196)

Consultation Time	n (%)	Costs of Care (USD)	Length of Stay (Days)
<7 days	129 (65.8)	Mean: 21,324.17 Median: 1,387.80 Min-Max: 264.56–17,910.59	Average: 10.6 Median: 8 Min-Max: 1–91
7-14 days	32 (16.3)	Mean: 3,769.73 Median: 3,281.13 Min-Max: 412.23–17,071.30	Average: 17.8 Median: 15.5 Min-Max: 1–43
>14 days	35 (17.9)	Mean: 6,467.53 Median: 5,138.43 Min-Max: 476.43–15,599.54	Average: 29.17 Median: 28 Min-Max: 2–59

Table 4. Comparison of Length of Stay and Costs of Care Variables in Palliative Care Consultation

Variable	<7 vs. 7-14 days	<7 vs. >14 days	7-14 vs. >14 days
Length of stay*	0.003	<0.001	<0.001
Costs of care*	0.014	<0.001	<0.001

Note: *Mann-Whitney test

consultation subgroup (less than seven days) significantly differed from the 7–14 days subgroup and the more than 14 days subgroup, as shown in Table 4.

Discussion

The most common type of cancer in the group received consultations by the palliative team was cervical cancer; in the group that did not receive consultations, it was nasopharynx cancer. According to the WHO, in 2018, the most common types of cancer worldwide were lung, breast, colorectal, prostate, skin, and stomach cancer. Almost 80% of patients with cancer were in a terminal condition.¹⁵

This study showed that patients who received PCC had longer stays and higher hospitalization costs. The length of stay was almost the same as in Australia. The average length of stay was nearly twice as long as for all overnight hospitalizations (excluding same-day stays): 10 days (9.2 days for palliative care and 11.1 days for other end-of-life care) against 5.3 days for all hospitalizations.¹⁶ Studies by May, *et al.*, and Subramaniam, *et al.*, showed the economic benefits of reducing hospitalization costs.^{7,17}

This study found that those receiving early PCC (less than seven days) had a shorter length of stay and less cost than those receiving PCC later than seven days. These results were in line with a study by Fitzpatrick, *et al.*, reporting that early palliative intervention would be correlated with financial savings.¹⁸ The study reported that patients referred early had significantly shorter mean lengths of stay (4.5 days) and lower in-hospital mortality compared to those referred late, who had an average length of stay of 7.4 days.¹⁸

The recommendation by the American Society of Clinical Oncology and Oncology Nursing Society is that a consultation with the palliative team should be carried out for cancer patients with metastases and worsening symptoms.¹⁹ Clinicians were often late in connecting patients with the palliative team when patients' condition was poor. Also, there was an increased risk of death after various diagnostic or therapeutic interventions had been carried out.

Following a subgroup analysis in the PCC group, it was discovered that early consultation (less than seven

days) led to significantly different results than consulting from 7–14 days and later than 14 days. This study supported a previous systematic review stating that early palliative care interventions may have a greater impact on quality of life and symptom intensity in patients with advanced cancer than usual/standard cancer care alone.²⁰ A study by Zaborowski, *et al.*, of 711 patients revealed that the pilot group's pre-consult length of stay was reduced from 4.8 days to 3.7 days, direct cost savings were 26%, and the pilot group had a 2-day reduction in overall length of stay compared to the baseline and control groups.²¹

A study by Chanthong, *et al.*, showed the palliative care unit was associated with cost savings in caring for terminally ill patients in a tertiary hospital in Thailand.²² To improve early PCC, hospitals use screening tools. In Indonesia, three assessments have been validated to be used in hospitals as aids for identifying patients who require palliative care.²³⁻²⁵ According to a public health specialist, physicians and nurses are often cautious about discussing patients' care preferences near the end of life.

End-of-life care is as important as politicians assume, but not for the reasons frequently provided.²⁶ Efforts on end-of-life care have to be doubled to better understand the needs of patients with terminal illnesses; so that patients can receive intensive treatment if they want it and assistance in enabling a more peaceful death when they do not; healthcare providers must learn how to manage that transition. It is vital not to get sidetracked by promises of cost savings along the way.²⁶

This study had several limitations: the psychosocial, functional, and spiritual aspects were not evaluated. The risk of bias was reduced by limiting the inclusion and exclusion criteria. The advantage of this study was that the sample matched the sample size calculation. Moreover, studies on the length of stay and hospitalization costs of terminal cancer patients receiving palliative care intervention are still limited in Indonesia.

Conclusion

In the PCC group, those receiving early consultation have a shorter length of stay and lower costs of care. The length of stay and costs of care for patients with advanced cancer who receive PCC are longer and higher

than for patients who do not. This study suggests to hospital management that patients with progressive or advanced cancer should consult the palliative team immediately to reduce the length of stay and hospitalization costs. Further studies are needed to evaluate indirect costs and different service units.

Abbreviations

PC: Palliative Care; WHO: World Health Organization; PCC: Palliative Care Consultation.

Ethics Approval and Consent to Participate

Ethics approval was obtained from the Research Ethics Committee of the Faculty of Medicine, Universitas Indonesia, and Cipto Mangunkusumo Hospital No.: KET-362/UN2.F1/ETIK/PPM.00.02/2019.

Competing Interest

The authors declared no conflicts of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

Availability of Data and Materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Authors' Contribution

RP designed the study and collected data, and HS contributed to the analysis and writing. RP, HS, WR, S, EF, and S contributed to the manuscript's writing.

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Risk Factors of Worsening of Systemic Lupus Erythematosus in Patients at Two Tertiary Hospitals in Jakarta

Giri Aji¹, Ratna Djuwita², Mondastri Korib Sudaryo^{2*}, Sukamto³

¹Doctoral Study Program, Department of Epidemiology, Faculty of Public Health, Universitas Indonesia, Depok, Indonesia, ²Department of Epidemiology, Faculty of Public Health, Universitas Indonesia, Depok, Indonesia, ³Department of Internal Medicine, Cipto Mangunkusumo National Central General Hospital, Jakarta, Indonesia

Abstract

Systemic Lupus Erythematosus (SLE) is a prototypical multiorgan autoimmune disease with a fluctuating and chronic disease course. As an emerging disease in this century, SLE will burden stakeholders and the country. This study was conducted to determine the prognostic factors for SLE worsening, especially in ambulatory patients. This ambispective study used logistic regression to view the risk factors for worsening SLE in patients. Anemia, age, body mass index, education level, employment status, marital status, hydroxychloroquine, and immunosuppressants were the independent variables in this study. This study concludes that anemia is statistically significant and, therefore, a risk factor for worsening SLE in patients (RR = 5.31; p-value < 0.005), while age, body mass index, education level, employment status, marital status, hydroxychloroquine, and immunosuppressants are not statistically significant.

Keywords: anemia, risk factor for flare, systemic lupus erythematosus

Introduction

Systemic Lupus Erythematosus (SLE) is a chronic, systemic, and debilitating multiorgan autoimmune disease. Five million people have lupus worldwide.¹ The history of lupus begins with Hippocrates describing ulcers (suspected to be lupus) as herpes esthiomenos in 200 BC.² The SLE can attack various organs: the skin, with manifestations of malar rash; the kidneys (nephritis); blood, with manifestations of autoimmune hemolytic anemia or thrombocytopenia; the musculoskeletal system (arthritis); and the central nervous system (myelitis, psychosis).² Currently, no drug has been found to cure SLE. Management of this disease aims to keep it under control or in remission, although there has been no clear definition of remission in SLE. Women of reproductive age suffer from SLE more than men.³

In SLE, many autoantibodies are produced by B lymphocytes, and the diagnosis of SLE is usually based on their presence. Some autoantibodies seem to attack specific organs. As a protein produced by the body (but which attacks the body itself), the antibodies lose the ability to recognize themselves (self-recognized) and combine with blood complement to form immune complexes that deposit in tissues and trigger inflammation. This is what underlies the concept of autoimmunity.⁴

Experts have developed many instruments to assess lupus disease activity globally. Some instruments, like the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) and the British Isles Lupus Assessment Group (BILAG), include questions about the conditions of the organs affected by lupus, which are given the appropriate score (weighted).⁵ End organ damage or organ damage in lupus occurs due to continuous attacks by autoantibodies. This commonly happens in uncontrolled SLE or flares. The damage may occur in various systems, such as neuropsychiatry, renal, or hematology. Besides the disease activity, organ damage can be due to lupus therapy, such as glucocorticoids, which trigger osteoporosis, or hydroxychloroquine, which leads to retinal disorders.⁶

Corticosteroids have become the main choice for treating lupus in the last 60 years. Pulse steroid doses adopted by internists for kidney transplant patients have become the standard therapy for lupus patients experiencing a flare. While, oral administration is still favorable, but the side effects of steroids remain a problem for SLE patients. Other medicines taken to treat lupus are immunosuppressants, such as azathioprine, cyclosporine, and antimalarial hydroxychloroquine. They have been taken for a long time for the SLE treatment.⁷

Based on the 2013 Indonesian Ministry of Health

Correspondence*: Mondastri Korib Sudaryo, Department of Epidemiology, Building A 1st Floor, Faculty of Public Health, Universitas Indonesia, Kampus Baru UI Depok, Depok City 16424, Indonesia, E-mail: maqo1@ui.ac.id, Phone: +62-21 7884-9031 or +62-21 786-3474

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reports, there is no prevalence of SLE in the Indonesian people.⁸ Crude prevalence was around 4.3 to 45.3 per 100,000 people.⁹ Mok, *et al.*, reported that Asian SLE has different variations of Fcγ receptors from Caucasian SLE, which causes Asian SLE patients to have higher organ damage scores than Caucasian patients.¹⁰ It is related to IgG and lupus nephritis; while, renal outcomes and levels of immunosuppressant usage among Asians are the same as among African people. It means that they also experience worse conditions than Caucasians. Besides, socioeconomic factors, including access to health facilities, education, cultural factors, and beliefs, also affect the overall outcomes of SLE patients in Asia.¹¹ A previous study stated that conditions including cytopenia or major organ involvement, such as nephritis, trigger flares in lupus.¹²

Crampton proposed a pathophysiological model of SLE (Figure 1).¹³ It was a presentation of an unknown antigen to MHC class II that would cause the priming of CD4 cells, leading to class switching and maturation of B cells in the germinal center. They were autoreactive, becoming plasma cells that produced soluble IgG isotype autoantibodies. The autoantibodies would bind to autoantigens and become immune complexes or bind to complement and Fcγ receptors on other cell types. This supports inflammation and tissue damage by recruiting inflammatory cells to the tissue. Cells that undergo apoptosis will be taken by macrophage cells and be a new autoantigen that continues to lymphocyte priming and auto activity. Also, TLR activation by environmental influences like a viral infection or cell damage by ultraviolet (UV) light contributes to the above process through the secretion of IFN-1 and other cytokines that trigger the autoreactivity of lymphocytes and network damage.¹³

Human leukocyte antigens, or HLA-DR (D-antigen related), is a group of genes on chromosome 6 that produce proteins on the cell surface called major histocompatibility complex class II (MHC class II).¹³ They are originally associated with organ transplantation. A study in Saudi Arabia found that the HLA-A*29 gene was related to SLE (OR = 2.07; 95% CI = 1.03–7.08), HLA-DRB1*15 haplotype (OR = 2.01; 95% CI = 1.20–3.68, P = 0.008), and HLA-DQB1*06 (OR = 1.67; 95% CI = 1.19–3.36, P = 0.0032). HLA-DRB1*16 is negatively associated with SLE disease (OR = 0.18; 95% CI = 0.02–1.3, P = 0.055).¹⁴ While, a study in Malaysia found that HLA-DR2, DQB1*0501, and DQB1*0601 had a significant relationship with SLE (pcorr=0.03, rr = 3.83; pcorr = 0.0036 rr = 4.56; pcorr = 0.0048, rr = 6).¹⁵

This study aimed to look for risk factors for the worsening of SLE in patients undergoing outpatient care. The risk factors were based on the patients' ages, education levels, employment status, hemoglobin levels, and

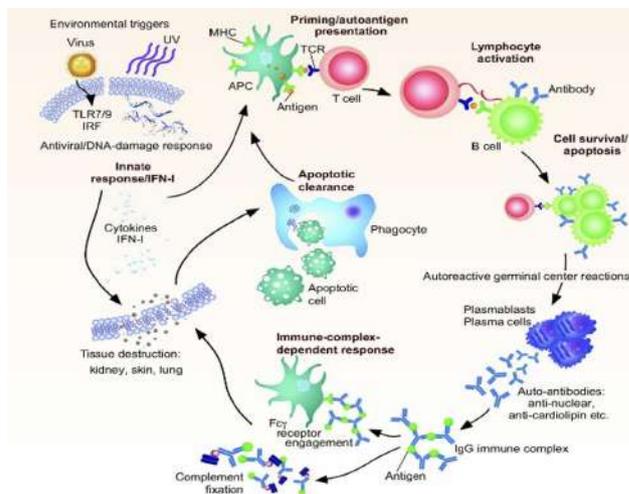


Figure 1. Disease Model and Mechanism¹³

administration of hydroxychloroquine and immunosuppressants. Due to the absence of genetic data on SLE patients in Indonesia, the genotyping analysis will be carried out on the subpopulation of study subjects as a form of descriptive data.

Method

The participants were 82 patients with SLE followed in an ambispective cohort study. A total of 22 subjects followed in a prospective cohort study, and 60 followed in a retrospective cohort study. The inclusion criteria were SLE patients diagnosed with the American College of Rheumatology 1997 criteria. While, the criteria for worsening was an increase in the SLEDAI, with a score of three or higher with a minimum of three months between the first and second measurements. The examined variables were anemia—defined as hemoglobin level <10 g/dL—education level, hydroxychloroquine, immunosuppressants, and employment status. The bivariate and multivariate methods aimed to check the significance of the relationship between the variables. The genotyping examination used the DNA typing PCR-based labeled sequence-specific oligonucleotide (SSO) that can read up to two digits.

Results

All of 82 participants were female (100%). Their average age was 33.3, with a maximum age of 55, and the youngest was 19. As many as 62 subjects (75.61%) were under 40, and 20 (24.39%) were over 40. Most respondents attended high school (47.56%), did not work formally (80.49%), and were married (60.98%). As many as 28.05% had a body mass index (BMI) of

≥25 (abnormal). Most respondents were not anemic (84.15%), and 64.63% received treatment with hydroxychloroquine. While, 68.29% received treatment with immunosuppressants, and 14.63% experienced an increase in the SLEDAI by three points.

Patients with SLE aged <40 years had a 1.61 times higher risk of worsening than those aged ≥40. Patients with SLE who work were at a 1.55 times higher risk, and patients without higher education were at a 1.48 times higher risk of worsening. While, based on the results of this study, being single/a widower/a widow was a protective factor against worsening, with an RR of 0.59 compared to married patients, and abnormal BMI (BMI≥25) was also a protective factor against worsening of SLE disease activity, with RR 0.24; however, all the variables above were statistically insignificant, with p-

value>0.05.

Another factor, anemia, was a risk factor for worsening in SLE patients with RR 5.31. However, in treating patients with the medicine, patients not given hydroxychloroquine had 1.31 times the flares/worsening, but immunosuppressants were protective factors against disease worsening, with RR 0.43. Statistically, the results of this bivariate analysis were only significantly related to the anemia variable, with a p-value of 0.003.

In contrast, other variables, such as age, education level, employment status, marital status, BMI, hydroxychloroquine, and immunosuppressants, produced p-values of >0.05, which were not statistically significant statistics. In this study, the predictor factor for worsening SLE activity in patients was statistically significant anemia. Patients who were anemic (indicated by Hb <10) had a higher risk of worsening the SLEDAI score (95% CI = 0.02–0.29).

Table 1. Respondents' Characteristic (N = 82)

Variable	Category	N	%
Age	≥40 years	20	24.39
	<40 years	62	75.61
Education	Elementary school	3	3.66
	Junior high school	6	7.32
	Senior high school	39	47.56
	Higher education	34	41.46
Employment status	Unemployed	66	80.49
	Employed	16	19.51
Marital status	Married	50	60.98
	Single/Widow/Widower	28	34.15
	Missing (no data)	4	4.88
BMI	BMI ≥25	55	67.07
	BMI >25	23	28.05
	Missing (no data)	4	4.88
Anemia	Not Anemia (Hb ≥10)	69	84.15
	Anemia (Hb <10)	13	15.85
Medication	Without Hydroxychloroquine	29	35.37
	With Hydroxychloroquine	53	64.63
	Without Immunosuppressant	26	31.71
	With Immunosuppressant	56	68.29
Genotype HLA (N = 19)	DRB1*12 DRB1*12	3	15.79
	DRB1*15 DRB1*15	6	31.58
	DRB1*12 DRB1*14	2	10.53
	DRB1*12 DRB1*15	2	10.53
	DRB1*7 DRB1*16	1	5.26
	DRB1*8 DRB1*15	1	5.26
	DRB1*7 DRB1*15	1	5.26
	DRB1*7 DRB1*12	1	5.26
	DRB1*14 DRB1*15	1	5.26
	DRB1*8 DRB1*12	1	5.26

Notes: Hb = Hemoglobin, BMI = Body Mass Index, HLA DR = Human Leucocyte Antigen

Table 2. Incidence of Worsening/Flare (N = 82)

Variable	Category	N	%
Worsening (Flare)	Not Flare	70	85.37
	Flare	12	14.63

Discussion

All respondents in this study were women. A previous study stated that women with lupus have a higher frequency than men (9:1 ratio).¹⁶ This is generally associated with differences in hormones and chromosomes; however, no studies can explain this with certainty. The average age of the respondents was 33.3. Although SLE can affect women in all age groups, a cross-sectional study in Germany showed an increased incidence of SLE in women in the 20–25 age group, with a rate of 3.6 per 100,000 persons per year (95% CI = 2.9–4.3).¹⁷ However, there is a second peak of incidence at menopause (95% CI = 1.5–3.8).¹⁸

The most vulnerable age group for SLE was 20–39 years for women.¹⁹ The age demographic in this study is not very different from the previous study. However, a study in Hong Kong stated that Asian SLE patients have a higher possibility of experiencing renal complications than Caucasians.¹⁰ Asian lupus patients tend to have higher organ damage scores due to late diagnosis. It is also necessary to think about the availability of access to health facilities.¹⁰

It is estimated that 20–25% of lupus patients will experience flares in the first 1–2 years, and 40–60% will experience them after 5–10 years.²⁰ While, a study in Italy reported an incidence of flares in SLE patients who were followed for the first year (5–7%).²¹ The incidence of flares (worsening) in this study was 14%, which is rather high compared to the incidence of flares in the Italian population. A previous study reported that in the Caucasian population, education level also affects the mortality of SLE patients.¹¹ Caucasian lupus patients with high educational levels have lower mortality rates, but this phenomenon is not found in other ethnic groups (African-American and Asia-Pacific Islander).¹¹

Table 3. Correlation between Worsening of Lupus (Flare) with Age, Education Level, Employment Status, Marital Status, Body Mass Index, Anemia, Hydroxychloroquine, and Immunosuppressants Status (N = 82)

Variable	Category	Flare				RR	95% CI	p-value
		Yes		No				
		N	%	N	%			
Age	<40 years	10	16.13	52	83.87	1.61	0.39–6.75	0.721
	≥40 years*	2	10	18	90			
Education	Lower education	7	14.58	41	85.42	0.99	0.71–6.01	0.237
	Higher education*	5	14.71	29	85.29			
Employment	Employed	4	25	12	75	2.06	0.34–2.86	1.000
	Unemployed*	8	12.12	58	87.88			
Marital status	Single/Widow/Widower	5	10.71	25	89.29	0.67	0.19–2.32	0.737
	Married*	8	16	42	84			
BMI	BMI >25	1	4.35	22	95.65	0.24	0.03–1.76	0.160
	BMI ≤25*	10	18.18	45	81.82			
Anemia	Anemia (Hb<10)	6	46.15	7	53.85	5.31	2.02–13.92	0.003 ^{*)}
	Not anemia (Hb≥10)*	6	8.70	63	91.30			
Medication	Without HCQ	5	17.24	24	82.76	1.31	0.46–3.75	0.746
	With HCQ*	7	13.21	46	86.79			
	Without Immunosuppressants	2	7.69	24	92.31	0.43	0.10–1.85	0.322
	With Immunosuppressants*	10	17.86	46	82.14			

Notes: RR = Relative Risk, CI = Confidence Interval, HCQ = Hydroxychloroquine, Hb = Hemoglobin, BMI = Body Mass Index, *Reference, *) Significant (p-value<0.05)

Table 4. Multivariate Analysis for Predictor Factors for Worsening Systemic Lupus Erythematosus Patients

Variable	RR Adjusted	95% CI	SE	p-value
Anemia	5.3	2.02–13.91	0.701	0.00

Notes: RR = Relative Risk, CI = Confidence Interval, SE = Standard Error

Table 5. Mean Size of The Erythrocyte Index in 15 Subjects with Anemia

	MCV (fl)	MCH (pg)	MCHC (g/dL)
Mean	69.4	26.3	32.4

Notes: MCV = Mean Corpuscular Volume, MCH = Mean Corpuscular Hemoglobin, MCHC = Mean Corpuscular Hemoglobin Concentration

In this study, the variable that affected the worsening condition of the SLEDAI score (flare) was anemia, defined as Hb<10 g/dl. Voulgarelis stated that anemia of chronic disease, autoimmune anemia, and iron deficiency anemia are often found in SLE patients.²² Iron deficiency anemia is associated with SLE disease activity.²² In contrast, anemia of chronic disease tends to be stable with no remission, regardless of other components of disease activity.²² While, autoimmune anemia is due to a severe decrease in hemoglobin levels.²² Inflammatory cytokines, such as tumor necrosis factor α , interferon β , and interleukin 1, seem to influence anemia, especially anemia of chronic disease, by inhibiting the proliferation of erythroblast progenitors, altering iron metabolism,

and suppressing erythropoietin production. Immunohistochemical studies in lupus nephritis patients also found CD4 lymphocytes and macrophages infiltration in the kidney’s interstitial areas, suppressing renal erythropoietin production.²²

From Table 5, the result of the calculation of the average MCV in 15 subjects is 79.2 fl. Djulbegovic stated that an MCV value of lower than 100 has a high specific value for iron deficiency anemia (although a definite diagnosis requires bone marrow examination).²³ The iron deficiency anemia in the subjects seems to be related to Voulgarelis’ statement that iron deficiency anemia is affected by disease activity. In contrast, anemia of chronic disease is more stable during observation.²² However, differentiating iron deficiency anemia from anemia of chronic disease is not easy. The mechanism of why cytopenia (anemia in this study) causes a flare in lupus patients may have many different pathways. Considering pro-inflammatory cytokines may cause anemia, it could be hypothesized that anemia is only the surrogate factor for predicting flare in lupus patients.

The Indonesian Ministry of Health reports show that anemia prevalence in women aged ≥15 years is 22.7%.²⁴ Assuming that this population is at risk of becoming afflicted with SLE in the future, it is expected that the burden of treatment could rise. In this study, two other variables (being employed or working and younger age) also posed a higher risk for lupus worsening (flare). Although not statistically significant, this could be explained by the theory that UV B induced apoptosis of keratinocytes in the skin; autoantibodies in lupus patients

may recognize autoantigens from this apoptotic cell, which then induced inflammation in the respondents who were working (with more sun exposure than the nonworking subjects); and subjects of a younger age had relatively more active estrogen (estrogen is known to modulate immune system function) compared to older respondents, which in turn caused a higher chance of flares.^{20,21}

In this study, genotyping was done on 19 subjects, with the examination target of the HLA DR gene. The highest frequency of the HLA gene was class 2, HLA DRB1*15 DRB1*15, with a frequency of 18.75%. While, Niu, *et al.*, stated that the HLA DR-3 gene is related to SLE.²⁵ A study in Malaysia used the PCR method and found HLA DR2 and DQB 1 to be associated with lupus.¹⁵ With the high variation of HLA genes in lupus, it should be considered that the HLA genes have high polymorphism. Therefore, the immune system can recognize different kinds of peptides. Later, the immune system can recognize various strange peptides, which will be presented to T lymphocytes.²⁶ The HLA gene DRB1*15 is commonly associated with multiple sclerosis, an autoimmune disease that primarily attacks the nervous system, especially the myelin membranes, and which is characterized by fatigue, pain, balance disorders, and paralysis.²⁷

The time for the second SLEDAI examination for prospective and retrospective cohorts in this study was set independently. Looking for the risk factors for flares in SLE patients is recommended so that future studies follow the subjects in a prospective cohort starting from a low SLEDAI score or remission until they have an increased SLEDAI score (flare). This step must be ethically reviewed. It is also necessary to consider the quantity factor of the frequency of repetition of the scoring tool or instrument to monitor disease activity. In this study, the SLEDAI tool and complement levels were only repeated twice. Also, there was a high risk of bias because it was an ambispective cohort carried out in two hospitals.

Conclusion

The risk factor for worsening (flare) of systemic lupus erythematosus was anemia, defined as a hemoglobin level of less than 10 g/dL, with RR = 5.31, p-value = 0.03, 95% CI = 2.02–13.92. While, age, body mass index, education level, employment status, marital status, hydroxychloroquine, and immunosuppressants are not statistically significant risk factors for worsening (flare) of systemic lupus erythematosus.

Abbreviations

SLE: Systemic Lupus Erythematosus; SLEDAI: Systemic Lupus Disease Activity Index; BMI: Body Mass Index; MCV: Mean Corpuscular

Volume.

Ethics Approval and Consent to Participate

This study was carried out after ethical approval was obtained from the Ethics Committee of the Faculty of Public Health, Universitas Indonesia, No. 814/UN2.F10/PPM.00.02/2018.

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 datasets generated and analyzed are available in the article.

Authors' Contribution

GA, RD, MKS, and S contributed to the conception and design, acquisition analysis and interpretation of data, and drafting and revising of the manuscript.

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Maternal Factors Influencing Postpartum Depression in Indonesia

Nurhalina Sari, Friska N M Dewi, Nova Muhani*

Public Health Study Program, Faculty of Health Sciences, Malahayati University, Bandar Lampung, Indonesia

Abstract

The estimated prevalence of postpartum depression differs in developed and developing countries. Due to the increasing number of cases in developing countries like Indonesia, postpartum depression has become a serious issue. This study aimed to identify factors influencing postpartum depression in Bandar Lampung City, Indonesia, in 2023 using the Edinburgh Postnatal Depression Scale instrument. This study employed a cross-sectional design with a sample size of 251 respondents, selected based on inclusion and exclusion criteria using a purposive sampling technique. The multiple logistic regression results indicated that women with abortion records had a three times higher risk (95% CI = 1.394–7.648; p-value = 0.013) of experiencing postpartum depression after controlling for other variables (record of depression, employment status, education, and family support). Postpartum women should be followed by midwives and given regular assistance from their loved ones, such as their spouse or family, to prevent depression. These experts can monitor the mother's well-being and share information on maternal and infant health.

Keywords: depression, Edinburgh Postnatal Depression Scale, postpartum

Introduction

Maternal mental health is a biopsychosocial state frequently brought on by a variety of stressors.¹ Mental health means a state of entire bodily, psychological, and social well-being, not just the absence of illness, incapacity, and weakness.¹ Mental health illnesses include anxiety, depression, bipolar disorder, obsessive-compulsive disorder, post-traumatic stress disorder, and psychosis.¹ Feelings of melancholy, a lack of interest or pleasure, guilt, low self-esteem, disturbed sleep or appetite, exhaustion, and poor concentration are all signs of depression.¹

Mothers often suffer from depression or other mental health conditions caused by hormonal changes during pregnancy and postpartum.² The changes involve a significant decrease in estrogen and progesterone hormone levels, leading to emotional instability in postpartum mothers.² The changes that pregnant women experience at different phases of pregnancy affect their mental health; therefore, they are more susceptible to mental health issues.³ During their pregnancy and after giving birth, nearly one in five pregnant women have mental

health issues.³ Psychological health disorders throughout pregnancy and after delivery increase the risks of premature birth, low birth weight, and impaired fetal development.^{3,4}

Beginning with conception, the mother's mental health affects the child's development. Prenatal and postnatal mental health difficulties can be the start of later mental health problems in the mother's life, according to studies in the field of prenatal mental health that concentrate on prevalent mental disorders, such as depression and anxiety.⁵ Age, education, occupation, financial situation, breastfeeding, family support, maternal and child health, social connections, and psychological background are a few aspects affecting maternal mental health.⁶

Postpartum depression is a type of stress-related depression in postpartum women; it ranges in severity from the mildest, known as baby blues syndrome, to the most severe, known as postpartum psychosis.^{7,8} According to the 2018 Indonesian Basic Health Research report, 6.1% of Indonesians over the age of 15 reported having depression.⁹ As a result, 700 people had depression overall.⁹ Following delivery, over 80% of women experience

Correspondence*: Nova Muhani, Public Health Study Program, Malahayati University, Pramuka Street No. 27, Kemiling, Bandar Lampung 35152, Indonesia, E-mail: muhaninova@malahayati.ac.id, Phone: +62 815-8335-9676

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depression, characterized by sad and erratic emotions occurring between two to 14 days later.¹⁰

The Indonesian Ministry of Health’s Family Health program has recorded an increase in maternal deaths, compared to 4,627 maternal deaths in 2020, there were 7,389 maternal deaths in Indonesia in 2021.¹¹ In Bandar Lampung City, Indonesia, mental health issues have not received adequate attention from many parties, especially spouses and families. Lack of prior childbearing experience or never having given birth are some causes of postpartum depression.⁸ A record of prior depression, social support, obstetric characteristics (such as cesarean section or instrument-assisted birth), and demographic factors affect postpartum depression.⁸

Due to their large populations and high fertility rates, emerging countries require early diagnosis and treatment.¹² The husband and family supports, the economic and employment situations, and the cultural aspects of childbirth are external variables that might cause postpartum depression.¹³ Age, records of complications, occupation, finances, the support of the spouse, and marital problems are all factors found to be associated with postpartum depression.¹⁴ Husbands are the first to express their wives love, support, and affection, assuring them of their bodily and spiritual safety.¹⁵ Therefore, this study aimed to identify factors influencing postpartum depression in Bandar Lampung City in 2023 using the Edinburgh Postnatal Depression Scale (EPDS) instrument.

Method

This quantitative study used a cross-sectional design. From February to May 2023, six practicing midwives in Bandar Lampung City participated in this study, with a relatively large number of deliveries compared to other midwives. Since the population size was unknown, the sample size was calculated using the Lemeshow formula, which required a minimum sample size of 119.3. This study utilized a sample consisting of 251 respondents. The participants were selected using a purposive sample technique with standard inclusion and exclusion criteria to find postpartum mothers who fit the study needs (mothers who were 2–8 weeks postpartum).

The most used postpartum depression screening method is EPDS.³ The EPDS questionnaire’s total score, which runs from 0 to 30, was used to determine the likelihood that depression would occur. Postpartum depression was diagnosed in mothers receiving a score of >9 on the EPDS questionnaire; while, postpartum depression was not suspected in those receiving a score of 9. The EPDS is a tool designed to measure postpartum mothers’ levels of depression; it enables the early detection of mothers who are assumably depressed.³ The EPDS questionnaire has been validated in various countries,

making its usage more reliable. This instrument can play a preventive role in managing mental health disorders in postpartum mothers.^{3,5,15}

By asking the mothers about 19 questions and analyzing how the fathers responded and helped their wives during the postpartum period, the study also evaluated the supports of the husband and the family. The husband support for his wife during pregnancy, childbirth, and postpartum was evaluated in various ways, including informational, emotional, practical, and evaluative assistance.¹⁶ To sustain the mother’s health and psychological well-being, which may change after giving birth for the first time or subsequent times, the husband’s support is essential during pregnancy and after.¹⁷

Validity and reliability tests were conducted at the midwifery practice in Lampung Selatan District, Indonesia, for the variables of age, parity, record of depression, record of abortion, employment status, education, husband support, and other family support items. Univariate analysis, bivariate analysis using the Chi-squared test, and multivariate analysis were all used in the data analysis. The percentage of univariate variables was explained via frequency distribution analysis. The Chi-squared test was used in bivariate analysis due to the unconditional nature of the data being analyzed. It was employed to establish the relationship between the dependent and independent variables. Multiple logistic regression was employed in the multivariate analysis to predict risk factors and determine the most influential variables on postpartum depression after controlling for other variables.

Results

Based on the information in Table 1, 19.1% of mothers are either under 20 or over 35 years old. Concerning the parity, 170 mothers (67.7%) had ≥2

Table 1. Frequency Distribution of Participant’s Characteristics (n = 251)

Variable	Category	n	%
Age	20–35 years	203	80.9
	<20 and >35 years	48	19.1
Parity	≥2 child	170	67.7
	<2 child	81	32.3
Education	Elementary education	68	27.1
	Middle education	144	57.4
	Higher education	39	15.5
Employment status	Unemployed	210	83.7
	Employed	41	16.3
Record of abortion	No	213	84.9
	Yes	38	15.1
Record of depression	No	245	97.6
	Yes	6	2.4
Husband support	Yes	195	77.7
	No	56	22.3
Family support	Yes	185	72.9
	No	68	27.1

Table 2. Relationship between Maternal Characteristics and Postpartum Depression (n = 251)

Variable	Category	Postpartum Depression						p-value	OR (95% CI)
		Yes		No		Total			
		n	%	n	%	n	%		
Age	<20 and >35 years	43	89.60	5	10.40	48	100	0.809	1.263 (0.459–3.480)
	20–35 years	177	87.20	26	12.80	203	100		
Parity	1–2	147	87.50	21	12.50	168	100	1.000	0.959 (0.429–2.142)
	>2	73	88	10	12	83	100		
Record of abortion	No	192	90.10	21	9.90	213	100	0.013	3.265 (1.394–7.648)
	Yes	28	75.70	10	26.30	38	100		
Record of depression	No	216	88.20	29	11.80	245	100	0.162	3.724 (0.653–21.241)
	Yes	4	66.70	2	33.30	6	100		
Employment status	Unemployed	186	88.60	24	11.40	210	100	0.306	1.596 (0.637–3.995)
	Employed	34	82.90	7	17.10	41	100		
Education	Elementary education	56	82.40	12	17.60	68	100	0.299	-
	Middle education	129	89.60	15	10.40	144	100		
	Higher education	35	89.70	4	10.30	39	100		
Husband support	Yes	172	88.20	23	11.80	195	100	0.646	1.246 (0.524–2.962)
	No	48	85.70	8	14.30	56	100		
Family support	Yes	165	90.20	18	9.80	183	100	0.054	2.167 (0.997–4.707)
	No	55	80.90	13	19.10	68	100		

Notes: OR = Odd Ratio, CI = Confidence Interval

children; while, 81 mothers (32.3%) had <2 children. Furthermore, Table 1 shows that 144 postpartum women (57.4%) have secondary education, which makes up the biggest percentage of postpartum mothers' education level. Most mothers in Bandar Lampung City had secondary education.

For the employment status, 210 (83.7%) and 41 (16.3%) of the respondents were unemployed and employed mothers, respectively. In the table above, 15% of the women had a record of abortion. The number of mothers previously diagnosed with depression was 6 (2.4%), while 245 (97.6%) did not. According to this study, postpartum women with a record of depression were less common than those without one.

The study on the frequency distribution of the variable "husband support" revealed that, of the 251 respondents, 77.70% of postpartum mothers had their husbands' support; while, 22.30% of postpartum mothers did not. In terms of the variable "family support," the findings of the frequency distribution analysis revealed that 72.9% of the mothers received help from their families, whereas 27.1% did not.

According to this study's findings, the risk factor of maternal age was not linked to the prevalence of postpartum depression because there were relatively few mothers under the age of 20 and over 35, and the number of respondents reported experiencing depression was only 31—a small number when compared to the study's total of 251 respondents. The Chi-squared test for statistical analysis produced a p-value of 0.013, less than 0.05. These results suggested an association between past abor-

Table 3. Multiple Logistic Regression of Maternal Characteristics

Variable	OR	95% CI	p-value
History of abortion	3.037	1.26–7.317	0.013
History of depression	2.927	0.435–19.684	0.269
Employment status	1.891	0.694–5.153	0.213
Education	0.652	0.35–1.212	0.176
Family support	1.949	0.868–4.379	0.106

Notes: OR = Odd Ratio, CI = Confidence Interval

tions by mothers and the prevalence of postpartum depression in Bandar Lampung City. However, there was no significant association between the incidence of postpartum depression in Bandar Lampung City and a prior record of depression; according to the statistical analysis using the Chi-squared test, the result's p-value was <0.05 (Table 2).

In this study, from the bivariate variables of age, parity, record of depression, record of abortion, education, employment status, husband support, and family support included in the multivariate modeling, record of abortion had the greatest influence. The odds ratio (OR) for past abortions was 3.037 (95% CI = 1.26–7.317), and the p-value for this variable was 0.013, according to the statistical analysis findings based on Table 3 of the multivariate modeling. In comparison to other variables, the variable "record of abortion" indicated a 3.037 times higher likelihood of having depression.

Discussion

This study revealed that there were still mothers giv-

ing birth at unsafe ages, especially after the age of 35, which was considered to be a high-risk age. It is recommended to get married at age ≥ 20 years, as advised by the National Family Planning Coordination Board.¹³ The results of this study were in contrast with several recent studies indicating a connection between postpartum depression and age because getting married under the age of 20 or over 35 makes individuals vulnerable to emotional instability.¹⁴ Other recent studies indicate that mothers aged 20-35 are more susceptible to developing depression.^{13,18} It is recommended to maintain a healthy lifestyle and get sufficient rest if pregnancy and childbirth occur at a risky age to protect the mother and child health.

However, this study also contradicted recent findings that discovered a substantial correlation between parity and incidence of postpartum depression; the results of this study do not indicate a relationship between parity and postpartum depression occurrence.¹⁷ Due to potential emotional instability that may increase the risk of complications during childbirth, resulting in feelings of fear, anxiety, and even depression, women expecting their first child and those who have given birth more than three times are particularly vulnerable to postpartum depression.¹⁹ Compared to women who have not previously experienced depression, women who have previously suffered from depression are more likely to be diagnosed with postpartum depression.²⁰ Previous depression might be treated with counseling, medication, or a mix of the two. Brain stimulation therapy, such as electroconvulsive therapy, might be considered if conventional treatments do not reduce symptoms.²¹

Compared to mothers who have never had an abortion, postpartum women with a record of abortion had a 3.265 times higher likelihood of being diagnosed with depression. This result is consistent with a previous study that points to a strong link between a record of abortion and the onset of postpartum depression.²² Multiple miscarriages and losses can have an emotional toll on a woman's mental health and preparation, which can result in emotions of fear and anxiety.²³

Additionally, the statistical analysis of the Chi-squared test indicated no connection between education level and the prevalence of postpartum depression in Bandar Lampung City. This finding conflicts with previous study showing a connection between a maternal education and the prevalence of postpartum depression.²³

There was no statistically significant association between employment status and the prevalence of postpartum depression in Bandar Lampung City, according to the statistical analysis of the chi-squared test. This result contradicted a previous study that claims a connection between the maternal employment status and the likelihood of depression.¹⁴ Overworked mothers may experi-

ence emotional instability and struggle to manage their lives.²²

In terms of the husband support, the statistical analysis using the Chi-squared test revealed no connection between the incidence of postpartum depression and the husband's support. This finding conflicted with another study that pointed to a link between the incidence of postpartum depression and support from the husband.¹⁶ Support from a partner helps lessen postpartum depression; it is a protective factor for postpartum depression and is thought to lower the incidence of postpartum depression while improving women's laboring experiences.¹⁶ So far, there might not have been any government programs regarding spousal support for postpartum mothers. However, it is advisable for husbands always to accompany and support the postpartum mother's health.^{16,17}

Furthermore, the statistical analysis of the Chi-squared test revealed no connection between the prevalence of postpartum depression and family support. This finding runs counter to a previous study that suggested that postpartum depression is correlated with family support.¹⁷ Women who do not receive support from their families—whether through care or assistance—are more susceptible to postpartum depression than those who do.²³

Prior studies have demonstrated that mothers with several miscarriages may find it challenging to conceive, and the number of children they bear also depends on how long it has been since their previous pregnancies. Additionally, several mothers who have previously struggled with depression may do so due to prior abortion experiences. Mothers with low levels of education will lack knowledge of the risks associated with a history of abortion, which may worsen postpartum depression. It has been demonstrated that a woman is more likely to have depression during subsequent pregnancies and childbirths if she has a record of abortion or miscarriage experiences. These emotional ordeals can have severe impacts on a woman. As a result, these women might experience worry and anxiety during subsequent pregnancies and deliveries.^{24,25}

Postpartum depression risk is increased by symptoms like pain from the curettage procedure of a miscarriage, which can engender feelings of trauma and anxiety.²⁶ Husbands and families should do a lot more to help wives with a record of abortion. Postpartum mothers should ideally receive extra attention from their families, and their partners should be by their side during every activity. Indeed, it is important not to let postpartum mothers feel like they are struggling alone.

A previous study has also shown that one of biggest risk factors for mothers developing postpartum depression is a record of abortion. Abortion can result in emo-

tional responses like sadness that impact one's physical well-being and increase the likelihood of postpartum depression.²⁷ It should be emphasized that depression and anxiety during pregnancy can result in miscarriages.²⁸ Employed women are more likely to miscarry because of the multiple activities and jobs they carry out, which causes exhaustion that might affect the health of the growing fetus and, as a result, increase the likelihood of miscarriage.²⁷

Conclusion

Postpartum depression is a mental health condition that affects new mothers and brought on by various reasons. A record of abortion is linked to the development of postpartum depression. Additionally, multivariate analysis reveals that the most important risk factor for postpartum depression is a record of abortion, age, parity, education, record of depression, employment status, and family support considered confounding factors. Postpartum women deserve support from their loved ones, such as their spouses or relatives, and they need to be with midwives who can keep an eye on their health and provide information on maternal and newborn health, thus preserving their mental health in the future.

Abbreviations

EPDS: Edinburgh Postnatal Depression Scale.

Ethics Approval and Consent to Participate

This study is ethically feasible, with a statement of ethical feasibility (ethical clearance): No. 3047/EC/KEP-UNMAL/1/2023.

Competing Interest

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

Availability of Data and Materials

The data presented in this study are available and can be provided by the first author.

Authors' Contribution

NS conceived the idea and sampling design, analyzed the data, and interpreted the study results. FNMD performed data collection and analyzed the data. NM critically analyzed and interpreted the study results and drafted the manuscript.

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Not Applicable.

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Analysis of Climate and Environmental Risk Factors on Dengue Hemorrhagic Fever Incidence in Bogor District

Ririn Arminsih Wulandari^{1*}, Tria Rahmawati¹, Al Asyary¹, Fajar Nugraha²

¹Department of Environmental Health, Faculty of Public Health, Universitas Indonesia, Depok, Indonesia, ²Centre of Biostatistics and Health Informatics Studies, Faculty of Public Health, Universitas Indonesia, Depok, Indonesia

Abstract

Dengue Hemorrhagic Fever (DHF) is transmitted through the bites of *Aedes aegypti* and *Aedes albopictus* mosquitoes and remains an endemic in Bogor District. This quantitative correlation study with an ecological approach aimed to analyze how DHF incidence was influenced by climate factors, population density, Larvae Free Rate, and the area altitude factor. Secondary data were obtained from the Bogor District Health Office, Bogor District Central Bureau of Statistics, and the Meteorology, Climatology, and Geophysics Agency. The spatial analysis method was used for the area altitude factor. The results showed a significant relationship between climate factors, such as air humidity at a Time Lag of 0 months ($r = 0.394$) and the altitude factor ($r = -0.350$), and DHF incidence in the Bogor District from 2017 to 2022. Spatial data showed that DHF incidence tends to be higher in districts with lower altitudes. Therefore, the Bogor District Health Office and the community can enhance efforts to prevent and control DHF, especially during seasonal transitions and in areas with lower altitudes. Cross-sector collaboration with the Meteorology, Climatology, and Geophysics Agency is also necessary to remain vigilant during climate fluctuations.

Keywords: altitude area, climate, dengue hemorrhagic fever, Larvae Free Rate, population density

Introduction

Dengue hemorrhagic fever (DHF) is an infectious disease caused by the dengue virus, spread through female mosquitoes from the *Aedes aegypti* and *Aedes albopictus* species.¹ The DHF is the fastest-growing vector-borne disease. It is a public health problem with the potential to cause a significant number of deaths worldwide.² In the last few decades, the incidence of DHF has increased up to 30 times globally, with an estimated 50 million dengue infections occurring each year and around 2.5 billion people living in dengue-endemic countries.³

A total of 1.8 billion (>70%) of the populations at risk live in Southeast Asia and the Western Pacific.³ Indonesia ranks second among the 30 dengue-endemic countries globally, with the highest number of DHF cases.⁴ Bogor District in West Java Province had fluctuating, relatively high DHF cases each year from 2017 to 2022. In 2017, there were 276 cases, which increased to a peak of 2,220 cases in 2021 before falling slightly to 1,953 cases in 2022.⁵⁻⁶

The distribution and increase in DHF cases can be attributed to various risk factors, including the population

levels of *Aedes* mosquito vectors, dengue virus virulence, population immunity, population mobility, population density, socioeconomic status, and community behaviors that can create mosquito breeding habitats.⁷ Population density is closely related to DHF transmission. In densely populated areas, the proximity of houses allows *Aedes* mosquitoes to more easily transmit the dengue virus, as the flight range of female *Aedes* mosquitoes is around 50-100 meters.⁸ One indicator used to measure the success of mosquito eradication programs is the Larvae Free Rate (LFR), for which the national standard at $\geq 95\%$.⁹

Climate factors, such as rainfall, air temperature, and humidity, also affect the DHF incidence.¹⁰ Rainfall is particularly relevant to the life cycle of *Aedes* mosquitoes. Heavy rainfall may saturate the soil, creating numerous water puddles that serve as breeding sites for mosquitoes, thus increasing the mosquito vector density.¹¹ Increased air temperature is associated with the development of mosquito larvae and the dengue virus within them.¹² While, air humidity is closely related to the physiological processes and respiratory systems of mosquitoes. Humidity levels above 85% lead to longer mosquito lifespans.¹³

Correspondence*: Ririn Arminsih Wulandari, Department of Environmental Health, Faculty of Public Health, Universitas Indonesia, C Building 2nd Floor Campus FKM-UI, Depok, 16424, Indonesia, E-mail: ririn.arminsih@gmail.com, Phone: +62 21-7865479

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Another environmental risk factor is the area altitude. *Aedes aegypti* mosquitoes thrive at altitudes of 0-500 meters above sea level; while, they are not well-suited to survive at altitudes greater than 1,000 meters above sea level.^{9,14} Given the relatively high number of DHF cases in Bogor District each year from 2017 to 2022, this study aimed to analyze the climate and environmental risk factors associated with DHF incidence in Bogor District from 2017 to 2022.

Method

This quantitative correlation study with an ecological approach was analyzed using time series data. Secondary data was used for disease factors, including the total number of dengue patients, dengue incidence rate (IR), and the LFR in Bogor District recorded by the Bogor District Health Office from January 2017 to December 2022. As for the environmental risk factors, climate data (air temperature, air humidity, and rainfall) was obtained from the Central Meteorology, Climatology, and Geophysics Agency; while, the population density and area altitude data were sourced from the Bogor District Central Bureau of Statistics.

Data processing was conducted in two ways. First, statistical tests through univariate analysis were used to describe the frequency distribution of variables, and bivariate analysis was used to determine the relationship between two variables using Pearson and Spearman Correlation Tests. For climate correlation tests, three analyses were conducted: climate data for the same month (Time Lag 0), climate data from one month earlier (Time Lag 1), and climate data from two months earlier (Time Lag 2) correlated with the dengue IR.

The climatic factors did not directly influence DHF incidence immediately, but rather, they affected the mosquito vector's life cycle. In the mosquito's life cycle, from egg to infective adult, a time lag can occur between climate fluctuations and the increase in DHF cases.¹⁰ The second test involved spatial analysis using ArcGIS 10.8 to determine the spatial depiction of information. In this study, spatial analysis was conducted only on the area altitude factor to depict the relationship between the area altitude and DHF incidence.

Results

Incidence Rate of Dengue Hemorrhagic Fever

The DHF incidence in Bogor District increased from 2017 to 2021, then decreased in 2022. The highest number of DHF cases was recorded in 2021, with 2,220 cases and an IR of 40.44 per 10,000 population. While, the lowest occurred in 2017, with 276 cases and an IR of 4.83 per 100,000 population (Figure 1).

Rainfall, Air Temperature, and Air Humidity

Rainfall in Bogor District showed a fluctuating trend from 2017 to 2022. The highest rainfall, 33.54 mm, occurred in April 2019. In contrast, the lowest rainfall, 4.44 mm, occurred in January 2022. The optimal rainfall for mosquitoes was below 50 mm, peaking between 15-35 mm (Figure 2).

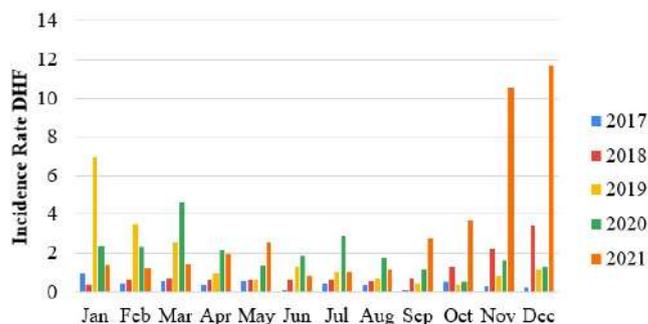


Figure 1. Overview of Dengue Hemorrhagic Fever Incidence Rate in Bogor District, 2017-2022

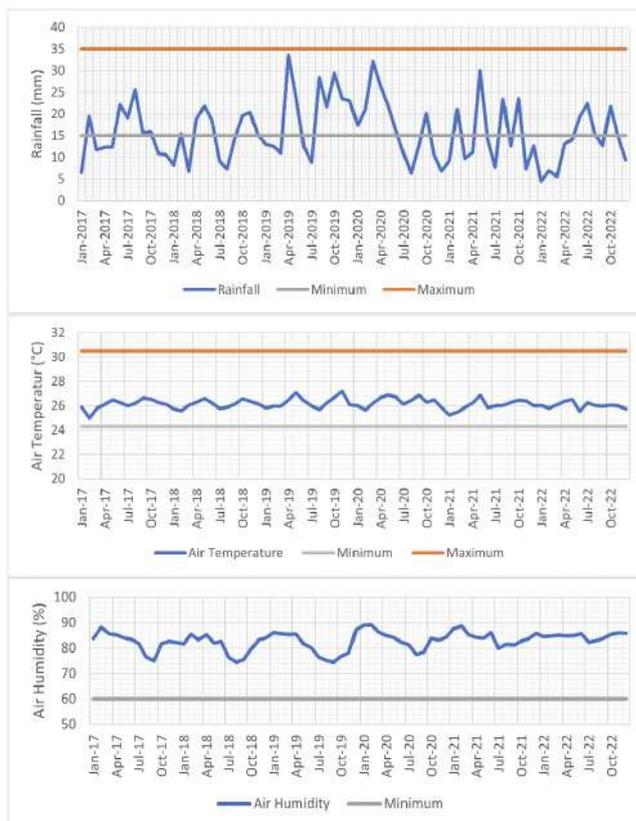


Figure 2. Monthly Distribution of Rainfall, Air Temperature, and Air Humidity in Bogor District, 2017-2022

Air temperature in Bogor District from 2017 to 2022 did not show drastic monthly changes and remained relatively stable. The air temperature falls within the optimal range for mosquito infection in range of 24.3 and 30.5°C. The highest air temperature, 27.20°C, was recorded in November 2019, while the lowest, 24.97°C, was recorded in February 2017 (Figure 2).

Air humidity in Bogor District showed a fluctuating trend from 2017 to 2022. The air humidity in Bogor District, which ranged from 70-85%, was optimal for mosquito survival (>60%). The highest air humidity, 89.21%, occurred in February 2020, and the lowest, 74.43%, occurred in September 2019 (Figure 2).

Population Density

Population density in Bogor District was assessed based on the average population density per subdistrict from 2017 to 2022. The highest population density was found in the Cijeruk, Cigombong, and Bojong Gede Subdistricts, while the lowest was in the Sukajaya Subdistrict.

Larvae Free Rate

Due to incomplete LFR data, the analysis was limited to 2019-2022. The average LFR in Bogor District from 2019 to 2022 was 93.25%. From 2019 to 2021, LFR values in Bogor District were below a national standard of ≥95%. The highest LFR value, 95%, was recorded in 2022 (Figure 3).

Area Altitude

The altitudes of the subdistricts within Bogor District vary significantly. The Cisarua Subdistrict had the highest altitude, 789 meters above sea level, while the Parung Panjang Subdistrict had the lowest altitude, 51 above sea level. Given the classification of altitude between lowland (<200 asl) and highland (>200 asl), Bogor District has

19 subdistricts in the highland (47.5%) and 21 subdistricts in the lowland (52.5%) (Figure 4).

Normality Test

The results of the normality test, using the Kolmogorov-Smirnov test, indicated that all variables from 2017 to 2022 were normally distributed (p-value>0.05), except for the air humidity variable at Time Lag 0 and the altitude variable (p-value<0.05). Normally distributed variables will be analyzed via bivariate analysis using the Pearson correlation test. While, non-normally distributed variables will be analyzed using the Spearman correlation test.

Correlation of Climate Factors, Population Density, Larvae Free Rate, and Altitude with Dengue Hemorrhagic Fever Incidence Rate in Bogor District, 2017-2022

The correlation test for climate variables was conducted using three time lag scenarios (Time Lag 0, Time Lag 1, and Time Lag 2). It was because climate factors did not directly affect DHF occurrence but instead influenced

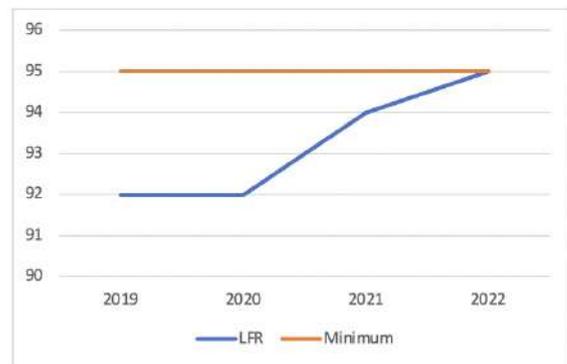


Figure 3. Distribution of Larvae Free Rate in Bogor District, 2019-2022

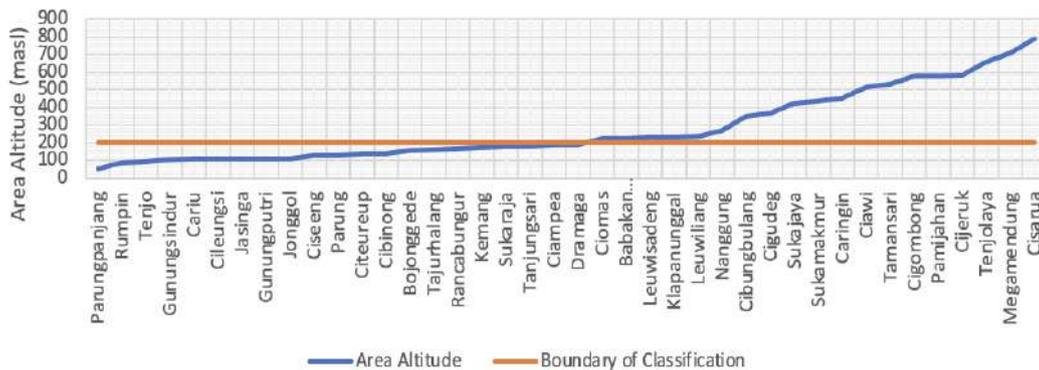


Figure 4. Distribution of Area Altitude in Bogor District in 2017-2022

the mosquito life cycle. In the mosquito life cycle, from eggs to infective adults, there may be a time lag between climate fluctuations and an increase in DHF cases; therefore, the time lag testing for climate factors needs to be considered.

The correlation test results for the three time lag scenarios of climate variables showed that only the air humidity at Time Lag 0 had a significant relationship with the DHF IR (p-value = 0.001). Additionally, the altitude variable showed a significant relationship with the DHF IR (p-value = 0.027). However, population density and the ABJ did not show significant relationships with DHF IR (p-value>0.05; p-value>0.05) (Table 1).

Map of Correlation between Area Altitude and Dengue Hemorrhagic Fever Incidence in Bogor District, 2017-2022

The correlation map showed that the area altitude significantly affected DHF occurrence. In subdistricts with lower altitudes, such as the Cibinong, Cileungsi, and Gunung Putri Subdistricts, DHF incidence tends to be higher. On the contrary, DHF incidence tended to be lower in subdistricts with higher altitudes. These results indicated that higher altitudes had lower temperatures, which led to the suboptimal and slower breeding process of *Aedes aegypti* mosquitoes, resulting in reduced dengue virus transmission. (Figure 5).

Discussion

The highest DHF IR in Bogor District was recorded in 2021 (IR = 40, 44 per 100,000 population). This condition was due to climate factors, including rainfall, air

temperature, and air humidity within the optimal range for mosquito breeding. Furthermore, in 2021, the LFR was below the national standard of <95%, indicating a high larval density. With the persistently high larval density, the risk of DHF transmission remained high.

Rainfall is an important factor in DHF transmission, as it can create containers of stagnant water, which serve as breeding sites for *Aedes aegypti* mosquitoes.¹¹ More breeding sites result in easier egg-laying for mosquitoes, leading to an increase in mosquito population and an elevated risk of DHF transmission.^{11,13} The optimal rainfall for mosquitoes is below 50 mm, peaking between 15-35 mm.^{15,16}

Rainfall can increase air humidity, prolonging the lifespan of adult mosquitoes.¹¹ However, the correlation analysis did not show a significant relationship between

Table 1. Correlation Test Results between Climate, Population Density, Larvae Free Rate, Area Altitude and Dengue Incidence

Variable	Dengue Incidence		
	Coef. Correlation (r)	p-value	
Rainfall	Time Lag 0	-0.165	0.167
	Time Lag 1	-0.145	0.228
	Time Lag 2	-0.096	0.431
Air temperature	Time Lag 0	-0.050	0.675
	Time Lag 1	-0.122	0.313
	Time Lag 2	-0.153	0.207
Air humidity	Time Lag 0	0.394	0.001*
	Time Lag 1	0.169	0.159
	Time Lag 2	0.196	0.105
Population density		-0.755	0.083
Larvae Free Rate		0.861	0.139
Area altitude		-0.350	0.027*

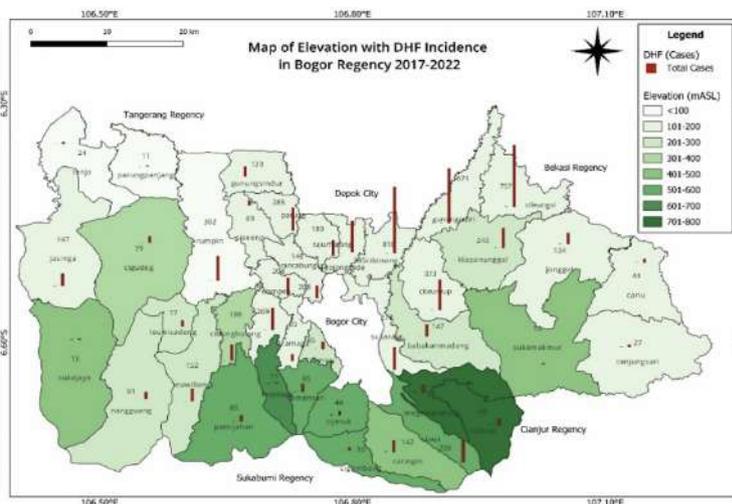


Figure 5. Correlation Map of Area Altitude with Dengue Hemorrhagic Fever in Bogor District, 2017-2022

rainfall and DHF in Bogor District from 2017 to 2022. The implementation of the “3M Plus” activities, through the actions of draining, closing, and utilizing or recycling all mosquito breeding habitats, to prevent DHF before the rainy season can also influence mosquito presence.⁹ Prolonged rainfall can eliminate mosquito breeding sites, as the mosquito larvae get carried away by the current and perish.¹⁷

Air temperature is an environmental variable that can enhance vector proliferation and reduce the time required for the dengue virus to replicate in mosquito bodies (the extrinsic incubation period of the dengue virus).¹⁸ A shortened incubation period allows the virus to replicate faster, leading to an increased viral count in mosquitoes.¹⁸ Moreover, higher temperatures promote larval development.¹⁸

The optimal air temperature range for mosquito infection is 24.3-30.5°C.¹⁵ However, the correlation analysis indicated that air temperature did not significantly correlate with the DHF IR in Bogor District from 2017 to 2022. The air temperature in Bogor District during this period ranged from 24.97°C to 27.20°C. Although these temperatures were optimal for mosquito development, it was possible that the mosquitoes were not infective.

Air humidity affects the respiratory systems and physiological processes of *Aedes aegypti* mosquitoes.¹³ The optimal humidity for mosquito survival is >60%.¹⁹ Low air humidity (<60%) shortens the lifespan of mosquitoes, as it causes the fluid in their bodies to evaporate.¹³ On the contrary, high air humidity (>85%) prolongs their lifespan.¹³

The correlation analysis between air humidity and DHF IR showed a significant relationship with moderate correlation strength and a positive correlation direction at Time Lag 0. These results indicated that higher air humidity was associated with increased DHF incidence, confirming the results of a previous study in Surabaya City.¹³ However, there was no significant correlation between Time Lag 1 or Time Lag 2 humidity and DHF IR, possibly due to other dominant factors, such as the physical environmental house conditions, including ventilation and lighting, which can influence mosquito activities. Mosquitoes prefer dark and moist places to rest and lay eggs.²⁰

Population density is a risk factor for DHF transmission.⁷ High-density settlements with low socioeconomic status have higher DHF transmission rates, given that female *Aedes* mosquitoes have a flight range of about 50-100 meters. The denser the population, the easier *Aedes* mosquitoes can transmit the dengue virus.⁸ However, the correlation analysis between population density and DHF incidence rate showed no significant relationship, consistent with a previous study in the South Minahasa

District.⁸ The lack of significant correlation may be due to the relatively small number of analyzed population data, which consisted of only six data points. Data quantity could affect the significance value of the relationship between variables.

The LFR is one indicator used to assess the presence of *Aedes* mosquitoes in an area, with the standard LFR value set at $\geq 95\%$. The LFR value in Bogor District from 2019 to 2022 was in the low category ($\leq 95\%$). Existing theories suggest that a low LFR value ($\leq 95\%$) indicates high mosquito larval density and an elevated risk of DHF transmission.^{9,13} However, the correlation analysis between the LFR value and the DHF incidence rate did not show a significant relationship. This might be due to technical errors during the reporting process, such as a less meticulous larval survey, leading to suboptimal examination of mosquito larvae. This result aligned with a study by Nuranisa, et al.²¹ The LFR value is calculated by comparing the number of houses or buildings without larvae to the total number of examined houses.⁹ The number of houses or buildings examined could also affect an area's LFR value.

Altitude is another environmental factor that can influence the proliferation of *Aedes aegypti* mosquitoes as the DHF vector.²² Area with altitudes greater than 1,000 meters above sea level did not have *Aedes aegypti* mosquitoes, resulting in low DHF transmission risk. This condition is due to altitude's impact on climate factors, such as rainfall, temperature, and humidity.²² Higher areas experienced lower temperatures due to higher rainfall and humidity. These conditions lead to sub-optimal and slower mosquito breeding, resulting in reduced dengue virus transmission.²³

The correlation analysis in this study was consistent with existing theories,^{22,23} indicating that altitude has a significant relationship with the DHF incidence rate. Moreover, the correlation had a moderate strength, with a negative correlation direction. This means that higher areas had lower DHF incidence. This correlation result was further supported by the correlation map, which showed that most DHF occurrences happen in lowland areas, aligned with a study by Tamengkel, et al.²²

Conclusion

In Bogor District, from 2017 to 2022, the highest incidence of DHF occurred in 2021, and the lowest incidence is in 2017. The DHF incidence in Bogor District is significantly influenced by climatic factors such as air humidity at Time Lag 0 and geographical factors such as area altitude. The Health Office is encouraged to collaborate and work with the Meteorology, Climatology, and Geophysics Agency to prevent increases in DHF cases during climate fluctuations. Community participation in DHF prevention and control efforts is also crucial, for instance, by

implementing the "1 House 1 Mosquito Larva Inspector" movement and "3M Plus" activities. Moreover, maintaining health and environmental cleanliness is essential to eliminate mosquito breeding sites, particularly during seasonal changes and in areas with low altitudes where people reside.

Abbreviations

DHF: Dengue Hemorrhagic Fever; LFR: Larvae Free Rate; IR: Incidence Rate.

Ethics Approval and Consent to Participate

This study has been approved by the Ethic Commission for Health Research, Faculty of Public Health, Universitas Indonesia No. Ket-612/UN2.F10.D11/PPM.00.02/2023.

Competing Interest

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

Availability of Data and Materials

Data and information used as study materials can be obtained from the corresponding author upon reasonable request.

Authors' Contribution

RAW is responsible for the ideas created, analysis, preparation of writings, supervising the study, writing review, and editing. TR and RAW performed formal analysis, investigation, interpretation, and writing-original draft preparation. AA and FN were subsequently involved in conceptualization, methodology, software, validation, resources, data curation, writing review, and editing. All authors have made substantial contributions to the final manuscript for publication.

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