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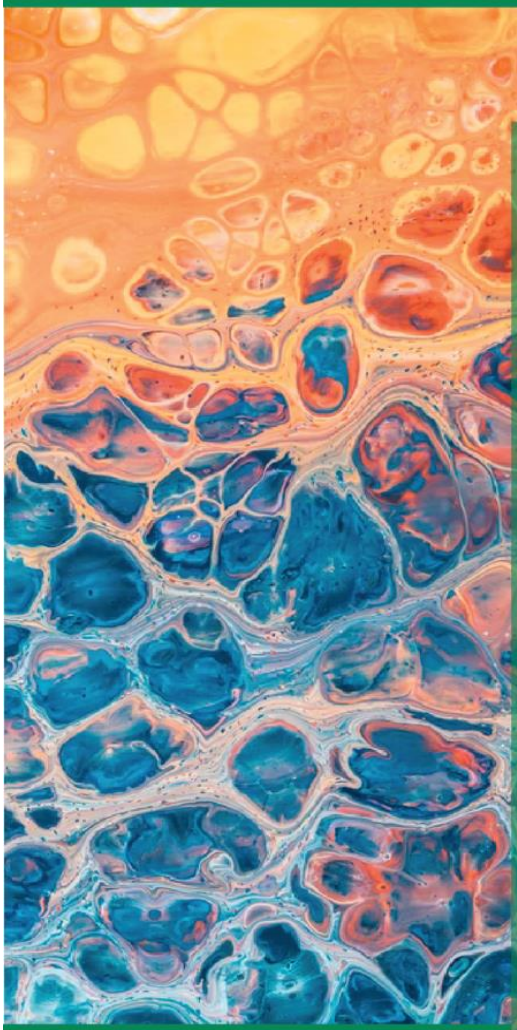

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EDITORIAL PREFACE

Dear Readers,

Alhamdulillah, we are pleased to announce the publication of the first edition of the fifth volume of the Jambura Medical and Health Science Journal (JMHSJ), a peer-reviewed journal published by Faculty of Medicine Universitas Negeri Gorontalo. This edition features six original research articles, one review article, and one case report contributed by esteemed researchers from various institutions, including Warmadewa University, Dr. Soetomo University, East Kalimantan Ministry of Health Polytechnic, Padjadjaran University, Education University of Indonesia in Bandung, Wijaya Kusuma University, Airlangga University, and Universitas Negeri Gorontalo. The diversity of submissions showcases the growing interest in JMHSJ among academics, researchers, and practitioners across Indonesia.

This issue presents a collection of original research articles covering diverse topics: the neurobiological impact of noise exposure on the frontal lobe in a rat model, maternal health indicators associated with low birth weight, a comparison of two non-pharmacological interventions for anxiety in primigravida, immediate effects of thoracic expansion exercises on breath-holding capacity in adolescents, the relationship between micronutrient intake and malaria infection, and the association of serum IL-8 levels with knee osteoarthritis severity. A systematic review examines the success and failure factors of free school meal programs, and a case report discusses drug therapy monitoring in a patient with abdominal colic.

We anticipate that future editions will continue to attract a diverse range of articles from various medical fields, reflecting our commitment to advancing knowledge and enhancing the quality of our journal, which has recently achieved accreditation from SINTA 3. We extend our heartfelt gratitude to all contributors and reviewers for their dedication and support. We wish you an insightful reading experience.

Gorontalo, February 2026

Dr. dr. Muhammad Isman Jusuf, Sp.N

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ORIGINAL ARTICLE **Open Access**

Negative Impact of Noise Exposure on the Mean Number of Neurons in the Frontal Lobe of Adult Wistar Rats

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ABSTRACT

Introduction: Noise exposure can induce oxidative stress and alter neurotransmitter dynamics within the nervous system. This oxidative stress is also associated with structural changes in the layers of the cerebrum. However, the effects of noise exposure on neuronal populations remain inadequately understood. This study aims to quantify the mean number of neurons in the frontal lobe of Wistar rats subjected to noise exposure.
Method: This study utilized an experimental design characterized by a randomized post-test only control group framework. A total of 30 male Wistar rats were selected through simple random sampling and subsequently divided into two groups: a control group without treatment (C1, n=15) and an experimental group exposed to 95 dB noise (E1, n=15) for four hours daily. Following a two-week exposure period, their brain tissue was excised and preserved in 10% neutral buffered formalin. Histological assessment was conducted using Hematoxylin and Eosin staining to evaluate the mean number of neurons in the frontal lobe. Statistical analysis was performed using the independent T-test.
Results: The mean number of neurons was 1053.33 ± 55.529 in the E1 group and 720.167 ± 61.135 in the C1 group. The mean neurons of the frontal lobe of Wistar rats in the E1 group ws lower than the C1 group significantly ($P < 0.001$).
Conclusion: Neuronal death in the frontal lobe resulting from noise-induced stress can induce structural alterations within this region, leading to detrimental effects on cognitive function and behavior.

Keywords: Frontal lobe, neuron, noise, stress

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Introduction

Sound influences the transmission of impulses within the central nervous system, particularly in the auditory cortex, encompassing Brodmann areas 41 and 42 located in the temporal lobe.[1] Exposure to an acoustically enriched environment affects the auditory system, resulting in alterations to neuronal structure and function.[2] Auditory stimulation can impact memory, autonomic functions, consciousness, cognitive abilities, and decision-making processes in the frontal lobe via the reticular formation.[3–5] Additionally, auditory stimulation has implications for cognition during rapid eye movement (REM) sleep.[6]

In contemporary society, exposure to sound can have detrimental effects, particularly in the form of noise, defined as unwanted sound and considered a significant environmental stressor. Noise pollution poses serious health risks, contributing to issues such as hearing loss, cognitive impairment, sleep disturbances, and negative emotional responses like stress, anger, and dissatisfaction.[7–10] Chronic exposure to environmental stressors, such as transportation noise, has been associated with increased rates of deafness and hindered cognitive development, including reading skills. A study examining the impact of ambient noise on the cognitive performance of schoolchildren found significant impairments at elevated noise levels, especially among students aged 11 to 13, underscoring the necessity for effective noise mitigation strategies in educational settings.[11] Conversely, other research indicated that white noise could have beneficial effects as a sleep therapy for patients with acute myocardial infacrtion.[12]

A study involving adult male rats demonstrated that exposure to noise at an intensity of 80 dB for two hours daily over six weeks resulted in deficits in spatial learning and memory, as assessed by the Morris water maze, alongside elevated serum corticosterone levels and increased malondialdehyde (MDA) and superoxide dismutase (SOD) levels in hippocampal tissues.[13]

The effects of noise, including varying intensities, on cognitive function have been extensively investigated. One notable study reported a reduction in neurogenesis within the motor and somatosensory cortices of rat pups subjected to noise exposure.[14] However, the effects on the average number of neurons in the frontal lobe remain less understood. The quantity of neurons in this region plays a critical role in decision-making, reasoning, personality, self-regulation, and planning. Oxidative stress resulting from noise exposure adversely affects memory, sensory processing, autonomic function (e.g., elevated heart rate), and cognitive capabilities.[13] Exposure to noise levels exceeding 80 dB for durations of up to two hours over 1.5 months can induce oxidative stress within the central nervous system,

comparable to conditions experienced on public roadways. Bali, as a prominent tourist destination, has seen a rise in transportation density. In 2018, noise levels in Lumintang City Park (Denpasar, Bali) reached 92 dB on the roadway, surpassing the quality standard for green spaces set at 50 dB.[15] This indicates a concerning increase in sound intensity that can act as an environmental stressor. This study aims to investigate the effects of noise on the average number of neurons in the frontal lobe of adult Wistar rats.

Methods

The Ethics Commission of the Faculty of Medicine at Udayana University had approved this study, under approval number 487/UN14.2.2.VII.14/LT/2023. The research employed an analytical experimental design with a randomized post-test control group approach. Male Wistar rats, aged three months and weighing between 240 and 260 grams, were utilized for the study. The subjects were divided into two equal groups: the treatment group (E1), which was subjected to noise exposure, and the control group (C1), which received no exposure. According to Federer's formula, a total sample size of 30 male Wistar rats was determined, and the subjects were assigned to groups through simple random sampling.

The rats in the treatment group were exposed to white noise generated by Real Time Analyzer software (version 5.2.0; Yoshimasa Electronic Inc., Japan) at an intensity of 95 dB for a duration of four hours daily over two weeks. The noise source, a loudspeaker (Sony SRS XB30, Japan), was positioned in a soundproof enclosure at a height of 30 cm above the rats. The control group (C1) was similarly housed in a soundproof box for the same duration without exposure to white noise.

On day 15, the Wistar rats were euthanized via intraperitoneal injection of ketamine at a dosage of 300 mg/kg body weight. The brains were subsequently fixed in 10% neutral buffered formalin. Histological preparations commenced with slicing paraffin-embedded blocks into 6 μm sections, followed by staining with hematoxylin-eosin.

Neuronal counts were conducted in the frontal lobe using a CX 41 microscope (Olympus, Japan) at 400x magnification, with independent assessments performed twice across four visual fields per animal. Data processing was carried out using Jamovi, and results are presented as mean values, with comparisons made between groups. An independent T-test was employed for statistical analysis to determine significance (p-value < 0.05), and findings were presented in both tabular and graphical formats.

Result

This study utilized 30 Wistar rats, which were divided into two equally sized groups maintained throughout the duration of the experiment. Both sets of numerical data were

subjected to Levene's test, yielding a *P*-value of 0.608, and the Shapiro-Wilk test, yielding a *P*-value of 0.132, indicating that the data were normally distributed and homogeneous. Subsequently, in Table 1, the C1 and E1 groups were compared using an independent samples T-test to assess for statistically significant differences in neuronal counts between the groups. The results indicated that the mean neuronal count in the group exposed to 95 dB noise for four hours daily was significantly lower than that of the control group that was not exposed to noise ($P < 0.05$), as shown in Figure 1.

Table 1. Results of the mean neurons of the frontal lobe of wistar rats.

Groups	Number (n)	Mean ± SD	*P*-value
C1	15	1054 ± 56.6	< 0.001
E1	15	720 ± 62.0	

Data were analyzed with independent T-test
C1 = control group; E1 = experimental group

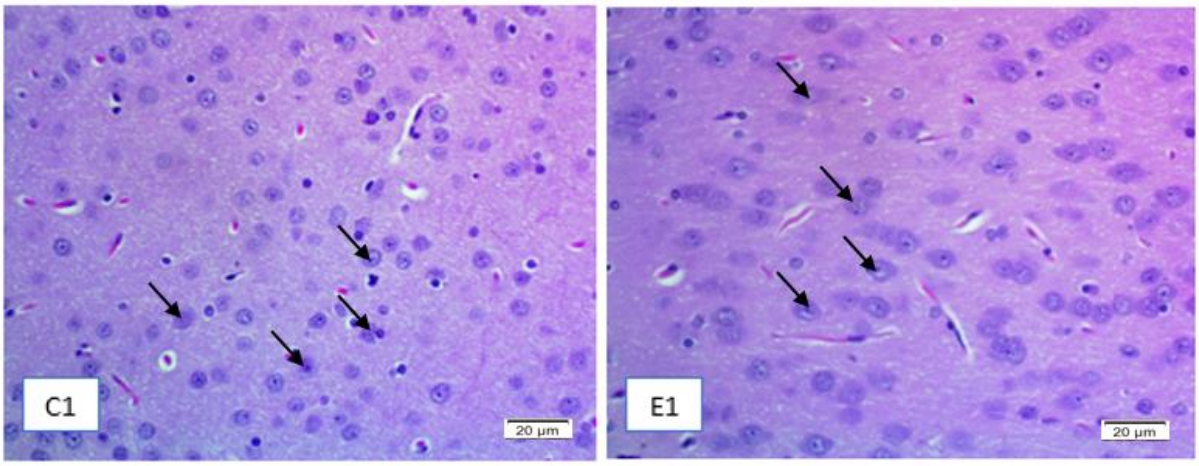

Figure 1. Histology of the frontal lobe of Wistar rats with HE staining at 400x magnification. In the C1 group, the neuron mean was higher than the E1 group. The black arrows indicate neurons.

Discussion

The present finding indicates that Exposure to 95 dB noise in the E1 group significantly reduced the mean number of frontal lobe neurons in Wistar rats compared to the C1 group. Auditory stimuli are initially transmitted to the primary auditory cortex (Brodmann areas 41 and 42) within the temporal lobe and subsequently processed in the auditory association cortex. Beyond perceptual processing, auditory input exerts significant influence on emotional regulation through projections from the medial and inferior temporal gyri to the amygdala. The amygdala provides efferent outputs to the hypothalamus via the bed nucleus of the stria

terminalis and the amygdalofugal pathways, thereby modulating autonomic and neuroendocrine activity. In parallel, auditory signals engage the hippocampus, contributing to memory formation and consolidation, with reciprocal hippocampal–hypothalamic connections further integrating auditory input into neuroendocrine regulation. Auditory information also reaches the reticular activating system, facilitating cortical arousal and consciousness. Within this network, the reticular formation—particularly the locus coeruleus—plays a central role in mediating motor and behavioral responses during heightened arousal states.[1] Chronic or acute exposure to noise levels above 85 dB is associated with adverse effects not only on the auditory system but also on extra-auditory physiological functions as showed on Figure 2. Such stress-related outcomes are mediated through activation of the hypothalamic–pituitary–adrenal (HPA) axis, the sympatho-adrenomedullary (SAM) system, and the inflammatory response. Activation of the HPA axis results in increased levels of glucocorticoids and corticotropin-releasing hormone (CRH), both of which induce dysfunction of cortisol regulation.[16,17] This dysfunction is associated with elevated extracellular glutamate and enhanced glutamate receptor activity. Notably, nearly 50% of brain neurotransmission is mediated by glutamatergic pathways, with 90% of cortical neurons utilizing glutamate as their neurotransmitter. Elevated extracellular glutamate levels facilitate an influx of Ca^{2+} ions, which can trigger neuronal death.[18]

Chronic exposure to noise also activates the NLRP3 inflammasome, which is associated with neuroinflammation and cognitive decline. While neuroinflammation is known to play a critical role in noise-induced cognitive deficits, the underlying mechanisms responsible for this neuroinflammation remain poorly understood.[19] Reactive oxidative stress (ROS) is pivotal in inhibiting N-methyl-D-aspartate receptors (NMDARs), leading to glutamate excitotoxicity and increased intracellular Ca^{2+} concentrations. This cascade of events results in mitochondrial dysfunction and neuronal death, contributing to a reduction in neuronal cell count. The excessive oxidative conditions induced by ROS can also lead to lipid peroxidation, DNA oxidation, and protein modifications across various cellular compartments.[19–22] Furthermore, another study found that noise exposure decreases levels of brain-derived neurotrophic factor (BDNF) and its receptor TrkB, increases amyloid levels, and impairs cognitive functions in aged rats.[23]

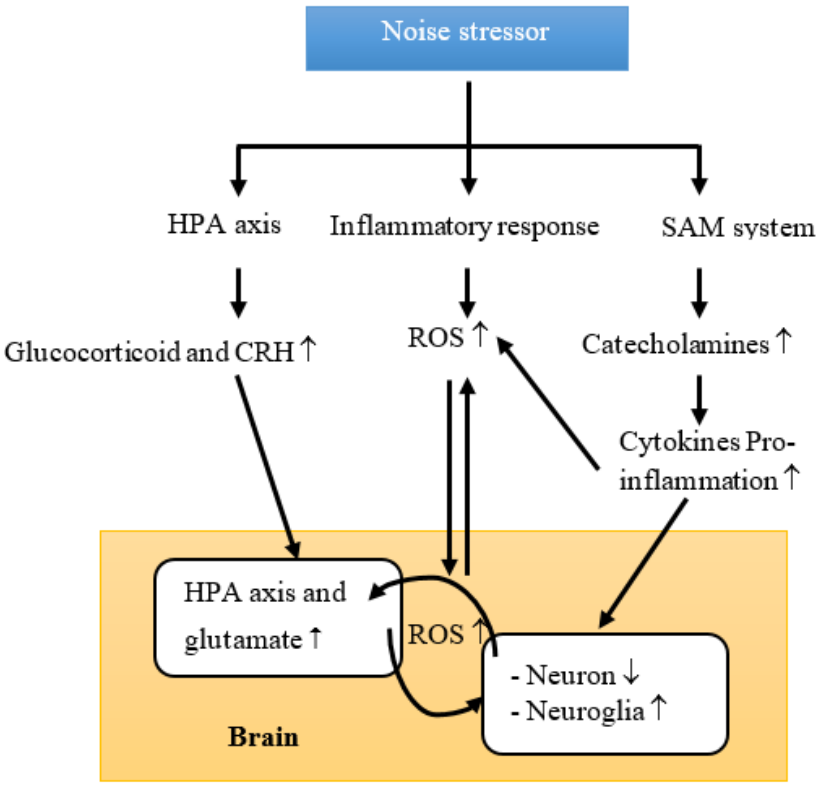

Figure 2. Noise can cause stress and activate the HPA axis, SAM system, and inflammatory cytokine interactions, ultimately leading to increased ROS in the brain.[17,20,21,24]

A study indicated that Wistar rats exposed to 95 dB noise for four hours daily exhibited a significant decrease in the number of neurons in the temporal lobes compared to control groups ($P < 0.005$).[25] In addition to affecting the temporal lobes, noise exposure can also alter the structural integrity of the amygdala, hippocampus and prefrontal cortex.[26,27] Neuronal loss in the frontal lobe due to oxidative stress can result in structural modifications that yield negative consequences. The frontal lobe is essential for executive functions, working memory, attention, decision-making, and emotional regulation. Damage to this region can lead to diminished cognitive abilities, including impairments in planning, organization, problem-solving, attention deficits, decision-making difficulties, and challenges in emotional regulation.[24,28–30] Furthermore, a study reported that 54 young participants exposed to 95 dB noise experienced significant reductions in mental workload and visual/auditory attention.[31] Oxidative stress is closely associated with the development and progression of Alzheimer's disease. Prolonged exposure to noise may contribute to the onset of Alzheimer's disease and related forms of dementia, which represent significant public health concerns.[32]

This study provides important insights into the impact of noise exposure on the central nervous system, highlighting mechanisms that remain relatively underexplored. However, the present work did not address the role of oxidative stress in noise-induced neurotoxicity. In addition, this study has limitations in the histological representation of other regions of the central nervous system, such as the temporal lobe, hippocampus, thalamus, and brainstem. Therefore, future investigations are warranted to evaluate oxidative stress in the frontal lobe and histological appearance in other regions as a potential pathway contributing to neuronal degeneration. Elucidating the molecular mechanisms underlying noise-related neuronal cell death may facilitate the identification of preventive strategies and the development of targeted therapeutic interventions.

Conclusion

This study concludes that noise exposure contributes to neuronal loss in the frontal lobe of Wistar rats, as evidenced by a lower mean neuronal count relative to the control group.

Conflicts of Interest

We have no conflicts of interest to report.

Funding sources

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ORIGINAL ARTICLE **Open Access**

Maternal Reproductive Health Indicators and Their Correlation with Low Birth Weight: Evidence from a Community-Based Cohort at Pasean-Pamekasan Health Center

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ABSTRACT

Introduction: Low birth weight (LBW) is a major cause of neonatal morbidity and mortality in developing countries. This study analyzed the relationship between maternal reproductive health indicators and LBW incidence at the Pasean Health Center, Pamekasan.
Method: A prospective cohort study was conducted on 72 third-trimester pregnant women followed until delivery. Data on maternal age, interpregnancy interval, nutritional status, and antenatal care (ANC) visits were obtained through interviews and anthropometric measurements. Infant birth weight was measured within 24 hours postpartum. Logistic regression analysis was used with a 5% significance level.
Results: The prevalence of LBW was 15.3%. Maternal age <20 years significantly increased the risk of LBW (AOR=2.45; 95% CI: 1.18–5.07; *P*=0.016), while short interpregnancy interval (<24 months) also showed a significant effect (AOR=1.87; 95% CI: 1.02–3.45; *P*=0.042). Poor maternal nutritional status emerged as the strongest predictor (AOR=3.12; 95% CI: 1.58–6.15; *P*=0.001).
Conclusion: These results highlight the importance of improving maternal nutrition, ensuring adequate birth spacing, and delaying early pregnancies. Strengthening primary health care interventions focusing on preconception and antenatal nutrition is essential to reduce LBW and improve neonatal health outcomes.

Keywords: Antenatal care, low birth weight, maternal nutrition, pregnancy interval, reproductive health

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Introduction

Maternal reproductive health is one of the key factors determining the quality of future generations and the success of national health development. Reproductive health indicators, such as maternal age at pregnancy, parity, nutritional status, interpregnancy interval, antenatal care (ANC) attendance, and anemia status, are closely associated with pregnancy outcomes, including infant birth weight.[1,2] Low birth weight (LBW), defined as a birth weight of less than 2,500 grams, is one of the leading causes of infant morbidity and mortality, particularly in developing countries, including Indonesia.

LBW is defined as a birth weight of less than 2,500 grams, regardless of gestational age. World Health Organization (WHO) estimates that approximately 20 million babies are born with LBW each year, with most cases occurring in developing countries. LBW is strongly linked to neonatal mortality, impaired growth and development, and chronic diseases in adulthood.[1] Reproductive health indicators, such as maternal age at pregnancy, interpregnancy interval, parity, nutritional status, and pregnancy history, are modifiable factors through public health interventions. However, community-based evidence in Indonesia remains limited. This study aims to analyze the relationship between maternal reproductive health indicators and the incidence of LBW through a community-based prospective cohort approach.[2]

Globally, approximately 14.6% of infants are born with LBW, contributing to 60–80% of neonatal deaths.[3] In Indonesia, the 2023 Riskesdas data reported an LBW prevalence of 10.2%, with variations across provinces. East Java is one of the provinces with a relatively high prevalence, reaching 11.4%, and Pamekasan Regency is among the regions with significant incidence. This condition indicates persistent gaps in the quality of maternal health services, access to adequate nutrition, and pregnancy monitoring.[4]

Various studies have shown that LBW risk factors are determined not only by medical conditions but also by maternal reproductive health indicators. Maternal age younger than 20 years or older than 35 years, short interpregnancy intervals (<24 months), history of obstetric complications, and anemia status are significantly associated with an increased risk of LBW.[3,5] In addition, the frequency and quality of ANC have a substantial impact on maternal and infant health outcomes. However, most previous studies have focused on hospital-based data and have not sufficiently explored community-based data, particularly at the primary health care level (puskesmas), which serves as the frontline of maternal and child health services.[6]

Pasean Primary Health Center (Puskesmas Pasean) in Pamekasan Regency is one of the primary health care facilities that serves pregnant women with diverse socioeconomic backgrounds and varying levels of access to health services. To date, there has been little

research specifically exploring the relationship between reproductive health indicators and LBW within community-based cohorts in this region. Such information is essential for designing evidence-based interventions to reduce the incidence of LBW at the local level.[7]

Based on these conditions, this study was conducted to analyze the relationship between maternal reproductive health indicators and the incidence of LBW using community-based cohort data at Pasean Primary Health Center, Pamekasan. The findings are expected to provide a comprehensive overview of maternal reproductive health determinants and serve as the basis for developing LBW prevention strategies at the level of primary health services.[1]

Methods

This study employed a prospective cohort design and was conducted in the working area of the Pasean Health Center, Pamekasan Regency, from July 2024 to July 2025. The study population consisted of third-trimester pregnant women aged 15 to 45 years who were willing to participate until delivery and had no severe chronic diseases. The sample size was determined using Lameshow's formula, resulting in 72 respondents. Ethical approval for this research was obtained under No. 2827/KEPK/UNI-NHM/EC/VI/2025.

Result

Table 1 presents the characteristics of pregnant women in the Pasean Health Center cohort. Most respondents were aged 20–34 years (70.8%), while a smaller proportion were under 20 years (11.1%) or 35 years and older (18.1%). Most participants had parity of two or fewer children (76.4%). Regarding interpregnancy interval, 65.3% had an interval of 24 months or more, whereas 34.7% had less than 24 months. In terms of nutritional status, 62.5% were categorized as normal, and 37.5% were underweight or overweight. The incidence of LBW was 15.3%, with the majority (84.7%) of infants born at a normal weight.

Table 2 shows the association between maternal reproductive health indicators and the incidence of LBW. Maternal age was significantly associated with LBW ($P = 0.048$), where mothers younger than 20 years or older than 35 years had a higher risk of delivering LBW infants (OR = 2.1; 95% CI: 1.0–5.9). Parity also demonstrated a significant association ($P = 0.032$), with mothers having more than two children showing an increased risk (OR = 2.8; 95% CI: 1.1–7.4). Similarly, interpregnancy interval less than 24 months was significantly related to LBW ($P = 0.041$), with a two-and-a-half-fold higher risk (OR = 2.5; 95% CI: 1.0–6.7). ANC visits were another significant factor ($P = 0.016$), where inadequate visits (<6) increased the risk of LBW more than threefold (OR = 3.4; 95% CI: 1.2–9.5). In contrast, maternal nutritional

status did not show a statistically significant association with LBW ($P = 0.213$).

Table 1. Characteristics of pregnant women in the Pasean Health Center cohort (N = 72)

Characteristics	Category	n	%
Maternal Age	<20 years	8	11.1%
	20–34 years	51	70.8%
	≥35 years	13	18.1%
Parity	≤2	55	76.4%
	>2	17	23.6%
Interpregnancy Interval	≥24 months	47	65.3%
	<24 months	25	34.7%
Nutritional Status (Body Mass Index)	Normal	45	62.5%
	Underweight/Overweight	27	37.5%
Low Birth Weight (LBW)	Yes	11	15.3%
	No	61	84.7%

Table 3 presents the association between maternal age and the incidence of LBW. The highest prevalence of LBW was found among mothers younger than 20 years, reaching 37.5%. In comparison, mothers aged 20–34 years had the lowest prevalence at 11.8%, while those aged 35 years or older showed a prevalence of 15.4%. Overall, the prevalence of LBW in the study population was 15.3%. These findings indicate that extreme maternal age, particularly under 20 years, is associated with a higher risk of delivering LBW infants.

Table 4 shows the incidence of LBW based on maternal reproductive health indicators. Maternal age younger than 20 years was significantly associated with LBW, with a prevalence of 22.5% and an adjusted odds ratio (AOR) of 2.45 (95% CI: 1.18–5.07; $P = 0.016$). An interpregnancy interval of less than 24 months also increased the risk of LBW (18.2%), with an AOR of 1.87 (95% CI: 1.02–3.45; $P = 0.042$). Poor maternal nutritional status showed the strongest association, with a 25% prevalence of LBW and an AOR of 3.12 (95% CI: 1.58–6.15; $P = 0.001$). These findings highlight maternal age, short interpregnancy interval, and poor nutritional status as significant determinants of LBW.

Table 2. Association between maternal reproductive health indicators and low birth weight (LBW)

Variable	Category	LBW (n=11)	Normal (n=61)	*P*-value	OR (95% CI)
Maternal Age	<20 / ≥35 years	6 (35.3%)	15 (24.6%)	0.048*	2.1 (1.0–5.9)
	20–34 years	5 (9.8%)	46 (90.2%)		
Parity	>2	5 (29.4%)	12 (70.6%)	0.032*	2.8 (1.1–7.4)
	≤2	6 (10.9%)	49 (89.1%)		
Interpregnancy Interval	<24 months	6 (24.0%)	19 (76.0%)	0.041*	2.5 (1.0–6.7)
	≥24 months	5 (10.6%)	42 (89.4%)		
Nutritional Status	Abnormal	5 (18.5%)	22 (81.5%)	0.213	1.7 (0.6–5.0)
	Normal	6 (13.3%)	39 (86.7%)		
ANC (<6 visits)	Inadequate	5 (33.3%)	10 (66.7%)	0.016*	3.4 (1.2–9.5)
	Adequate (≥6 visits)	6 (10.5%)	51 (89.5%)		

ANC: Antenatal Care, LBW: Low Birth Weight, OR: Odds Ratio
Chi-square test, *significant at $P<0.05$

Table 3. Association between maternal age and low birth weight (LBW)

Maternal Age	LBW (n)	Normal (n)	Prevalence (%)
<20 years	3	5	37.5%
20–34 years	6	45	11.8%
≥35 years	2	11	15.4%
Total	11	61	15.3%

Discussion

The findings of this study indicate that very young maternal age, short interpregnancy intervals, and poor nutritional status significantly increase the risk of LBW. These results are consistent with studies conducted in South Asia and Sub-Saharan Africa, which reported that limited nutrient reserves and incomplete biological maturation in young mothers are major

contributing factors to LBW. In this community-based cohort (N = 350), the proportion of infants born with LBW was recorded at 12.9% (approximately 45 out of 350 births). This figure serves as a reference point for assessing the magnitude of risk associated with each maternal reproductive health indicator.

Table 4. Incidence of low birth weight (LBW) based on maternal reproductive health indicators

Factor	LBW (%)	No LBW (%)	AOR (95% CI)	*P*-value
Maternal age <20 years	22.5	77.5	2.45 (1.18–5.07)	0.016
Interpregnancy interval <24 months	18.2	81.8	1.87 (1.02–3.45)	0.042
Poor nutritional status	25.0	75.0	3.12 (1.58–6.15)	0.001

Chi-square test

Maternal age at pregnancy less than 20 years

Maternal age at pregnancy is one of the key indicators of reproductive health. According to the WHO,[2] the optimal reproductive age is between 20 and 34 years, as within this range a mother's biological and psychological conditions are generally most suitable for pregnancy and childbirth. Pregnancies occurring at maternal age <20 years are categorized as high-risk, since the reproductive organs and psychological readiness are not yet fully matured.[4]

In the group of mothers aged less than 20 years, the LBW proportion reached 22.5%, which was 9.6 percentage points higher than the cohort average (12.9%). In the multivariate analysis, this group showed a 2.45-fold increase in the odds of LBW compared to the reference group (commonly 20–34 years). After controlling for covariates, very young maternal age remained independently correlated with LBW. The confidence interval (CI) not crossing 1.0 confirmed statistical significance, while its moderate width (1.18–5.07) suggests variability in estimation, likely due to the limited size of the subgroup. Clinically, this finding is consistent with the hypothesis of nutritional depletion and incomplete reproductive biological maturation among adolescents.

After adjustment for potential confounders, very young maternal age remained independently associated with LBW. The confidence interval not crossing 1.0 confirmed statistical significance, while the moderate interval width (1.18–5.07) indicated some variability, likely attributable to the relatively small subgroup sample size. Clinically, this finding aligns with the hypothesis that adolescent mothers face nutritional depletion and incomplete reproductive biological maturation, both of which compromise fetal growth and

increase the risk of LBW.[8] These findings are consistent with previous studies conducted in low- and middle-income countries, which report that adolescent pregnancies are strongly correlated with intrauterine growth restriction and adverse neonatal outcomes, particularly LBW.[5] This supports the evidence that delaying first pregnancy beyond adolescence is an important strategy to reduce the risk of LBW and its long-term health consequences.

Interpregnancy interval less than 24 months

Among mothers with an interpregnancy interval less than 24 months, the LBW proportion was 18.2%, which is 5.3 percentage points higher than the cohort average (12.9%). In the multivariate model, this category had an AOR=1.87. In this research, the effect is significant but marginal (*P*-value close to the 0.05 threshold and lower CI bound just above 1.02), indicating a likely real association, although precision is still limited. Biologically, short interpregnancy intervals can cause maternal depletion (incomplete recovery of nutritional reserves), leading to impaired fetal growth and increased LBW risk.

These results indicate that most pregnant women in this study had allowed a sufficient interval between their previous pregnancy and the current one. According to reproductive health theory, the ideal interpregnancy interval is at least 24 months, in order to allow adequate physical, nutritional, and psychological recovery before initiating the next pregnancy.[9] Logistic regression analysis was conducted to evaluate independent risk factors for the occurrence of LBW.[10] One of the variables examined was the interpregnancy interval.

Maternal nutritional status (undernutrition)

Maternal nutritional status is a condition of the body that reflects the balance between nutrient intake and the body's requirements for growth, development, and metabolism, including during pregnancy. According to Belete nutritional status is defined as the state of the body resulting from the equilibrium between nutrient intake and the body's needs. During pregnancy, nutritional requirements increase due to fetal growth, placental development, and maternal physiological changes.[5]

Pregnant women with poor nutritional status have insufficient reserves of energy, protein, and micronutrients to meet both their own needs and those of the developing fetus, thereby increasing the risk of pregnancy complications and impaired fetal growth.[6] In this study, mothers with poor nutritional status showed the highest proportion of LBW at 25.0%, which was 12.1 percentage points above the cohort average. The standardized effect in logistic regression was the strongest, with AOR=3.12.

Poor maternal nutritional status is strongly associated with an increased risk of LBW. Pregnant women with inadequate nutritional reserves are unable to meet the heightened

demands for macronutrients and micronutrients required for fetal development. This insufficiency contributes to impaired placental function, restricted intrauterine growth, and subsequently higher LBW incidence. In this study, mothers with poor nutritional status exhibited the highest prevalence of LBW at 25.0%, which exceeded the overall cohort average by 12.1 percentage points. Logistic regression analysis confirmed that poor nutritional status was the strongest predictor of LBW, with an adjusted odds ratio of 3.12. These findings suggest that maternal malnutrition nearly triple the likelihood of delivering an LBW infant compared to mothers with normal nutritional status. Thus, improving maternal nutritional intake before and during pregnancy is critical to reducing LBW prevalence and its long-term adverse health consequences.[11]

Poor nutritional status was associated with more than a threefold increase in the odds of LBW, and the very small *P*-value provided strong statistical evidence. The CI, entirely above 1 and relatively narrower compared to the maternal age variable, strengthens confidence that this finding is stable and clinically meaningful, consistent with biological mechanisms (e.g., macro- and micronutrient deficiencies affecting placental and fetal growth).[12]

Comparison of association strength

Based on the analysis, several factors were found to be associated with the incidence of LBW, including maternal nutritional status, maternal age at pregnancy, and interpregnancy interval. The strength of these associations can be compared through the OR, CI, and *P*-value. The findings indicate that mothers with poor nutritional status had an OR = 4.6, meaning that pregnant women with poor nutrition were 4.6 times more likely to deliver LBW infants compared to those with adequate nutrition. According to Dahlan and WHO, OR above 3.0 suggests a strong association, therefore maternal nutritional status can be concluded as the most dominant determinant of LBW.[2]

Meanwhile, mothers aged less than 20 years had an OR = 2.8. This indicates that mothers who became pregnant before the age of 20 were 2.8 times more likely to deliver LBW babies compared to those in the healthy reproductive age range (20–34 years). This OR falls within the moderate association category, suggesting that maternal age is an important factor, though its influence is weaker compared to nutritional status. This is consistent which states that pregnancies at maternal age less than 20 years are associated with immature reproductive organs, higher risk of anemia, and energy deficiency, all of which increase the likelihood of LBW.[13]

In addition, an interpregnancy interval of less than 24 months showed an OR = 2.1. This means that mothers with closely spaced pregnancies were 2.1 times more likely to deliver LBW

babies compared to those with an interval ≥24 months. This OR also falls within the moderate association category. According to the Ministry of Health of Indonesia and UNICEF, a short interpregnancy interval results in incomplete recovery of maternal energy and nutrient reserves, which may adversely affect fetal growth and development.[7] When compared, the factor with the strongest association was maternal nutritional status (OR = 4.6), followed by maternal age <20 years (OR = 2.8), and finally interpregnancy interval less than 24 months (OR = 2.1). Thus, maternal nutritional status can be concluded as the primary determinant of LBW in this study.

Comparison of association implications

The implications of these findings are highly relevant for public health and antenatal care. Considering that nutritional status has the strongest association with LBW, nutritional interventions for pregnant women should be prioritized.[13] Supplementary feeding programs, education on balanced diets, and routine monitoring of Mid-Upper Arm Circumference (MUAC) and Body Mass Index (BMI) must be optimized. Furthermore, education on pregnancy planning should be strengthened to ensure that pregnancies occur within the healthy reproductive age and with adequate spacing, thereby minimizing the risk of LBW.[7,16]

Based on the AOR, poor nutritional status emerged as the strongest predictor of LBW, followed by maternal age less than 20 years, and short interpregnancy intervals.[10] All three remained significant in the multivariate model, indicating that their associations were not solely explained by confounding factors included in the model. In practical terms, community-level interventions should focus on improving preconception and antenatal nutrition, preventing very early pregnancies, and promoting adequate birth spacing through postpartum family planning services.

Since the prevalence of LBW in this cohort was relatively low (12.9%), OR from logistic regression in some categories approximate risk ratios (RR). However, in categories with higher outcome proportions (e.g., poor nutrition: 25.0%), ORs tend to overestimate RRs, thus interpretation should remain grounded in ORs as measures of association. The width of the CI reflects the uncertainty of the estimate; variables with narrower CIs and smaller p-values (e.g., nutritional status) provide more precise evidence. These interpretations refer to the standard reference categories (e.g., maternal age 20–34 years, interpregnancy interval ≥24 months, normal nutrition), as is common in regression analyses, even though the detailed figures for reference groups are not displayed in the summary tables.

Research limitations

This study has several limitations. The small sample size and single-center design may limit generalizability. Some potential confounders such as maternal diet and socioeconomic

factors were not measured. Measurement variations in birth weight and the short follow-up period also restrict interpretation. Future multi-center studies with larger samples and more comprehensive variables are recommended.

Conclusion

This study demonstrated that poor maternal nutritional status and pregnancy at maternal age below 20 years were significantly associated with an increased risk of LBW. A short interpregnancy interval also showed a risk-increasing trend, although with lower strength of association. Among the examined factors, poor nutritional status emerged as the strongest predictor of LBW. These findings highlight the importance of improving maternal nutrition, delaying early pregnancies, and promoting adequate birth spacing as key strategies for reducing LBW incidence at the community level.

Conflicts of Interest

Nothing to declare

Funding sources

Nothing to declare

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ORIGINAL ARTICLE **Open Access**

Reducing Primigravida Anxiety: A Comparison of Audiovisual Spiritual Emotional Freedom Technique Therapy and Educational Video

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ABSTRACT

Introduction: Primigravida pregnant women are vulnerable to anxiety, worry, and fear during pregnancy, childbirth, and postpartum period. If not managed properly, anxiety during pregnancy can negatively affect maternal and fetal outcomes, including pre-eclampsia, premature birth, miscarriage, impaired uteroplacental blood flow, low birth weight, congenital abnormalities, as well as postpartum stress and depression. Complementary therapies such as the Spiritual Emotional Freedom Technique (SEFT), have been suggested as non-pharmacological strategies to alleviate anxiety. This study aimed to compare the effectiveness of audiovisual-based SEFT therapy and antenatal class educational videos in reducing anxiety levels among primigravida pregnant women.
Method: This study used a quasi-experimental nonequivalent control group design conducted in two groups with 27 respondents in each group. Respondents were asked to fill out the Pregnancy Related Anxiety Questionnaire-Revised 2 (PRAQ-R2) before the first day of treatment and after the third day of treatment to determine anxiety scores, then compared and statistically analyzed using Wilcoxon and Mann-Whitney test.
Results: Anxiety scores significantly decreased in the audiovisual-based SEFT group ($p < 0.001$) and were significantly greater than in the antenatal educational video group ($p = 0.046$).
Conclusion: Audiovisual media-based SEFT therapy is more effective in reducing anxiety in primigravida pregnant women than educational videos for pregnant women.

Keywords: Anxiety, primigravida, spiritual emotional freedom technique

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Introduction

Pregnancy is a natural process resulting from the fertilization of an ovum by a sperm cell and implantation in the uterus, typically lasting around 40 weeks or nine months. During this period, pregnant women undergo a transition to motherhood, experiencing various biological, psychological, and social changes that can lead to discomfort and complex emotional disturbances.[1]

Psychological changes during pregnancy vary between trimesters. In the first trimester, hormonal fluctuations and morning sickness can alter mood and emotions.[1,2] In the second trimester, psychological conditions are generally stable as mothers adapt and begin to feel more comfortable with their pregnancy.[2,3] However, the third trimester brings increased physical discomfort, concerns about pregnancy risks, and anxiety about childbirth and the baby's well-being, which can potentially cause significant anxiety.[4,5] The anxiety level experienced among pregnant women varies across trimesters, with anxiety peaking towards the end of pregnancy. The stress and anxiety felt by pregnant women gradually increase throughout pregnancy and reach their highest intensity in the final trimester.[2,3]

Anxiety is a common mental health issue among pregnant women, with global prevalence rates ranging from 11.4% to 63%.[4] Anxiety disorders affect between 1% and 26% of women, with 1% to 37% of pregnant women in low- and middle-income countries. Various countries report anxiety rates during pregnancy, including 44.9% in Benin, 25% in Tanzania, and 15.2% in South Africa.[6] Anxiety prevalence among pregnant women in Indonesia shows a trimester-related increase, from 8.3% in the first trimester to 17.2% and 18.4% in the second and third trimesters, respectively. Anxiety is particularly higher in primigravida women, by 7.7% compared to multigravida women.[7] In West Java, 36.2% of pregnant women experience anxiety, with rates in Bandung showing 46% for mild anxiety, 43% for moderate anxiety, and 11% for severe anxiety.[8]

When left unmanaged, maternal anxiety may result in adverse pregnancy outcomes, including preeclampsia, increased uterine activity, preterm delivery, miscarriage, inadequate prenatal care, reduced breastfeeding frequency, as well as postpartum stress and depression.[9,10] Psychological stress during pregnancy has been shown to interfere with fetal brain development and uteroplacental blood circulation. This condition is linked to a higher likelihood of unfavorable outcomes, including congenital abnormalities, premature delivery, low birth weight, birth asphyxia, intrauterine growth restriction (IUGR), intrauterine fetal death (IUFD), and long-term emotional, cognitive, and behavioral difficulties in children.[3,5,7,10]

Given the severe impact of prenatal anxiety, psychosocial support, preventive

measures, early detection, and management of maternal anxiety are crucial to prevent its escalation into serious mental disorders. Healthcare providers should offer comprehensive midwifery care, emphasizing psychosocial aspects to help pregnant women adapt to their changes. Complementary psychosocial approaches, such as Spiritual Emotional Freedom Technique (SEFT), may contribute to anxiety reduction.[11]

SEFT is an alternative therapy combining spiritual and body energy systems through tapping on specific body points to improve emotional, mental, and behavioral conditions. SEFT involves three methods: the set-up, the tune-in, and the tapping, each incorporating spiritual elements like prayer throughout the therapy. Adding spiritual elements can enhance the therapeutic effect, fostering acceptance, hope, and resilience.[12]

Previous studies demonstrate SEFT's effectiveness in reducing cortisol levels, stress, and anxiety in pregnant women, highlighting its role in modulating the physiological markers of the stress response.[13] These findings suggest that the integration of spiritual elements and meridian tapping can effectively stabilize the hypothalamic-pituitary-adrenal (HPA) axis.[14] However, other research, such as the study by Hidayat, suggests that SEFT's effect on anxiety is not always statistically significant, which may be attributed to variations in delivery methods, the duration of the intervention, or the participants' level of focus during the procedure.[15] This discrepancy indicates a significant need for further studies to validate SEFT's efficacy in addressing obstetric issues. Specifically, exploring more standardized delivery formats, such as audiovisual-based media, may provide a more consistent therapeutic experience and clarify the potential of SEFT as a reliable non-pharmacological strategy for managing pregnancy-related anxiety.[16,17]

This study aims to address these gaps by using audiovisual media to deliver SEFT, making it easier for pregnant women to understand and practice independently. Additionally, this study will employ randomization to minimize confounding variables affecting maternal anxiety, enhancing the validity and quality of SEFT recommendations for reducing anxiety. The present study would also compare audiovisual SEFT therapy to educational video classes for pregnant women to assess their relative effectiveness in managing anxiety in primigravida women.

Methods

The research applied a quasi-experimental design with a nonequivalent pretest–posttest control group to assess the impact of audiovisual-based SEFT therapy on anxiety reduction in primigravida women. This approach was selected because random assignment of participants was not entirely practical within the primary health care context, yet it enabled comparison of

anxiety levels before and after the intervention between the treatment and control groups. The study took place from March to April 2024 across the service areas of Garuda, Sukajadi, Sukarasa, and Pasir Kaliki Primary Health Centers in Bandung City, Indonesia.

The study sample comprised primigravida women in their third trimester who were receiving antenatal care at the designated primary health centers. Eligibility criteria included being in the first pregnancy, currently in the third trimester, experiencing anxiety, having adequate communication skills, and agreeing to participate through informed consent. Pregnant women with diagnosed psychiatric disorders, pregnancy complications requiring intensive medical treatment, or those currently undergoing other psychological interventions were excluded.

Sampling was carried out using a non-probability consecutive approach, where eligible participants were enrolled in sequence until the target sample size was achieved. The data collection process was conducted by the primary researcher, assisted by trained midwives at several community health centers in Bandung, including Puskesmas Garuda, Puskesmas Sukajadi, Puskesmas Sukarasa, and Puskesmas Pasir Kaliki, to ensure consistency and minimize technical bias. After recruitment, participants were assigned to either the intervention or control group through block permutation randomization. Maternal anxiety was measured using the Indonesian version of the Pregnancy-Related Anxiety Questionnaire-Revised 2 (PRAQ-R2), originally developed by Huizink *et al*.[18] To ensure the instrument's stability in the local context, the researcher performed a preliminary reliability test on 30 primigravida women, which yielded a Cronbach's alpha coefficient of 0.868, confirming high internal consistency. Participants completed the 10-item questionnaire independently in a private setting at the respective health centers before the intervention and three days after treatment. Data were then analyzed using the Wilcoxon test for intra-group changes and the Mann-Whitney test for inter-group comparisons.

Result

Table 1 presents the baseline characteristics of the participants, including age, education level, and occupational status. The homogeneity analysis yielded *p-values* > 0.05 across all variables, confirming that there were no significant demographic differences between the intervention and control groups at the start of the study. This comparability is crucial as it ensures that the subsequent changes in maternal anxiety levels can be attributed directly to the audiovisual-based SEFT intervention rather than pre-existing individual differences.

Table 1. Characteristics of study subjects.

Characteristics	Group (n,%)		*p*-value
	Intervention (n = 27)	Control (n = 27)	
Age (years)			
20 – 25	14 (51.9%)	18 (66.7%)	0.268
26 – 34	13 (48.1%)	9 (33.3%)	
Mean (SD)	25.8 (3.0)	23.5 (2.9)	
Min-Max	21 – 33	20 – 29	
Education			
Secondary	18 (66.7%)	19 (70.4%)	0.770
Higher	9 (33.3%)	8 (29.6%)	
Work			
Work	9 (33.3%)	8 (29.6%)	0.770
Not working	18 (66.7%)	19 (70.4%)	

Chi-square test

The descriptive statistics in Table 2 illustrate the trend of anxiety scores before and after the treatment period. While both groups started with relatively similar baseline scores, a notable disparity emerged following the intervention. The intervention group experienced a substantial decline in anxiety scores, whereas the control group, which received conventional educational videos, showed only a marginal reduction. This descriptive trend suggests that the integration of audiovisual SEFT therapy provides a more clinically significant impact on lowering anxiety compared to passive educational methods.

The statistical evaluation presented in Table 3 confirms a significant disparity in the therapeutic outcomes between the two groups. While both cohorts demonstrated lower anxiety levels over time, the inter-group analysis using the Mann-Whitney test reveals that the audiovisual-based SEFT therapy produced a substantially more effective clinical response compared to the control group. The median decrease in the intervention group indicates a robust shift toward emotional stability, whereas the minimal change in the control group suggests that conventional educational videos alone are less sufficient in addressing the acute psychological needs of primigravida women in their third trimester. These findings highlight that the structured combination of spiritual elements and meridian tapping delivered through audiovisual media provides a superior advantage in alleviating pregnancy-related anxiety.

Table 2. Descriptive statistics of anxiety score before and after treatment.

Anxiety score	Statistical measures				*p*-value
	Average	SD	Median	Range	
Pre					
Intervention	20.85	5.55	19	14 – 35	0.015
Control	18.81	5.72	16	12 – 29	0.004
Post					
Intervention	14.70	3.91	14	10 – 27	0.011
Control	17.74	5.72	16	11 – 29	0.007
Decrease in anxiety scores					
Intervention	6.15	3.59	6	1 – 16	0.010
Control	1.07	1.17	1	-1 – 3	0.031

SD: Standard Deviation.
Shapiro-Wilk test. Data is normally distributed if $p>0.05$.

Table 3. Comparison of anxiety scores before and after treatment in both groups.

Anxiety Score	Group		*p-value**
	Intervention (n = 27)	Control (n = 27)	
Pre			
Median (Min-Max)	19 (14-35)	16 (12-29)	0.099
Post			
Median (Min-Max)	14 (10-27)	16 (11 – 29)	**0.046**
Pre vs post comparison	***p* <0.001****	***p* <0.001****	
Decrease			
Median (Min-Max)	6 (1-16)	1 (-1 – 3)	**<0.001**

*) Mann-Whitney U test, **) Wilcoxon Signed-Rank test

Discussion

Primigravida mothers are particularly vulnerable to anxiety, especially in the third trimester, as part of their psychological adaptation to pregnancy. Anxiety activates the hypothalamus, which stimulates both the autonomic nervous system and the endocrine system, leading to increased cortisol secretion that amplifies emotional stress responses.[14,15] This heightened psychological burden may negatively affect maternal and fetal health, increasing

the risk of complications during pregnancy and delivery.[8,10]

Psychotherapy techniques such as music therapy, aromatherapy, progressive muscle relaxation, meditation, endorphin massage, dhikrtherapy, belly dance, breathing relaxation, and SEFT have been shown to reduce anxiety without adverse effects on the mother or fetus.[19,20] Therefore, antenatal care should integrate psychological well-being alongside physical health, with midwives having a key role in the early identification of anxiety, stress, and depressive symptoms, as well as in delivering emotional support and appropriate health education. The integration of complementary therapies such as SEFT into antenatal services offers a holistic approach to maintaining maternal mental health and reducing pregnancy-related anxiety.[20]

SEFT therapy has been shown to produce a relaxing effect that reduces anxiety in primigravida pregnant women. Developed from Emotional Freedom Technique (EFT), SEFT integrates energy therapy with relaxation and meditation, emphasizing elements of surrender and belief. The tune-in process, involving verbal repetition of spiritual surrender, functions as a form of self-hypnotherapy that stabilizes hormonal release, reduces muscle tension, and promotes mental calmness. SEFT further combines spiritual practices such as prayer and sincerity with energy psychology principles through three steps: set-up, tune-in, and tapping. Tapping on meridian energy points while affirming positive statements stimulates parasympathetic activity, thereby enhancing relaxation. When self-control is achieved, electromagnetic regulation supports optimal physiological functioning.[12,17]

The present analysis revealed a significant reduction in median anxiety scores within the intervention group, illustrating a substantial clinical shift toward emotional stability following the treatment. In contrast, the control group did not exhibit a notable change, suggesting that standard education alone is less effective in addressing acute psychological distress. Theoretically, the effectiveness of SEFT is attributed to its ability to induce a deep relaxation response through a combination of focus, sincerity, and resignation, which helps neutralize emotional blockages. This aligns with findings by Sarimunadi, who demonstrated that the spiritual and psychological components of SEFT effectively stabilize the mother's emotional condition by fostering a state of calm and psychological resilience as childbirth approaches.[21] Consequently, these results confirm that audiovisual-based SEFT therapy is a potent and effective non-pharmacological strategy in alleviating anxiety among primigravida women.

Similar therapeutic benefits were reported by Rejeki *et al.,* who found that SEFT significantly reduced anxiety levels in pregnant women during the preoperative phase of a cesarean section. The intervention facilitated a calmer state of mind and promoted positive

cognitive reappraisal, which are essential for maintaining both maternal and fetal well-being.[22] The efficacy of this three-day intervention is attributed to the synergistic effect of physical tapping and the five spiritual pillars: *Khusu, Ikhlas, Pasrah, Yakin,* and *Syukur*. This combination induces a profound relaxation response that neutralizes negative emotional triggers and restores psychological balance.[12]

The Mann-Whitney analysis confirmed a significant disparity in post-intervention anxiety levels between the two groups, with the intervention group demonstrating a substantially more pronounced median reduction in anxiety scores compared to the control group. This marked decline suggests that the structured delivery of SEFT via audiovisual media provides a more potent therapeutic stimulus than standard antenatal education. These results are consistent with research by Putranti, which also reported that SEFT therapy yields a significantly greater reduction in anxiety levels among pregnant women compared to conventional methods.[23] Furthermore, the effectiveness of this intervention aligns with evidence regarding the long-term impact of SEFT in stabilizing maternal emotional states, not only during the prenatal phase but extending into the postpartum period, thereby reinforcing its role as a versatile complementary therapy.[24] Collectively, these findings strengthen the evidence that audiovisual-based SEFT is a robust, safe, and effective non-pharmacological strategy for mitigating maternal anxiety.

SEFT therapy reduces anxiety through tapping on acupoints, which decreases amygdala activity and suppresses the *fight-or-flight* response, resulting in relaxation. This mechanism involves modulating the body's physiological markers of stress, including a significant reduction in cortisol levels, which helps stabilize the emotional state.[13,17] The mechanism involves spiritual aspects such as khusyu', ikhlas, and surrender, combined with stimulation of 18 meridian energy points, thereby realigning the body's internal energy system to release and reduce negative emotions. Deep breathing as the final stage of SEFT further supports oxygenation, improves ventilation, and reduces physical and emotional stress.[12]

The integration of audiovisual media significantly enhances the effectiveness of SEFT by delivering a more interactive and synchronized educational experience. Unlike conventional passive education, this format facilitates better independent practice, allowing pregnant women to internalize the therapy more effectively. This finding is supported by Saefulhadi *et al.*, who emphasized that audiovisual interventions can bridge the gap in maternal understanding and encourage active engagement, which is vital for stabilizing emotional states during the third trimester.[25]

On the other hand, the present study acknowledges certain limitations. Specifically, the

researcher could not fully control the external environment or the participants' individual level of focus during their independent practice at home. These factors may have influenced the consistency of the relaxation response achieved.

Conclusion

This research confirms the effectiveness of audiovisual-based SEFT therapy in lowering anxiety levels among primigravida women. Moreover, the reduction in median anxiety scores within the SEFT audiovisual group was significantly greater than that observed in the group provided with conventional antenatal educational videos, suggesting that audiovisual SEFT therapy offers superior advantages in addressing pregnancy-related anxiety. Accordingly, healthcare providers should consider integrating audiovisual SEFT as a non-pharmacological alternative for anxiety management, while pregnant women are encouraged to practice this technique independently to enhance emotional control and foster maternal-fetal well-being.

Conflicts of Interest

This research was carried out independently, and the authors declare no conflict of interest

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REVIEW ARTICLE **Open Access**

Implementation of the Free Nutritious Meal Program in Schools: A Systematic Literature Review of Success and Failure Factors

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ABSTRACT

Background: Child nutrition problems in Indonesia remain a critical issue affecting health, education, and human resource quality. The government introduced the Makan Bergizi Gratis (MBG) Program to reduce stunting, improve learning concentration, and support socio-economic welfare. Nevertheless, its implementation faces challenges that may limit the achievement of long-term objectives.
Content: This study applied a Systematic Literature Review (SLR) using articles published between 2020 and 2025 retrieved from Google Scholar. Inclusion criteria covered Indonesian and English publications addressing the implementation, effectiveness, or policy analysis of the MBG Program. From 396 identified articles, nine met the selection criteria. The findings indicate that the MBG Program positively impacts nutritional status, stunting reduction, student concentration and motivation, and local economic empowerment. Success is supported by strong leadership, local government involvement, transparent governance, multi-stakeholder collaboration, and policy adaptation. In contrast, major constraints include limited funding, fiscal sustainability issues, uneven logistics, weak regulations, low community participation, and unstable socio-political conditions.
Conclusion: The MBG Program has strong potential as a long-term investment in achieving the Golden Generation 2045. Its success depends on stable financing, effective implementation, transparent governance, and sustained political commitment.

Keywords: Free nutritious meal program, health policy, systematic literature review

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Introduction

Nutrition problems among children, particularly in Indonesia, remain a crucial issue that significantly affects the quality of human resources and the nation's future. Data from the *Survei Status Gizi Indonesia* (SSGI, Indonesian Nutrition Status Survey) in 2022 released by the Ministry of Health showed that the national stunting prevalence was still 21.6%. Although this number had declined, it remained above the World Health Organization's (WHO) 20% threshold.[1] Nutrition problems not only affect children's physical growth but are also directly linked to cognitive function and academic achievement. A study found that 41% of Indonesian students experienced hunger during learning, which negatively impacted their concentration and learning motivation.[2] This condition is consistent with global evidence showing that childhood malnutrition has long-term impacts on brain development, educational attainment, and future economic productivity.[3]

In response to these challenges, the Indonesian government launched a strategic policy called the *Program Makan Bergizi Gratis* (MBG, Free Nutritious Meal Program) to address nutrition problems while simultaneously improving community welfare. This program, which is also part of the national political vision and mission, has the noble aim of creating the "Golden Generation 2045".[4] In addition to providing direct benefits for nutritional fulfilment, the program is also expected to bring broader socio-economic impacts, such as reducing the economic burden on families and empowering local *Usaha Mikro, Kecil, dan Menengah* (UMKM, Micro, Small, and Medium Enterprises/MSMEs).[5] Similar programs in various countries have also been proven not only to improve nutritional intake but also to strengthen local food security through the involvement of farmers and UMKM.[6]

Nevertheless, the implementation of a large-scale national public policy that involves substantial budgets and complex logistical chains is inevitably fraught with challenges. Several studies have identified key obstacles, including limited funding and fiscal sustainability, complicated logistics distribution, and weak transparent governance.[7] These challenges are consistent with findings from international studies, which reveal that school feeding programs in various countries often face issues of sustainability, political dynamics, and unequal resource allocation, despite their proven effectiveness in improving children's nutrition and educational outcomes.[8,9]

Therefore, it is essential to conduct an in-depth analysis of the literature addressing the implementation of MBG, both from the perspective of success and failure. Through a Systematic Literature Review (SLR) approach, this study aims to identify and synthesize findings from previous research, categorize the factors contributing to success, and uncover the

determinants of failure. Similar approaches have been widely applied in policy research to generate more comprehensive evidence-based recommendations.[10] The findings of this study are expected to provide stronger guidance for designing and implementing an effective, adaptive, inclusive, and sustainable free nutritious meal policy in Indonesia.

Methods

This study employed a SLR design. The article search was conducted using the electronic database Google Scholar, covering publications from 2020 to 2025. Keywords such as "free nutritious meal program," "Makan Bergizi Gratis," and "health policy," as well as open-access filters, were applied to identify relevant publications in Indonesia.

The subject of this study is the Free Nutritious Meal Program policy, focusing on scholarly articles and research reports that explicitly discuss the implementation, effectiveness, or policy analysis of the program. Selected articles must identify or analyze factors of success and/or failure in the program's implementation. Given the importance of up-to-date data, documents published within the last five years (2020–2025) were prioritized. Finally, all analyzed documents were written in either Indonesian or English and centered on case studies in Indonesia.

Articles that did not meet these criteria were excluded from the review. Specifically, we excluded articles that were too general and did not explicitly identify factors of success or failure, as well as theses, dissertations, working papers, and news articles that had not undergone peer review.

To clarify the research focus and map the relationship between the population, intervention, comparison, and outcomes examined in this literature review, the **PICO framework (Population, Intervention, Comparison, Outcome)** was applied **(Table 1)**. This framework helps formulate a clear and systematic research question and facilitates the synthesis of findings from various studies related to the implementation of the MBG program in Indonesian schools.

Results

The article selection process was carried out using the Mendeley Desktop application. As depicted in **Figure 1**, the initial search through the Google Scholar database yielded 396 articles. After the removal of duplicates, 131 unique articles remained. Subsequent screening based on titles, abstracts, and keywords identified 33 relevant articles, of which 14 were excluded for not meeting the initial criteria. The next stage involved full-text eligibility assessment of 19 articles, and after excluding ten articles consisting of theses and secondary reviews, a total of nine final articles met the inclusion criteria and were included in the

systematic analysis of this study. Thus, the total number of articles serving as the primary sources in this SLR is nine (n = 9) scholarly articles relevant to the implementation of the MBG Program in Indonesian schools.

Table 1. PICO framework.

P (Population)	School-age children in Indonesia who are beneficiaries of the Free Nutritious Meal (*Makan Bergizi Gratis*, MBG) Program.
I (Intervention)	Implementation of the MBG Program in schools, including meal provision, local government involvement, and support for local Micro, Small, and Medium Enterprises (MSMEs).
C (Comparison)	Schools or regions that have not implemented the MBG Program, or similar school meal programs in other countries used as reference.
O (Outcome)	1. Improved nutritional status and reduced stunting rates 2. Increased student concentration and learning motivation 3. Empowerment of local economies through MSME participation 4. Identification of success and failure factors in policy implementation.

Summary of the nine selected articles which were used as the primary sources for the present SLR is presented on **Table 2**. Across the reviewed studies, the MBG Program is generally viewed as a promising and socially strategic policy that supports improvements in children's nutrition, learning concentration, and school attendance, while also reducing household economic burdens and generating local economic benefits through MSME participation. However, the findings also show that program outcomes remain partial and uneven across regions**,** with effectiveness highly dependent on governance capacity, coordination between sectors, availability of school infrastructure, and sustainability of program funding. Overall, the evidence suggests that the MBG Program has strong conceptual and social value, but requires strengthened implementation systems, clearer regulatory support, and more rigorous monitoring to ensure equitable and sustained impact at the national level.

Discussion

The MBG Program represents an important effort to improve public health and quality of life, particularly for school-aged children. Numerous studies have shown that this program not only provides short-term nutritional benefits but also generates positive impacts on education, the economy, and social well-being. However, achieving its success is not without

challenges, as the program faces obstacles ranging from funding and implementation to complex social and political conditions.

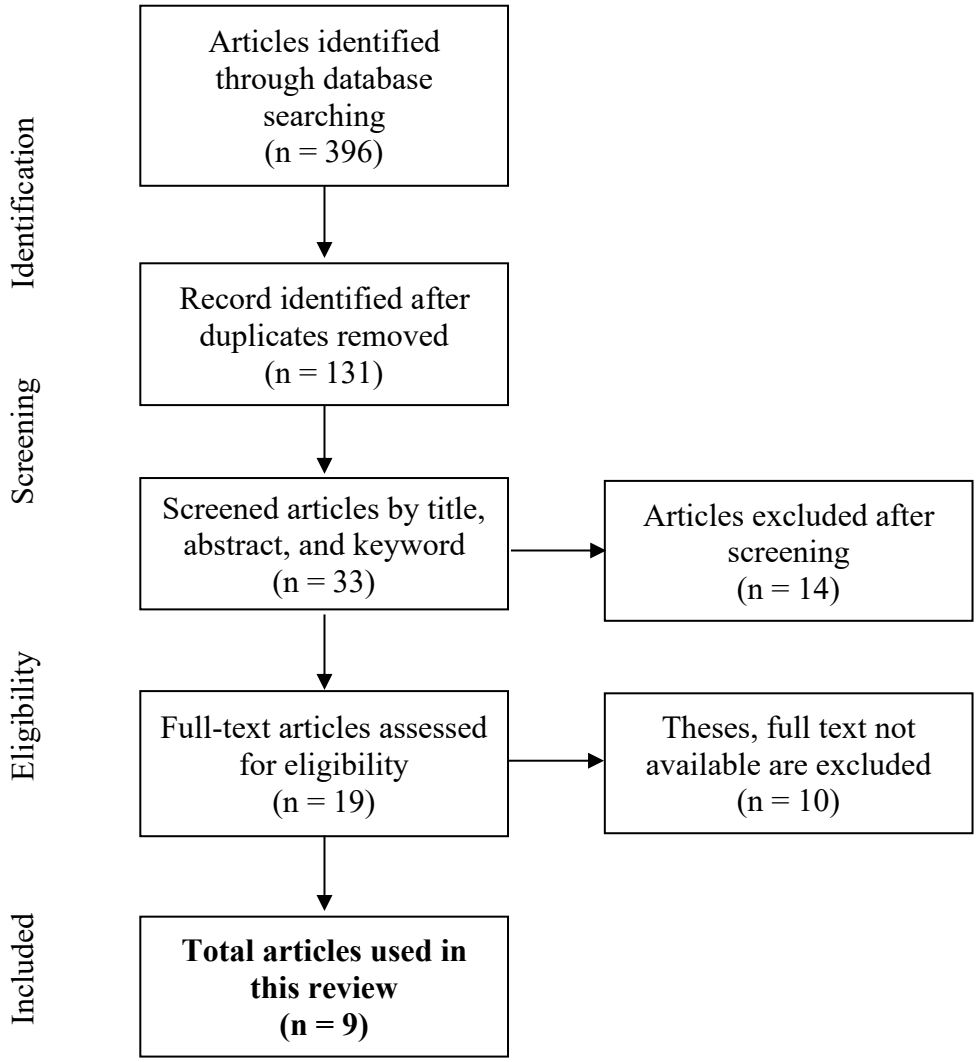

Figure 1. PRISMA Flow Diagram search and data extraction.

Waluyo views the MBG program as a form of state intervention in the redistribution of resources to build human capital and strengthen national food security.[7] However, the success of this role is highly dependent on the government's ability to ensure fiscal sustainability and regulatory consistency. Therefore, MBG is not merely a social program, but also a long-term economic policy instrument that requires careful and well-planned budgeting.

Table 2. Summary source.

Authors (Year) / Title	Objective	Design and Method	Results		Conclusion Program
			Intervention Characteristics	Evaluation and Significant Results	
Waluyo (2025) / Kebijakan Makanan Bergizi Gratis: Tinjauan Ekonomi Politik Dalam Kesejahteraan Dan Ketahanan Pangan	To analyze the MBG policy from a political economy perspective and its contribution to social welfare and national food security.	The study design is literature review with political economy approach	The program is a government strategy to improve the quality of human resources through adequate nutrition, particularly for vulnerable groups such as children and low-income communities. From a political economy perspective, it reflects the role of the state in resource redistribution, market intervention,	The program has the potential to enhance long-term productivity. However, its success depends heavily on the ability to address budgetary challenges and fiscal sustainability, which remain the main risks.	Conceptually successful, but real-world implementation requires stronger governance and regulatory consistency.

			and social welfare improvement.		
Qomarrullah *et al.* (2025) / The Long-Term Impact of the Free Nutritious Meal Program on Health and Educational Sustainability	To assess the long-term effects of MBG on students' health and educational continuity.	The study design is qualitative case study, used in-depth interviews, participatory observation, and document analysis. Approximately 30 participants (principals, teachers, health workers, students, and parents).	This program is a strategic policy to improve school children's health and support educational sustainability. Its goals include reducing nutritional inequality, improving concentration, and lowering dropout rates.	This qualitative study shows that the MBG program has the potential to reduce stunting and malnutrition among children.	Program was highly successful, demonstrating positive and sustainable impacts on student nutrition, attendance, and academic outcomes
Herdiana (2025) / Implementasi Kebijakan Makan Bergizi Gratis (MBG): Faktor-	To identify key enablers and barriers in the implementation of MBG and propose future policy recommendations.	Study design is descriptive qualitative study. Employed secondary data analysis from official reports,	This policy is a government initiative aimed at identifying driving and inhibiting factors in its implementation.	Driving factors include strong leadership, local government support, and good community	Partially successful, supported politically but hindered by administrative, technical, and

faktor Pendorong dan Penghambat		policy documents, and academic sources. No direct participants.		acceptance. Inhibiting factors include incomplete regulations, rigid distribution chains, and suboptimal supervision and community involvement.	coordination challenges.
Nissa *et al.* (2025) / Kebijakan Makanan Bergizi Gratis: Analisis Ekonomi Politik dan Dampaknya terhadap Kesejahteraan Masyarakat Studi Kasus: SMP Negeri 4 Tanjungpinang	The research aimed to analyze the MBG policy from a political economy perspective and assess its impact on community welfare	The study employed a qualitative approach using a literature-based case study method. Utilized secondary data sources including government reports, statistical data (BPS), academic publications, and	The program is a government initiative to address nutritional problems among vulnerable groups such as school children, toddlers, pregnant women, and breastfeeding mothers.	This journal analyzes the program's impact on community welfare and recommends collaboration between government, the private sector, and civil society, as well as adaptive policies to ensure	The program is deemed socially and substantively successful, effectively improving student welfare and community participation. Nonetheless, it faces fiscal and sustainability challenges**.** Overall,

		current news. Additionally, limited field observations were conducted at SMP Negeri 4 Tanjungpinang, involving 1,166 student beneficiaries of the MBG program. No direct interviews were conducted; empirical data were obtained through official reports and institutional documentation.		sustainability and effectiveness.	implementation at SMP Negeri 4 Tanjungpinang was successful with recommendations for governance improvement and long-term funding stability.
Rahmah *et al.* (2025) / Analisis Efektivitas Program Makan Bergizi	To evaluate how effective the Free Nutritious Food (MBG) Program is at the	The study design is literature review. This study use synthesis analysis of	The program was introduced by the Indonesian government in 2025	The program shows positive impacts on children's nutritional status,	Partially successful — positive effects but requires stronger monitoring,

Gratis di Sekolah Dasar Indonesia Tahun 2025	primary-school level in Indonesia.	previous studies, program reports, and government data related to program implementation.	to address nutritional issues among children, reduce stunting, and improve the quality of primary education.	stunting reduction, and increased student concentration and attendance. It also reduces household economic burdens and empowers local entrepreneurs. However, challenges include uneven distribution, lack of facilities, and varying levels of nutritional awareness.	infrastructure, and food-quality standards.
Aji (2025) / Makan Bergizi Gratis di Era Prabowo-Gibran: Solusi	To examine policy readiness, budgeting, and political–implementation	This study is a literature review and public-policy reflection.	The program is a flagship vision and mission of President and Vice President Prabowo-Gibran,	The study raises concerns about the sustainability of the program due to the large budget	Does not measure direct outcomes; focuses on policy analysis and

untuk Rakyat atau Beban Baru?	challenges of the program		aimed at improving the quality and health of human resources to build the "Golden Generation 2045."	requirements (800 billion IDR per day).	implementation readiness.
Basit and Ramdani (2025) / Analisis Implementasi Program Makan Bergizi Gratis Terhadap Perkembangan Ekonomi	To analyze program implementation and its micro–macro economic effects on households and the food sector.	The study design is descriptive qualitative study based on literature review and economic policy analysis. Used secondary-data analysis (BPS, national reports, economic studies, education data).	The program is a government initiative to address malnutrition, improve human resource quality, and reduce the economic burden on poor households.	The program not only improves children's nutritional status but also generates a multiplier effect on agriculture, MSMEs, and household purchasing power.	Economically effective, though based on modeled and secondary data, requiring field validation.
Merlinda and Yusuf (2025) / Analisis Program Makan Gratis Prabowo Subianto	To analyze how the Free Nutritious Meal Program contributes to improving students' learning motivation	The study used a qualitative design. Data were collected through non-participant school	The program is a strategic initiative aimed at improving student nutrition and learning motivation,	This discourse analysis study provides insights into the program's	Conceptually successful strategic for learning motivation, but findings are analytical rather than

Terhadap Strategi Peningkatan Motivasi Belajar Siswa di Sekolah Tinjauan dari Perspektif Sosiologi Pendidikan	through nutrition improvement and socio-educational support.	observation, documentation of social-media and news content, and secondary literature review; data collection lasted half a month.	based on data showing that 41% of students in Indonesia experience hunger during learning.	impact on student learning motivation.	quantitative field-impact evaluation.
Kiftiyah *et al.* (2025) / Program Makan Bergizi Gratis (MBG) dalam Perspektif Keadilan Sosial dan Dinamika Sosial – Politik	To examine whether the MBG program is well-targeted from a social-justice perspective and to analyze its socio-political implementation dynamics.	The study is library research using a Systematic Literature Review (SLR). Data sources include reputable journals, mass media, and supporting literature; data were identified, evaluated, and qualitatively described.	This flagship program of the Prabowo Subianto–Gibran administration aims to improve community welfare, particularly among students.	The study recommends prioritizing schools in *daerah 3T* (disadvantaged, frontier, and outermost regions). Program sustainability depends on budget, policy stability, and government commitment.	No direct success/failure outcome measured; the program is strategic and socially-just in intent, but success depends on governance and equitable targeting.

The study conducted by Waluyo views the success of the MBG Program as a strategic long-term investment from a political economy perspective.[7] The program not only provides immediate nutritional benefits, but also builds healthier and more productive human resources, which in turn can improve the quality of the workforce and contribute positively to the national economy. However, financial challenges cast a shadow over the program's success. Issues of funding and fiscal sustainability remain the primary obstacles, as without a stable budget allocation and a clear financing mechanism, the program risks becoming a financial burden and failing to achieve its long-term objectives.

This statement is consistent with another study conducted by Aji,[4] which evaluated the success of the program in terms of its noble objective of creating the "Golden Generation 2045" through improving the quality of human resources. Nevertheless, the issue of substantial funding emerges as a major concern, with sustainability risks that could potentially impose a new burden on the *Anggaran Pendapatan dan Belanja Negara* (APBN, State Budget) if the sources of financing are not clearly defined. Both perspectives underscore the critical importance of funding as a key factor for ensuring the program's sustainability, while simultaneously highlighting it as the primary challenge.

Another study conducted by Qomarrullah *et al.* emphasized the success of the program in generating long-term impacts beyond physical health.[11] The program has the capacity to address nutritional inequalities, which are the root cause of educational challenges, by providing nutritious meals that directly improve students' concentration and reduce dropout rates. This finding aligns with Merlinda's work, which highlighted the program's success in social and educational contexts. The primary positive outcome—increased student learning motivation—was attributed to the fulfillment of nutritional needs, which reduces hunger during learning.[2] Together, these studies reaffirm the program's positive impact on both students' health and education, particularly in enhancing concentration and learning motivation.

According to Basit and Ramdani, stress the program's success in generating significant multiplier effects by empowering local farmers and small enterprises, supported by transparent governance and optimized supply chains. Failures, however, may arise from a lack of transparency and ineffective supply chain management, leading to financial leakages.[13]

The findings of these two studies are consistent with the research conducted by Nissa *et al.*, which emphasized that the success of the program lies in its ability to remain adaptive and sustainable, particularly in aligning policies with diverse geographical and socio-economic contexts. Program failure may occur if rigid and uniform approaches are applied without taking local conditions into account, thereby preventing the achievement of equitable community

welfare outcomes.[14] Collectively, these studies underline the importance of leadership, collaboration, transparency, and policy adaptation to local contexts as critical determinants of successful implementation.

According to the study by Kiftiyah *et al.*, the success of the program depends on prioritizing implementation in 3T regions as an effective way to reduce social inequality. However, the sustainability of the program largely relies on socio-political dynamics, with a significant risk of failure if political commitment weakens or if policy changes lead to its termination, which would negatively impact vulnerable communities.[15] This perspective highlights social justice and political dynamics as critical factors for sustainability, complementing the more economic and technical implementation perspectives discussed in other studies.

The success of the MBG program is not determined by a single aspect, but rather is the result of various interrelated factors that influence both its implementation and impact. The authors argue that the effectiveness of the program depends largely on the synergy between stable funding, effective execution, and policy alignment with local social and political conditions. Financial stability serves as the primary foundation to ensure the program can run sustainably without being hindered by budgetary constraints. Furthermore, strong leadership, support from local governments, and collaboration among stakeholders are essential to successful implementation. Community involvement and the adaptation of policies to local characteristics are also essential to ensure that the program delivers maximum and equitable benefits. However, without transparency, good governance, and consistent political commitment, the program risks failure, which would hinder the achievement of its long-term objectives in health, education, and social welfare. Therefore, the success of the MBG program should be viewed as the outcome of integrated factors working in synergy and the sustained commitment of all relevant parties.

Driving factors for successful implementation

The successful implementation of the MBG Program is strongly influenced by governance factors. Herdiana identifies strong leadership, support from local governments, and cross-sectoral coordination as key determinants of program success. Regions with well-defined institutional structures and adaptive implementation mechanisms tend to demonstrate more optimal implementation outcomes.[12]

In addition, policy adaptation to local conditions is a crucial aspect. Nissa *et al.* emphasizes that implementation approaches which take into account geographical, social, and economic differences can enhance both the effectiveness and acceptability of the program

within communities.[14] Kiftiyah *et al.* also recommends prioritizing 3T regions as a social justice strategy to ensure that the most vulnerable groups receive maximum benefits from the MBG Program.[15]

Inhibiting factors and risks of program failure

Despite its considerable potential, the MBG Program continues to face various structural challenges. One of the main issues is funding sustainability. Several studies highlight the substantial budgetary requirements and the risk of dependence on political dynamics in budget allocation, which may threaten the long-term sustainability of the program.[4,7] Without stable and transparent financing mechanisms, MBG risks becoming a fiscal burden that is difficult to sustain.

Operational challenges also represent significant barriers. Rahmah *et al.* and Herdiana point out uneven food distribution, limited school infrastructure, and weak monitoring and evaluation systems as major constraints.[5,12] Furthermore, limited community involvement in program planning and oversight may reduce accountability and increase the risk of inefficiency.

From a socio-political perspective, Kiftiyah *et al.* emphasizes that the stability of political commitment is a fundamental prerequisite for the sustainability of the MBG Program. Changes in leadership or policy direction may lead to implementation uncertainty and directly affect vulnerable groups who are the primary targets of the program.[15]

Strengths and limitations of the study

This study's primary strength lies in its use of a SLR approach, which enables the integration of findings from multiple disciplines and provides a comprehensive overview of the implementation of the MBG Program. The focus on recent literature (2020–2025), along with the application of the PICO framework, enhances the precision and relevance of the analysis.

Nevertheless, several limitations should be acknowledged. The number of articles included in the review is relatively limited (n = 9), and most of the studies employ qualitative approaches or rely on secondary data, with a lack of large-scale quantitative evaluations assessing nutritional and educational impacts. Variations in study designs and outcome indicators also constrain the generalizability of the findings.

Overall, the results of this review indicate that the MBG Program has a strong conceptual and empirical foundation as an instrument for improving health, education, and social welfare. However, its success is highly dependent on the synergy between effective governance, fiscal sustainability, and consistent political commitment to ensure equitable and

sustainable impacts.

Conclusion

This systematic literature review concludes that the MBG Program is a strategically important public policy with strong conceptual and empirical evidence for improving children's nutrition, educational participation, and broader social welfare in Indonesia, while also generating local economic benefits through MSME involvement. However, its impacts remain uneven across regions and are highly dependent on governance quality, leadership, intergovernmental coordination, cross-sector collaboration, adaptive policy design, and alignment with local socio-economic and geographical contexts, including prioritization of 3T regions to ensure equity. The program's sustainability is challenged by fiscal constraints, political dependence, uneven logistics and infrastructure, weak monitoring and evaluation, and limited community participation. Therefore, the MBG Program should be viewed as a long-term investment in human capital rather than a short-term social assistance scheme, requiring strengthened governance, fiscal sustainability, adaptive implementation, and rigorous impact evaluations to achieve equitable and sustainable national health, education, and social welfare outcomes.

Conflicts of Interest

The authors declare no conflict of interest regarding the publication of this manuscript.

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Author's Contribution

Design and conceptual framework: SPN. Literature search: SPN, SFFL, RN, NM, RFS. Drafting manuscript: SPN. Data analysis and synthesis: SPN, RN, RFS. Writing—review and editing: SPN, SFFL, RN, NM, RFS. All authors had read and validated the manuscript.

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Immediate Effects of Thoracic Expansion Exercises on Breath-Holding Capacity in Adolescents: A Quasi-Experimental Study

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ABSTRACT

Introduction: Breath-holding time (BHT) is a practical indicator of respiratory endurance and thoracic function. Thoracic expansion exercises (TEE) are widely implemented to enhance chest mobility and ventilatory performance, particularly among adolescents involved in physical training. This study evaluated the short-term effects of TEE on breath-holding time.
Method: A quasi-experimental pre–post design was employed with 30 participants aged 14–19 years. The sample consisted of 18 males (60%) and 12 females (40%), with a mean age of 16 ± 0.95 years. BHT was assessed before and after the intervention using a standardized digital timer. Participants completed a structured TEE protocol involving repeated deep-inhalation cycles with controlled thoracic expansion. Statistical analysis was performed using a paired-samples t-test at a 95% confidence level.
Results: Mean BHT increased from 39.77 seconds at baseline to 47.04 seconds post-intervention. The paired t-test indicated a significant improvement following TEE ($t = -4.194$, $p < 0.05$), demonstrating that the exercise effectively enhanced respiratory endurance in the short term.
Conclusion: TEE produces a significant immediate improvement in breath-holding capacity among adolescents. These findings support the integration of TEE into school-based or training programs aimed at optimizing respiratory function. Longitudinal studies are warranted to examine long-term effects.

Keywords: Adolescent health, breathing exercises, physiotherapy, quasi-experimental study, respiratory endurance

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Introduction

Pulmonary function is a fundamental indicator of respiratory health and serves as a critical determinant of overall physiological development during childhood and adolescence. This developmental period is characterized by rapid maturation of the respiratory system, including increases in lung volume, airway diameter, and respiratory muscle strength.[1] Disruption of these developmental processes, particularly due to modifiable risk factors such as early exposure to smoking, may hinder the achievement of optimal lung capacity and result in long-term respiratory impairment.[2]

Emerging evidence from contemporary cohort and longitudinal studies indicates that cigarette smoking initiated during adolescence is consistently associated with impairments in the normal trajectory of pulmonary function development**,** particularly in small-airway flow and expiratory parameters. Recent research shows that smoking exposure in youth correlates with attenuated forced expiratory volume in one second (FEV_1) and forced mid-expiratory flow ($FEF_{25–75}$), markers that reflect early airway dysfunction and compromised lung growth.[3] Moreover, smoking during the critical period of lung maturation has been linked to reduced lung function indices and altered growth slopes compared with non-smoking peers, suggesting that tobacco exposure during adolescence can suppress the attainment of peak lung function later in life.

Additional analyses indicate that individuals initiating smoking during adolescence and continuing into young adulthood tend to achieve lower predicted FEV_1 and expiratory flow values, suggesting that early tobacco exposure limits lung functional potential.[2,3] Similar findings have been reported in adolescent populations, highlighting smoking during the critical period of lung development as a major determinant of long-term respiratory health.

One clinically relevant consequence of diminished pulmonary function, particularly among young smokers, is the reduction in Breath-Holding Time (BHT). BHT serves as a simple, non-invasive proxy for functional ventilatory capacity and reflects the complex interplay between oxygen reserves, tolerance to rising CO_2 levels, chemoreceptor sensitivity, and chest wall mechanics.[4] Operationally, BHT refers to the maximum duration for which an individual can voluntarily suspend breathing after achieving full inspiration. Despite its simplicity, BHT is a valuable clinical indicator used in respiratory physiology, rehabilitation sciences, and pulmonary function research due to its sensitivity to subtle changes in lung capacity and ventilatory control.

Standardized BHT assessment typically involves instructing the subject to perform maximal inspiration, followed by voluntary breath-holding until the initial urge to exhale.

Timing begins at the end of inspiration and concludes at the initiation of the subsequent exhalation. To enhance reliability and reproducibility, established protocols recommend repeated trials with consistent instructions and rest intervals. Methodological frameworks such as the Jones and Meade protocol remain widely adopted for ensuring measurement consistency in both clinical and research contexts.[5]

Interventions aimed at improving thoracic mobility and inspiratory capacity may play an important role in enhancing BHT, especially among adolescents at risk for reduced lung function. Thoracic Expansion Exercise (TEE) is one of the most widely utilized breathing techniques within physiotherapy for promoting deeper inspiration, increasing thoracic cage compliance, and augmenting lung volumes. TEE typically includes cycles of slow, maximal inspiration followed by controlled expiration, often accompanied by manual facilitation or thoracic measurement to quantify chest expansion.[6] Through repeated deep-breath training, TEE is believed to enhance alveolar recruitment, increase diaphragmatic excursion, improve ventilation distribution, and elevate oxygen reserves, physiological changes that cumulatively contribute to prolonged breath-holding ability.[7,8]

However, evidence on the short-term impact of TEE on BHT among adolescents remains limited. Given that adolescence represents a vulnerable period for both pulmonary development and the initiation of smoking behavior, targeted non-pharmacological interventions are urgently needed to mitigate early functional decline.

This study therefore aims to evaluate the short-term effects of Thoracic Expansion Exercise on Breath-Holding Time among Grade X students at SMK Gotong Royong, a population in which smoking behaviors are commonly reported. By administering TEE across three consecutive repetitions and measuring thoracic expansion and BHT before and after intervention, this research seeks to determine whether a brief session of targeted respiratory training can yield measurable improvements in ventilatory function. Findings from this study are expected to contribute important empirical evidence for clinical physiotherapy practice, while also supporting early preventive strategies for respiratory health promotion among adolescents, both smokers and non-smokers.

Methods

Study design

This study employed a quasi-experimental one-group pretest–posttest design**.** This design was selected to evaluate short-term changes in breath-holding time following TEE within the same group of participants. The absence of a control group was considered appropriate due to practical and ethical considerations in a school-based setting, where all

eligible students were encouraged to participate in the intervention.

Study setting and period

The study was conducted at SMK Gotong Royong, Gorontalo City, Indonesia, in a quiet and well-ventilated classroom environment. Data collection was carried out in December 2025. All measurements were performed at 09:00 a.m. to minimize potential circadian-related physiological variations that could affect respiratory performance.

Population and sample

The target population consisted of all tenth-grade students at SMK Gotong Royong**.** A total of 30 students (male and female) participated in the study. Because it was not feasible to include the entire population, a purposive sampling technique was employed to recruit participants who met the predefined inclusion criteria. Participants were included if they were enrolled as tenth-grade students at SMK Gotong Royong, aged 14–19 years**,** able to understand and follow instructions, and agreed to participate by providing written informed consent. Participants were excluded if they were unable to complete the measurement procedures, had difficulty following instructions, or declined to provide informed consent. These criteria ensured that all participants could safely complete the intervention and provide reliable data.

Variables and measurements

The primary outcome variable was BHT, measured in seconds as an indicator of respiratory endurance. Age and sex were considered potential covariates due to their known influence on pulmonary function.

Initially, BHT was conducted prior to the intervention. Participants were seated in an upright position and instructed to perform a maximal inspiration followed by breath-holding for as long as possible. The duration was measured using a calibrated digital timer until spontaneous expiration occurred. Furthermore, TEE intervention was performed which consisted of three consecutive repetitions involving maximal nasal inspiration, active thoracic expansion, and full oral expiration. A 30-second rest interval was provided between repetitions. All procedures were administered by the researcher using standardized verbal instructions to ensure consistency. Finally, following the intervention, BHT was reassessed using the same protocol as the pretest. Demographic data, including age and sex, were collected using a standardized participant information form.

Statistical analysis

Data analysis was performed using SPSS software. Descriptive statistics were used to summarize participant characteristics and BHT values. The Shapiro–Wilk test was applied to assess data normality. Differences between pretest and posttest BHT values were analyzed

using a paired-samples t-test, with statistical significance set at $p < 0.05$ and a 95% confidence interval (CI).

Ethical considerations

The study was conducted in accordance with the Declaration of Helsinki and national research ethics guidelines. Ethical approval was obtained from an institutional ethics committee prior to data collection. Written informed consent was obtained from all participants and their legal guardians. Participation was voluntary, confidentiality was maintained, and all data were anonymized.

Result

Sample characteristics

This study involved 30 tenth-grade students from SMK Gotong Royong, Gorontalo City, who met the predefined inclusion and exclusion criteria. The participants consisted of 18 males (60.0%) and 12 females (40.0%)**.** The age ranged from 14 to 19 years, with a mean age of 16.0 ± 0.95 years**.** Most participants were 16 years old (50.0%)**,** indicating that most respondents were in mid-adolescence. Detailed sample characteristics are presented in Table 1**.**

Table 1. Sample characteristics (N=30).

Characteristics	Frequency	Percentage
Age (years)		
14	1	3.3 %
15	7	23.3 %
16	15	50.0 %
17	6	20.0 %
19	1	3.3 %
Gender		
Male	18	60.0 %
Female	12	40.0 %

Prerequisite test: normality analysis

Prior to conducting the paired-samples t-test, the normality of BHT data was assessed. The Kolmogorov–Smirnov test indicated that both pre-intervention and post-intervention BHT values were normally distributed ($p > 0.05$). Although the Shapiro–Wilk test showed a

deviation from normality in post-intervention BHT ($p < 0.05$), the sample size of 30 participants supports the use of parametric testing, as the paired-samples t-test is considered robust to minor violations of normality. Therefore, parametric analysis was deemed appropriate.

Paired-samples T-test results

The descriptive statistics of breath-holding time before and after the intervention are presented in Table 2**.** The mean BHT before the intervention was 39.77 ± 12.48 seconds**,** which increased to 47.04 ± 14.77 seconds after the intervention. A paired-samples t-test was conducted to evaluate the effect of TEE on BHT. The analysis demonstrated a statistically significant improvement in BHT following the intervention, with a mean difference of 7.27 seconds ($t(29) = 4.19$, $p < 0.001$) and a 95% confidence interval of 3.73 to 10.82 seconds.

Table 2. Breath-holding time before and after the intervention.

Indicator (seconds)	BHT Before	BHT After	*p*-value
Mean ± SD	39.77 ± 12.48	47.04 ± 14.77	<0.001
Min–Max	19.00–65.05	30.03–96.01	
95% CI	35.11–44.43	41.53–52.56	

BHT: Breath-Holding Time, CI: Confidence Interval, SD: Standard Deviation.
Data analyzed with Paired T-Test.

Effect size

The magnitude of the intervention effect was assessed using Cohen's *d*. The analysis yielded a Cohen's *d* value of **0.77**, indicating a large effect size and suggesting that TEE has a substantial short-term impact on respiratory endurance.

Discussion

This study aimed to evaluate the short-term effects of TEE on BHT among tenth-grade students of SMK Gotong Royong using a quasi-experimental pretest–posttest design with repeated measures. The results demonstrated a significant improvement in breath-holding capacity following a single session of TEE, as evidenced by an increase in mean BHT from 39.77 to 47.04 seconds and a significant paired t-test result ($t = –4.194$; $p < 0.05$). These findings indicate that TEE can elicit measurable physiological effects even after one intervention session.

The observed increase in BHT can be explained by acute physiological adaptations in the respiratory system. TEE stimulates maximal inspiratory volume through the activation of respiratory musculature, including the diaphragm, external intercostal muscles, and accessory

muscles such as the sternocleidomastoid and scalene muscles. This activation enhances lung inflation and increases alveolar oxygen reserves, which directly contributes to prolonged breath-holding capacity.[7]

Additionally, TEE improve chest wall compliance, thereby reducing mechanical resistance during breath retention. Recent studies suggest that breathing exercises focusing on inspiratory volume can modulate chemoreceptor sensitivity to CO_2, enhancing tolerance to elevated CO_2 levels during breath-holding.[9,10] These mechanisms are consistent with the significant increase in BHT observed in the present study.

Thoracic circumference measurements taken after each TEE repetition confirmed progressive chest wall mobility during the intervention. Adequate thoracic mobility is associated with greater vital capacity, improved ventilation efficiency, and increased end-inspiratory lung volume, all key determinants of breath-holding capacity.[8]

TEE's immediate effects on chest wall elasticity and neuromuscular respiratory control support the short-term enhancement of respiratory endurance. Studies involving adolescent populations have similarly reported that simple breathing-based interventions can rapidly influence respiratory function by improving inspiratory coordination and volume.[11]

The study sample comprised 30 students, with most aged 16 years (50%). Adolescence represents a developmental phase during which respiratory structures are still maturing, allowing greater adaptability to breathing exercises compared with adults.[1] Sex-related physiological differences and smoking status are potential covariates, as males generally demonstrate higher lung vital capacity, whereas smoking behavior can reduce lung elasticity and gas exchange efficiency.[11] Despite these variations, the significant improvement observed across the sample suggests that TEE exerts a consistent effect across basic demographic profiles.

The pretest–posttest design with repeated measures offers the advantage of detecting intra-subject changes, as each participant functions as their own control. This design is well-suited for assessing short-term physiological responses, particularly for acute interventions such as TEE. Conducting the intervention at 09:00 a.m. minimized circadian-related variability, as respiratory performance can fluctuate with hormonal cycles and fatigue.[12]

Standardized instruction by a single researcher and the use of consistent timing instrumentation ensured measurement reliability. Participant compliance, combined with a quiet and well-ventilated environment, further enhanced the study's internal validity.

The increase in BHT by approximately seven seconds following a single session suggests that TEE is effective as a rapid-effect intervention for enhancing breath-holding

capacity. In educational or sports settings, this exercise may serve as a useful warm-up or breathing regulation strategy for students engaged in physical activities. Clinically, TEE can be utilized as a simple modality in respiratory rehabilitation, especially for individuals requiring enhanced ventilatory capacity or breathing control, such as those with mild asthma or non-pathological restrictive conditions.[13]

This study has limitations, including the absence of a control group and the lack of additional respiratory variables such as vital capacity, inspiratory reserve volume, or ventilatory rate. Future research should employ randomized controlled designs, investigate long-term effects, and incorporate a broader range of physiological measurements to provide a more comprehensive understanding of TEE's impact.

Conclusion

This study demonstrates that a single session of TEE produces a significant short-term improvement in breath-holding time among adolescents. From an application perspective, TEE may be practically implemented as a brief breathing exercise within school-based physical education programs, sports training sessions, or routine physiotherapy interventions to enhance respiratory endurance and breathing control in adolescents. For future research, randomized controlled trials with larger sample sizes, inclusion of control groups, and longer intervention durations are recommended to evaluate the long-term effects of TEE and to examine its impact on additional respiratory parameters such as lung volumes, respiratory muscle strength, and ventilatory efficiency.

Conflicts of interest

The authors declare that they have no conflicts of interest. All authors have completed the ICMJE Conflict of Interest Disclosure Form, and the disclosures indicate that there are no relevant financial or non-financial relationships to report.

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Relationship between Micronutrient Intake and Malaria Infection: A Cross-Sectional Study

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ABSTRACT

Introduction: The incidence of malaria infection is influenced by several factors, including micronutrient intake. Micronutrient intake is essential for maintaining normal nutritional status and maintaining a healthy immune system. Vitamin A, zinc, and iron are micronutrients that function to boost the immune system. This study aims analyze the relationship between micronutrient intake and the incidence of malaria infection at the Paguat Community Health Center.
Method: This study used a cross-sectional study method with an analytical observational approach. The population in this study consisted of 37 people obtained from the medical records of the Paguat Community Health Center for the period January-July 2025, using total sampling techniques. The study used primary data in the form of questionnaires and 3x24-hour food recall interviews. The 3x24-hour food recall method was calculated using the Nutrisurvey application to determine the nutritional content of each food item. Data analysis was performed using univariate, bivariate, and multivariate methods.

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Results: Bivariate analysis showed that micronutrient intake such as vitamin A (*P*-value = 0.680) and iron (*P*-value = 0.080) had no significant association with malaria infection. Meanwhile, zinc micronutrient intake (*P*-value = 0.030) had a significant association with malaria infection. Based on multivariate analysis, *P*-value of 0.025 ($P < 0.05$) was obtained, with a confidence interval (95% CI: 0.035–0.798). Zinc micronutrient intake has a significant effect on the incidence of malaria infection.
Conclusion: The analysis shows no statistically significant relationship between vitamin A and iron intake with malaria infection. Zinc intake is statistically significantly associated with malaria infection.

Keywords: *Anopheles sp*., malaria, nutritional status, *Plasmodium sp.*

Introduction

Malaria is a disease caused by parasites of the genus Plasmodium.[1] *Plasmodium sp.* protozoan parasites are transmitted to humans through the bite of female Anopheles mosquitoes. Malaria is the most life-threatening parasitic disease worldwide, despite various control strategies that have been implemented. Malaria causes deaths or more each year, and children under five years of age are the most vulnerable population to these deaths.[2]

The World Health Organization (WHO) in 2020 stated that in 2019, there were approximately 229 million cases of malaria worldwide, with 94% occurring in Africa. These malaria cases are estimated to have caused 409,000 deaths globally, with 67% occurring in children. Malaria has a negative impact on women's health during pregnancy, childbirth, and the postnatal period.[3] Malaria is also endemic in India and many countries in Southeast Asia.[4] Indonesia is one of the countries in Southeast Asia with the second highest number of malaria cases after India.[5] Although Indonesia's annual parasite incidence declined from 2010 to 2014, progress stagnated between 2015 and 2019.[6]

Malaria is largely concentrated in Eastern Indonesia, with 27 districts and cities showing high endemicity.[6] In 2019, Papua Province accounted for 86% of the highest malaria cases in Indonesia. Papua consistently has the highest incidence of malaria in the country.[7]

Gorontalo Province is one of the provinces with a fairly high incidence of malaria. One of the areas affected by malaria from 2023 to 2025 is Pohuwato Regency. A sharp increase in malaria cases, particularly in mining areas, was the main factor in determining this status. Based on epidemiological investigations, it was revealed that there was malaria transmission that met the criteria for an outbreak. Since 2023, the early warning system in use has indicated the potential for a malaria outbreak in Pohuwato Regency. The number of malaria cases in

Pohuwato has increased, with 814 cases recorded throughout 2023, 824 cases in 2024 accompanied by two deaths, and 170 new cases reported as of February 2025. Of the total 170 malaria cases recorded in 2025, approximately 56% originated from the mining area in Hulawa Village, 18% from the mine in Puncak Jaya Village, and the remaining 10% from Karya Baru Village.[8]

The results of a survey conducted by an emergency response team led by the Deputy Regent of Pohuwato in 2025, in an epidemiological investigation and vector survey, identified the habitat of Anopheles mosquitoes, the main vector for the spread of malaria, showing that one breeding site can reach several villages within a 2 km radius. These malaria cases occurred in the productive age group, namely 19 to 59 years old, with 95% of sufferers being men who work as miners, especially people who are active around mining sites.

Based on interviews with malaria officials, Paguat is one of the areas that has reported a spike in malaria cases. This was conveyed through an interview with one of the malaria officers at the Paguat Community Health Center, who stated that they have been receiving malaria patients since 2023. Malaria cases have become a concern due to mining activities that cause malaria infections, especially in the Paguat Community Health Center's working area.

Malaria infection is not only influenced by humans, mosquito, parasite, and environmental factors, but also by an individual's nutritional status. A person's nutritional status can be defined as the result of the intake of nutrients received and nutritional needs and their utilization to maintain nutrient reserves in the body.[9] An individual's nutritional status is influenced by various factors, including the intake of micronutrients through an individual's diet. Micronutrient intake consists of several vitamins and minerals such as vitamin A, iron, and zinc. Micronutrient intake is important for maintaining normal nutritional status so that the immune system is well maintained. Micronutrients such as vitamins and minerals function to boost the body's immunity through several mechanisms.[10] Research shows that an inappropriate diet can increase a person's risk of experiencing nutritional deficiency or excess.[11] Micronutrients include vitamin A, zinc, and iron, and their deficiency is often associated with a higher susceptibility to diseases such as malaria. Micronutrient deficiency has been linked to various infections, including malaria-related morbidity.[12]

Studies show that vitamin A in the form of retinol is used for immune cell development. Vitamin A is necessary for the development and function of T cells, a type of white blood cell that plays an important role in the immune response to malaria.[10] Vitamin A deficiency can impair the ability of T cells to kill malaria parasites.[12]

Iron has a complex relationship with malaria because it affects infection through several

opposing mechanisms. Iron deficiency can decrease erythropoiesis and reticulocyte production, thereby inhibiting the growth of Plasmodium, particularly *P. vivax*, which selectively infects red blood cells.[13] Morevoer, Zinc is an essential micronutrient required by the body. Zinc deficiency significantly affects antibody levels in varying malaria statuses and age groups.[14]

Nutrient deficiencies can cause disturbances in the immune response, where nutrients modulate metabolic processes that include the activation or inhibition of enzymes or immunoregulatory mediators that can result in changes in cellular immune function, especially in T lymphocyte-derived cells.[15] Many micronutrients and macronutrients that are essential for humans are also essential for parasites, making the host's nutritional status relevant not only to an adequate immune response but also to the development of the organism itself.[16] Intake of micronutrients such as vitamins and minerals functions to enhance immunity through several mechanisms.[10]

Thus, micronutrient and macronutrient deficiencies can affect an individual's immunity, making them more susceptible to disease or increasing the severity of disease in individuals. Therefore, this study aims to analyze the relationship between micronutrient intake and malaria infection incidence at the paguat community health center.

Methods

This study used a quantitative method with a cross-sectional study design. The study was conducted in the working area of the Paguat Community Health Center, Pohuwato Regency, Gorontalo Province. Data collection was carried out over a period of 2 months, from September to October 2025. The Health Research Ethics Committee of Gorontalo State University approved this study with number 162A/UN47.B7/KE/2025.

The population in this study is all patients suffering from malaria infection and having a history of malaria based on observations at the Paguat Community Health Center during the period from January to July 2025, totaling 37 people. The sample consisted of 37 people, selected using total sampling techniques.

Respondents in this study were drawn from medical records at the Paguat Community Health Center for the period January-July 2025. Initially, all respondents met the criteria for the target population through a screening process. The inclusion criteria were respondents with recorded age, gender, weight, tuberculosis (TB), and a history of malaria; respondents aged 15-64 years who had previously received malaria treatment and who had good communication skills. Exclusion criteria included patients with severe chronic illnesses such as tuberculosis; respondents experiencing acute infections (high fever and severe symptoms); patients with a

history of severe anemia; and those unwilling to participate in the data collection process. The entire data collection process after determining the criteria was conducted by visiting all patients selected for the study.

The dependent variable is the incidence of malaria infection, while the independent variables are micronutrient intake (vitamin A, iron, and zinc). Data were collected using a questionnaire for the dependent variable and a 3x24-hour food recall for the independent variable, namely micronutrient intake. The objective criteria for iron, zinc, and vitamin A intake were based on recommended dietary allowance (RDA).

Data analysis was performed using SPSS software. The data analysis in this study used an ordinal measurement scale, with univariate testing in the form of frequency distribution, bivariate using Fisher's exact test because the variables did not meet the chi-square test. Multivariate analysis (binary logistics) was used to assess the most relevant variables. The significance limit chosen was $P < 0.05$.

Result

The characteristics of the sample in this study were age, gender, and occupation. Table 1 shows the frequency distribution of respondents' gender with a 95% confidence interval. There were 36 male respondents (97.3%) and one female respondent (2.7%). The frequency distribution of respondents' ages was obtained. There were six respondents aged 19-23 years with a percentage of 16.2%, three respondents aged 24-28 years with a percentage of 8.1%, nine respondents aged 29-33 years, nine respondents aged 34 38 years with a percentage of 24.3%, two respondents aged 59-63 years with a percentage of 5.4%. The table shows that the respondents in the study ranged in age from 19 to 63 years. The largest age groups were 29-33 years and 34-38 years, each with nine people (24.3%). Meanwhile, the smallest age group was 49-53 years, with one person (2.7%). The frequency distribution of respondents' occupations shows that most of them work as mine laborers, namely 33 people (89.2%). A small number work as construction workers, namely three people (8.1%), and one person (2.7%) work as a farmer.

Table 2 shows the results of the frequency distribution of micronutrient intake, with 30 people (81.1%) classified as deficient in vitamin A intake, two people (5.4%) classified as adequate, and five people (13.5%) classified as excessive. These results indicate that most respondents do not meet their daily vitamin A intake requirements. Iron intake is divided into three categories, with most respondents having exceeded intake, namely 20 people (54.1%), 10 people (27.0%) in the adequate category, and seven people (18.9%) in the deficient category. These results indicate that most respondents have sufficient or higher than adequate daily iron

intake. For zinc intake, most respondents were in the deficient category, totaling 26 people (70.3%), while only 11 people (29.7%) were in the adequate category. These results indicate that most respondents did not meet their optimal daily zinc requirements.

Table 1. Respondent characteristics analysis (N=37).

Characteristics	Frequency	Percentage (%)
Gender		
Male	36	97.3
Female	1	2.7
Age (in years old)	6	16.2
19-23	3	8.1
24-28	9	24.3
29-33	9	24.3
34-38	5	13.5
39-43	1	2.7
49-53	2	5.4
54-58	2	5.4
59-63	6	16.2
Occupation		
Mining worker	33	89.2
Construction worker	3	8.1
Farmer	1	2.7

In Table 3, most respondents in this study experienced malaria infection, totaling 21 respondents (56.8%). Meanwhile, 16 respondents (43.2%) did not experience malaria. The results of the study indicate that the study population is still at risk of malaria exposure based on the observation period. The next step was to conduct a bivariate analysis to determine the relationship between the two variables. Zinc intake was obtained by calculating the total zinc intake for 3 days using a 24-hour food recall. Zinc intake was based on the Recommended Nutrient Intake in Permenkes No. 28 of 2019.

Based on Table 4, it was found that 16 respondents (53.3%) who suffered from malaria had deficient vitamin A intake, while three respondents (60.0%) had exceeded vitamin A intake. Many respondents who did not suffer from malaria were found in the group with deficient vitamin A intake, numbering 14 people (45.7%). The statistical test results showed a

P-value of 0.680 ($P > 0.05$), indicating no significant relationship between vitamin A intake and the incidence of malaria infection.

Table 2. Frequency distribution of micronutrient intake (N=37).

Micronutrient intake	Frequency	Percentage (%)
Vitamin A		
Deficient	30	81.1
Adequate	2	5.4
Exceeded	5	13.5
Iron		
Deficient	7	18.9
Adequate	10	27.0
Exceeded	20	54.1
Zinc		
Deficient	26	70.3
Adequate	11	29.7

Table 3. Frequency distribution of malaria infection incidence (N=37).

Malaria Incidence	Frequency	Percentage (%)
Positively Diagnosed	21	56.8
Negatively Diagnosed	16	43.2

Table 4. Relationship between vitamin A intake and malaria infection incidence at Paguat Community Health Center.

Vitamin A Intake	Malaria Incidence				*P-value*
	Positively Diagnosed		Negatively Diagnosed		
	n	%	n	%	
Deficient	16	53.3	14	46.7	**0.680**
Adequate	2	100.0	0	0	
Exceeded	3	60.0	2	40.0	
Total	**21**	**56.8**	**16**	**43.2**	

Fisher exact test

Based on Table 5, respondents with low iron intake had the highest proportion of malaria sufferers, namely six people (85.7%), while those who did not suffer from malaria were

mostly in the group with exceeded iron intake, namely 12 people (60.0%). The statistical test results showed a *P*-value of 0.080 ($P > 0.05$), indicating no significant relationship between iron intake and malaria infection incidence.

Table 5. Relationship between iron intake and malaria infection incidence at Paguat Community Health Center.

Iron Intake	Malaria Incidence				*P-value*
	Positively Diagnosed		Negatively Diagnosed		
	n	%	n	%	
Deficient	6	85.7	1	14.3	**0.080**
Adequate	7	70.0	3	30.0	
Exceeded	8	40.0	12	60.0	
Total	**21**	**56.8**	**16**	**43.2**	

Fisher exact test

Table 6 shows the relationship between zinc intake and the incidence of malaria infection. Respondents with deficient zinc intake had a higher proportion of malaria patients, namely 18 people (69.2%), compared to those with adequate zinc intake, namely three people (27.3%). The statistical test results obtained a *P*-value of 0.030 ($P < 0.05$), which means that there is a significant relationship between zinc intake and the incidence of malaria infection. Zinc intake in the deficient category is associated with an increased risk of malaria. Zinc intake, as a variable related to the incidence of malaria infection, was further tested using multivariate analysis to analyze the effect of zinc micronutrient intake. A simple logistic regression analysis in the form of Binary Logistic was performed with the following results.

Table 7 shows the logistic regression analysis to predict the probability of an event occurring. The interpretation of the probability calculation from the logistic regression model obtained a value of y = 0.981 for the category of respondents with low zinc intake (X = 0). The probability of malaria occurrence is p = 0.722 or 72.2%. This indicates that respondents with low zinc intake have a 72.2% chance of contracting malaria. Based on the interpretation results, a value of y = -0.748 was obtained for the category of respondents with good intake (X = 1). After being entered into the logistic equation, the probability of malaria occurrence was obtained as p = 0.321 or 32.1%. This result shows that respondents with good zinc intake have a 32.1% chance of experiencing malaria.

Table 6. Relationship between zinc intake and malaria infection incidence at Paguat Community Health Center

Zinc Intake	Malaria Incidence				*P-value*
	Positively Diagnosed		Negatively Diagnosed		
	n	%	n	%	
Deficient	18	69.2	8	30.8	**0.030***
Adequate	3	27.3	8	70.0	
Total	**21**	**56.8**	**16**	**43.2**	

*Significant at $P<0.05$. Fisher exact test

Table 7. Multivariate analysis of zinc intake and malaria infection incidence at the Paguat Health Center.

Variable	B	S.E.	Wald	df	Sig.	Exp (B)	95% CI for Exp (B)	
							Lower	Upper
Zinc intake	-1.729	0.799	5.025	1	0.025	0.167	0.035	0.798
Constant	0.981	0.677	2.099	1	0.147	2.667		

Simple logistic regression test

Discussion

Based on the analysis results, vitamin A and iron intake did not have a significant relationship with malaria incidence. Meanwhile, the related variable was zinc intake, obtained from bivariate and multivariate tests.

Relationship between Vitamin A micronutrient intake and malaria infection

Based on the analysis results, there was no significant relationship between vitamin A intake and the incidence of malaria infection. Variations in vitamin A intake among respondents did not directly affect the risk of malaria. Several studies have stated that vitamin A does not provide meaningful protection against Plasmodium infection. For example, studies conducted by Sandalinas et al. state that vitamin A is not always dominant in overcoming malaria infection, because malaria infection can reduce retinol (vitamin A) levels as an inflammatory response, which does not always indicate that vitamin A directly prevents malaria.[17] In addition, it is possible that studies using respondents as samples did not categorize the samples based on the requirement of having other diseases that may affect vitamin A metabolism.[18]

The relationship between iron micronutrient intake and malaria infection incidence

The analysis results show no significant relationship between iron intake and the incidence of malaria infection. This is due to the limitations of the study, which may have prevented any relationship from being identified. In previous study, it was shown that a lack of representative or non-representative samples could be one of the influencing factors, so that the statistical model used was unable to control for other confounding factors. In addition, there are several other factors that influence the incidence of malaria infection, including environmental factors, age, genetics, and exposure to malaria infection.[19]

The relationship between zinc micronutrient intake and the incidence of malaria infection

The bivariate analysis results show that zinc micronutrient intake has a significant relationship with the incidence of malaria infection. The results of the multivariate analysis of zinc intake and the incidence of malaria infection at the Paguat Community Health Center obtained a B value of -1.729, which means it has a negative relationship. This value interprets that the better the zinc intake, the lower the chance of contracting malaria. The standard error (S.E.) shows a value of 0.0799, which means it is still within reasonable limits or the model is quite stable, not too large. This means that the smaller the S.E. value, the more stable the model estimation.

Meanwhile, the Wald value produced for zinc intake of 5.025 indicates a fairly strong or significant effect on the dependent variable (incidence of malaria infection). The value $p = 0.025$ ($p < 0.05$) illustrates that zinc intake has a significant effect on the incidence of malaria infection. The Exp(B) value of 0.167 means that respondents with adequate zinc intake have a 0.167 times greater chance of contracting malaria than respondents with low zinc intake. The confidence interval (95% CI: 0.035–0.798) does not exceed 1, which reinforces the significance of the relationship between these variables. The constant value of 0.981 ($p = 0.05$) is not significant, but it is still needed as a component of the logistic regression equation. The results of this study indicate that there is a significant relationship between zinc intake and the incidence of malaria infection; low zinc intake increases the likelihood of malaria infection. These results are consistent with the study conducted by Sakwe et al. which shows a synergistic relationship between malaria incidence and malnutrition conditions such as nutritional deficiencies.[20]

The body requires adequate nutrient intakes for all its functions to operate optimally. Several types of micronutrients play an important role in supporting the immune system. Good nutrition has great potential in preventing and controlling infectious diseases, including malaria, by providing sufficient micronutrients to strengthen the body's resistance. Thus, good

nutritional status contributes to improving the body's defense mechanisms and makes individuals more resistant to malaria infection. Micronutrient deficiencies also have a major impact on reducing immunity, making individuals more susceptible to infectious diseases. Several nutrients such as carotenoids, vitamins A, C, E, selenium, and zinc are known to have immunomodulatory properties, where changes in the intake of these nutrients can affect immune function in both experimental models and humans.[21]

Zinc is a micronutrient that has significant immune modulation functions.[22] Zinc is a fundamental trace element in nutrition and is the second most abundant trace metal in the human body after iron. The total zinc content in the human body is 2–4 g, with a plasma concentration of 12–16 μM. Although it is a small plasma pool, zinc is exchangeable and moves rapidly. Adequate daily zinc intake is necessary to maintain stable conditions because, unlike iron, the body does not have a specific system for absorbing zinc. The highest concentrations of zinc are found in muscles, bones, skin, and liver.[23]

In humans, zinc deficiency is known to increase the risk of plasmodium infection and susceptibility to viral infections. Zinc plays a role in many metabolic and chronic diseases such as diabetes, cancer (esophagus, small cell oral carcinoma, breast cancer), and neurodegenerative diseases. There is also strong evidence linking zinc deficiency to several infectious diseases such as malaria, HIV, tuberculosis, measles, and pneumonia.[23]

Malaria parasites use zinc to protect themselves from attacks by the immune system (oxidative burst) in infected individuals, causing a decrease in zinc levels in the blood (plasma) of malaria patients.[22] According to the WHO, zinc deficiency is currently the fifth leading cause of death and morbidity in developing countries. It is estimated that about one-third of the world's population is zinc deficient. Globally, zinc deficiency contributes to approximately 18% of malaria cases. Although severe zinc deficiency is rare, mild to moderate deficiency is more common.[23] Zinc deficiency is associated with impaired immune function, resulting in increased morbidity from infection, growth disorders, and liver dysfunction. Therefore, zinc deficiency in infected humans may be a nutritional adaptation to endemic disease. Zinc deficiency is primarily related to dietary patterns; zinc is most abundant and easily absorbed from animal proteins, while consumption of vegetables and cereals reduces its absorption due to zinc binding to phytate.[22]

Zinc is found in many food groups, and its concentration and bioavailability vary greatly. Foods with the highest zinc concentrations include red meat, some shellfish, nuts, fortified cereals, and whole grains.[23] Zinc from animal sources has higher bioavailability than zinc from plant sources. People who do not consume red meat, vegetarians, and people living

in developing countries who rely primarily on plant-based foods are at higher risk of zinc deficiency due to inadequate zinc intake.[24] This consumption pattern causes zinc deficiency.

Malaria, a type of infectious disease, can potentially cause nutritional immunity, which is when the host organism absorbs trace minerals during infection, limiting their availability to pathogens. Zinc is an essential trace element for both the host and the pathogen. Pathogens need zinc to survive, reproduce, and cause disease. This triggers a competitive process between the host and the invading pathogen. There are three mechanisms that allow the host to compete for zinc and create a zinc-deficient environment for the pathogen. However, some pathogens have developed tactics to overcome some of these mechanisms. At the systemic level, the distribution of zinc in the body changes. This mainly involves a small amount of free zinc that is not bound in plasma because 99.9% of zinc remains inside cells and is not directly accessible to pathogens. During infection, plasma zinc levels decrease dramatically.[25]

Study limitations

This study used a cross-sectional design, which is limited in nature and associative, and cannot explain cause-and-effect relationships. The food recall method relies on respondents' memory, which may lead to recall bias and unavoidable errors in estimating consumption portions. This study did not measure nutritional status biomarkers. The relatively small sample size affects the statistical power of the analysis. Confounding factors that could influence the variables were not considered in this study.

Conclusion

Micronutrient intake of vitamin A and iron does not have a significant association with the incidence of malaria infection. Respondents with micronutrient zinc intake have a significant association; zinc deficiency provides a greater opportunity for malaria infection compared to individuals with adequate zinc intake.

Conflicts of Interest

The authors have no conflicts of interest in reporting.

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ORIGINAL ARTICLE **Open Access**

Association Between Serum IL-8 Concentrations and Severity of Knee Osteoarthritis: An Exploratory Cross-Sectional Study

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ABSTRACT

Introduction: Osteoarthritis (OA) is a chronic degenerative disorder of the joints that progresses over time, with inflammation playing a key role in its underlying mechanisms. Interleukin-8 (IL-8), a pro-inflammatory cytokine that participates in immune responses and neutrophil migration, has been associated with the process of cartilage breakdown in OA. This study was conducted to analyze the association between serum IL-8 concentrations and the radiographic severity of knee OA as exploratory evidence to enhance understanding of OA pathophysiology.
Method: This exploratory observational research applied a cross-sectional approach in patients diagnosed with knee OA. Seven participants were enrolled through total sampling at the Larasati Pondok Osteoarthritis Elderly Health Center, Faculty of Medicine, Wijaya Kusuma University, Surabaya. Radiographic severity of OA was determined using the Kellgren–Lawrence grading system. Venous blood specimens were obtained to determine serum IL-8 concentrations as an indicator of systemic inflammation.
Results: Statistical analysis demonstrated a significant inverse correlation between serum IL-8 concentrations and OA severity ($r = -0.866$, $P = 0.012$). These results indicate that IL-8 concentrations in serum are relatively elevated in the early phase of OA and tend to decline as the disease progresses.

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Conclusion: The findings of this exploratory study indicate that serum IL-8 may represent systemic inflammatory activity during the early stages of knee OA and holds potential as a biomarker candidate for future investigation. Further longitudinal studies involving larger sample sizes are necessary to validate its clinical relevance for OA detection and disease monitoring.

Keywords: Cartilage, inflammation, interleukin-8, joint diseases, osteoarthritis, risk factors

Introduction

Osteoarthritis (OA) is a long-term degenerative joint condition marked by the gradual breakdown of articular cartilage, changes in the subchondral bone, development of osteophytes, and inflammation of the synovial membrane, all of which contribute to joint pain and reduced functional capacity.[1,2] OA represents a major contributor to musculoskeletal disability in the elderly population and places a considerable strain on healthcare systems worldwide. Data from the Global Burden of Disease study indicate that OA affects hundreds of millions of people globally, with its prevalence rising alongside population aging and the growing occurrence of risk factors such as obesity and joint trauma. The worldwide prevalence of knee OA is estimated at around 16% among adults and exceeds 20% in individuals older than 40 years.[3]

Epidemiological studies show that the worldwide burden of OA has risen markedly since 1990 and is expected to keep increasing through 2050, in line with demographic shifts and the expanding prevalence of metabolic risk factors, including diabetes mellitus. Beyond its impact on individual quality of life, OA also creates significant economic pressure on healthcare systems because of the growing need for both conservative treatments and surgical interventions such as joint arthroplasty.[4,5]

From a pathophysiological perspective, OA is no longer viewed solely as a degenerative condition but as a multifactorial disorder characterized by persistent low-grade inflammation. This inflammatory response arises through interactions between chondrocytes, synoviocytes, immune cells, and various inflammatory mediators, including cytokines and chemokines. Key proinflammatory cytokines such as interleukin-1β (IL-1β), tumor necrosis factor-α (TNF-α), and interleukin-6 (IL-6) contribute significantly to extracellular matrix breakdown by promoting the activity of proteolytic enzymes, including matrix metalloproteinases (MMPs) and aggrecanases. In addition, these cytokines enhance chemokine production, facilitating immune cell infiltration into synovial tissue and thereby intensifying inflammation and

progressive joint damage.[1,6,7]

Interleukin-8 (IL-8) is a proinflammatory chemokine involved in the inflammatory mechanisms underlying OA. It is secreted by multiple cell types, including chondrocytes, synoviocytes, and immune cells, and functions as a chemoattractant for neutrophils. Activation of neutrophils within the joint environment may promote cartilage breakdown through the release of proteolytic enzymes and inflammatory mediators. Furthermore, IL-8 has been shown to stimulate chondrocyte differentiation and hypertrophic changes, as well as increase the expression of matrix metalloproteinase-13 (MMP-13), an essential enzyme responsible for the degradation of type II collagen in articular cartilage.[7,8]

Earlier research has shown that IL-8 concentrations are higher in the synovial fluid of individuals with OA than in healthy controls and are linked to enhanced MMPs activity and synovial inflammation. Experimental findings also indicate that blocking inflammatory pathways related to IL-8 may slow the progression of cartilage deterioration in OA models. Nevertheless, clinical data examining the relationship between systemic (serum) IL-8 concentrations and the severity of OA are still scarce and yield inconsistent results[7-9], indicating that the involvement of IL-8 in OA progression is multifaceted and may vary between the early and later stages of the disease.

The severity of OA is commonly assessed using the Kellgren–Lawrence (KL) radiographic classification, which evaluates structural joint changes based on osteophyte formation, joint space narrowing, and subchondral bone alterations. The KL grading system is widely used in epidemiological and clinical studies to classify OA severity from mild to severe.[10] Although radiographic classification provides valuable structural information, it does not capture early molecular and inflammatory changes, highlighting the need for exploratory studies investigating systemic inflammatory markers in relation to OA severity.

Considering this background, an exploratory cross-sectional study was undertaken to assess the relationship between serum IL-8 concentrations and the severity of knee OA. We hypothesized that serum IL-8 concentrations would be associated with the radiographic grading of knee OA. The findings from this study are intended to provide exploratory evidence to support further investigation into the systemic inflammatory processes involved in OA.

Methods

The research employed a cross-sectional observational analytic design in patients with confirmed knee OA. The research was carried out in compliance with the Declaration of Helsinki and applicable national ethical standards. The Research Ethics Committee of Husada Utama Hospital granted ethical clearance for this study (No. 35/KEP-RSHU/X/2024; October

14, 2024). The study sites included Husada Utama Hospital in Surabaya and the Institute of Tropical Disease, Airlangga University. The study subjects consisted of seven elderly patients recruited from the Larasati Pondok OA Posyandu, Faculty of Medicine, Wijaya Kusuma University, using total sampling between November 2024 and January 2025. Given the small sample size, this study was designed as an exploratory analysis. All participants gave informed consent and fulfilled the predefined inclusion and exclusion criteria.

The inclusion criteria were patients diagnosed with knee OA based on clinical and radiographic criteria, aged ≥50 years, with body weight ≥40 kg, and experiencing pain in one or both knees. The exclusion criteria were patients with autoimmune diseases, hepatitis, renal disorders, bone malignancies, osteoporosis, or radiographic findings showing no evidence of OA.

The primary variable was serum IL-8 concentrations, measured as a systemic inflammatory marker using a Bio-Rad iMark™ Microplate Reader. Serum IL-8 concentrations were categorized into low, moderate, and high groups based on quartile distribution because no standardized clinical cut-off values for IL-8 in OA were available. The severity of OA was assessed using knee radiographs based on the Kellgren–Lawrence classification by specialist radiologists at the Radiology Department of Husada Utama Hospital. Statistical analysis was conducted using the Spearman correlation test in SPSS version 25, taking into account the limited sample size and the nonparametric distribution of the data.

Result

The study included seven older individuals diagnosed with knee OA. Each participant met the eligibility requirements and completed the research without any exclusions. The distribution of OA severity based on the KL classification is presented in Table 1. Among the seven participants, four (57.14%) had grade 2 OA and three (42.86%) had grade 3 OA.

Table 1. Distribution of osteoarthritis severity based on Kellgren–Lawrence classification (N=7)

Osteoarthritis Severity	Frequency	Percentage
2	4	57.14%
3	3	42.86%

The distribution of serum IL-8 concentrations among the study participants is presented in Table 2. Serum IL-8 concentrations were categorized into low, moderate, and high groups based on sample quartile distribution due to the absence of established clinical cut-off values.

Table 2. Distribution of serum IL-8 concentrations among study participants (N=7)

Serum IL-8 concentrations (pg/mL)	Frequency	Percentage
Low (IL-8 < 113.85)	2	28.57%
Moderate (113.85 ≤ IL-8 < 136.5)	3	42.86%
High (IL-8 ≥ 136.5)	2	28.57%

Spearman's rank correlation analysis was conducted to evaluate the association between serum IL-8 concentrations and the severity of OA. The results demonstrated a strong negative correlation between serum IL-8 concentrations and OA severity ($r = -0.866$, $P = 0.012$), suggesting that serum IL-8 concentrations decreased as disease severity increased (Table 3). Given the small sample size, these findings should be regarded as exploratory and interpreted with caution.

Table 3. Association between serum IL-8 concentrations and osteoarthritis severity

Serum IL-8 concentrations	OA Severity		Total n (%)	Correlation Coefficient	*P*-value
	Grade 2, n (%)	Grade 3, n (%)			
Low	0 (0%)	2 (100%)	2 (100%)		
Moderate	2 (66.67%)	1 (33.33%)	3 (100%)	-0.866	0.012
High	2 (100%)	0 (0%)	2 (100%)		
Total (Percentage)	**4 (57.14%)**	**3 (42.86%)**	**7 (100%)**		

Discussion

Results from this study indicated that higher severity of knee OA was significantly associated with lower serum IL-8 concentrations, indicating that IL-8 concentrations are relatively elevated in the early stages of the disease and tend to decline as OA becomes more severe. Despite the small sample size, these results suggest that serum IL-8 may serve as a potential early systemic biomarker representing inflammatory activity during the initial phase of OA.

Osteoarthritis is currently recognized as a low-grade chronic inflammatory disease involving complex interactions among chondrocytes, synoviocytes, immune cells, and inflammatory mediators such as cytokines and chemokines.[11] IL-8 is a proinflammatory chemokine produced by chondrocytes and synoviocytes and plays an important role in neutrophil recruitment and activation within joint tissues.[11,12] Neutrophil activation may

accelerate cartilage degradation through the release of proteolytic enzymes and inflammatory mediators, thereby contributing to OA progression.[11]

Increased IL-8 concentrations in both plasma and synovial fluid have been documented in individuals with knee OA, supporting its role in the disease's pathogenesis.[13] The findings of the present study indicate that IL-8 concentrations, which are higher during the early stage of OA, tend to decline as the disease advances. This observation aligns with earlier reports demonstrating that IL-8 is linked to clinical manifestations as well as biomarkers of bone and cartilage metabolism and has been proposed as a potential marker for early detection, evaluation of disease severity, and monitoring of progressive damage to cartilage and subchondral bone.[14,15]

However, the association between systemic IL-8 concentrations and OA severity remains inconsistent across studies. García-Manrique et al. reported that synovial fluid IL-8 was associated with clinical severity, whereas plasma IL-8 was not, indicating heterogeneity in systemic inflammatory biomarker findings.[7] Several studies have indicated that IL-8 concentrations in synovial fluid may serve as a more robust clinical marker of OA severity than serum IL-8, possibly due to complex biological processes or systemic compensatory mechanisms.[7,14] The observed reduction in serum IL-8 concentrations in advanced OA could represent negative feedback regulation of systemic inflammation or a shift from an active inflammatory stage toward a later phase dominated by structural degeneration.

Most previous studies have focused on synovial fluid biomarkers that reflect local joint inflammation; however, these procedures are invasive and less feasible for population-based screening.[13] Evidence regarding serum IL-8 as a systemic biomarker remains limited and heterogeneous. This study contributes exploratory evidence to this research gap by demonstrating a significant negative correlation between serum IL-8 concentrations and OA severity, highlighting the potential role of IL-8 as an early systemic inflammatory biomarker in OA.

This study has certain limitations, notably the small sample size and the cross-sectional design, which does not allow conclusions about causality. In addition, potential confounding factors such as obesity and metabolic conditions were not fully controlled and may influence systemic inflammatory biomarker concentrations.[7,11] Therefore, longitudinal studies with larger sample sizes and adequate control of confounding factors are required to validate these findings.

Conclusion

This study indicates that serum IL-8 concentrations tend to be higher in the early stages

of knee OA and decrease as disease severity progresses, suggesting that systemic inflammatory activity may be more prominent in the initial phase of the disease. These results indicate that serum IL-8 could be regarded as a potential early marker of systemic inflammatory involvement in OA. However, the findings should be interpreted with caution because of the small sample size and the cross-sectional nature of the study. Additional longitudinal research involving larger populations is required to validate these observations and to further define the clinical significance of serum IL-8, including its possible utility in early diagnosis and in monitoring disease progression.

Conflicts of Interest

The authors state that there are no competing interests.

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CASE REPORT **Open Access**

Case Study: Drug Therapy Monitoring in a Patient with Abdominal Colic at a Regional Public Hospital in Gorontalo

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ABSTRACT

Abdominal colic is a common complaint of abdominal pain frequently observed in hospitalized patients, often associated with gastrointestinal infections. This study aims to evaluate the rationality of antibiotic use and identify potential drug-related problems (DRPs) in patients with abdominal colic. The report was conducted descriptively using a SOAP-based approach, utilizing inpatient medical record data at Gorontalo City General Hospital in February 2025. The case analysis showed that the use of ceftriaxone adhered to the 5R principles (right indication, right patient, right drug, right dose, and right duration). However, the concurrent administration of Fiocilas (ampicillin–cloxacillin) represented an unnecessary duplication of antibiotic therapy that was not supported by clinical indications or culture data. This was categorized as "unnecessary drug therapy" and posed a potential risk for antimicrobial resistance and adverse effects. The recommended pharmaceutical intervention was discontinuation of the additional antibiotic and continuation of the main therapy with clinical monitoring. To conclude, this case emphasizes the important role of pharmacists in monitoring the rational use of antibiotics to improve the safety and effectiveness of patient treatment.

Keywords: Abdominal colic, abdominal pain, drug interactions, drug rationality, pharmacotherapy

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Introduction

Abdominal colic is a type of occasionally abdominal pain, originating from the organs within the abdomen. This condition can be caused by various infections affecting the abdominal organs. Experts explain that abdominal colic is characterized by pain or cramping in the abdomen, often accompanied by nausea and vomiting. Obstruction in the abdominal organs can block the flow of intestinal contents, which then causes pain.[1]

According to data from the World Health Organization (WHO) in 2021, approximately 1.8 to 2 million people worldwide experience abdominal colic each year. The prevalence varies across countries, with rates ranging from 22% in the UK, 31% in China, 14.5% in Japan, 35% in Canada, and 29.5% in France. In Southeast Asia, approximately 583,635 people are affected annually. The prevalence of abdominal colic by age group is 1.3% in those aged 55-64, 1.2% in those aged 65-74, and 1.1% in those aged ≥ 75. By gender, the prevalence is higher in men (68.4%) than in women (31.6%). The prevalence of abdominal colic per 1,000 population varies by country. The number of medications a patient takes can lead to drug-related problems (DRPs).[2]

In Indonesia, abdominal pain remains one of the common causes of hospital admission, particularly related to gastrointestinal disorders. Data from the Ministry of Health of the Republic of Indonesia indicate that digestive system diseases are consistently among the leading causes of inpatient morbidity in regional hospitals. In Gorontalo Province, cases of abdominal pain and gastrointestinal infections are frequently reported in inpatient services, emphasizing the importance of rational drug therapy and antibiotic use in regional referral hospitals.

Drug-related problems are issues that arise during patient therapy that can hinder or potentially hinder the achievement of optimal therapeutic outcomes. These can be caused by various factors. Some types of DRPs include unmet drug needs, use of drugs without proper indications, errors in drug selection, drug interactions, and the use of doses that are too high or too low. Inaccurate drug selection and dosage are part of drug-related issues that can impact patient clinical outcomes. When a drug enters the body, interactions with other substances can affect its pharmacokinetics and pharmacodynamics, resulting in changes in therapeutic effects.[2]

Rational medication use must be carried out correctly and appropriately. If not managed properly, it can delay the achievement of therapeutic targets. Rational medication use occurs when patients take the appropriate dose, at the right time, and for the appropriate duration for their condition. This can speed the healing process and reduce the risk of side effects. Conversely, drug misuse can lead to organ damage, drug resistance, and even death.[3]

The importance of drug therapy monitoring is to ensure safe, effective, and rational drug therapy for patients. This activity includes assessing drug choice, dosage, route of administration, therapeutic response, adverse drug reactions (ADRs), and recommendations for changes or alternatives to therapy. Drug therapy monitoring must be conducted continuously and evaluated regularly at specific intervals to determine the success or failure of therapy.[4]

Based on the literature above, it is clear that abdominal colic can cause various complications and require varying medical treatments. Therefore, the author aims to conduct a retrospective study entitled "Case Study of Drug Therapy Monitoring in Patients with Abdominal Colic at the Regional General Hospital in Gorontalo."

Methods

This study is a descriptive analysis of the medical records of patients with abdominal colic. Patients were patients who underwent inpatient care at a hospital in Gorontalo province during February 2025. The analysis used the SOAP method (Subject, Object, Assessment, and Planning), with reference to the latest clinical literature to assess the suitability of management with medical practice standards.

The inclusion criteria in this study were adult inpatients diagnosed with abdominal colic who received antibiotic therapy and had complete medical record data. The exclusion criteria included patients with incomplete medical records, confirmed non-bacterial causes of abdominal pain, or patients discharged against medical advice.

Case Study

Mrs. X aged 43 years was admitted to a regional public hospital in Gorontalo of Februari 11, 2025 with a chief complaint of recurrent, sudden-onset abdominal pain accompanied by fever. The pain was localized to the left lower quadrant and described as cramping in nature. The patient also reported nausea and vomiting. Her past medical histrory was significant for an ovarian cyst diagnosed in 2021. The physical examination obtained blood pressure of 110/70 mmHg, pulse rate of 105 x/minutes and body temperature of 38.50C. Laboratory examination obtained Hemoglobin value of 8.8 g/dL, Leukocytes 13.000/mcl, Platelet 37.1000/mcl, random blood glucose 15 mg/dL. The pharmacological therapy given was Omeprazole twice daily intravenously, Antrain® three times daily intravenously, Ondansetron three times daily intravenously, Cefriaxone twice daily intravenously, Fiocilas® three times daily intravenously, and extra Paracetamol drips because the patient's body temperature was 38.50C. She also received normal saline eight drips per minutes infusion solution, Sucralfate syrup three times daily, Paracetamol 1 tablet three times daily, Dulcolax® syrup two times daily, Ibuprofen 1 tablet three times daily, Santramol 1 tablet three times daily,

Ferrous Sulfate 1 tablet once daily, Vipalbumin® 2 capsul three times daily, and Mefenamic Acid 1 tablet three times daily. During hospitalization, the patient showed gradual clinical improvement. At discharge, the patient was afebrile, abdominal pain had decreased significantly, leukocyte levels showed improvement, and the patient was discharged in stable condition. The patient's clinical characteristics, laboratory findings, and pharmacotherapy during hospitalization are summarized in Tables 1–4.

Table 1. Clinical data of presented cases.

SOAP components	Data
S (*Subjective*)	- Chief complaint: Abdominal pain that comes and goes suddenly, fever, pain in the lower left quadrant - Other symptoms: conjunctival derms, nausea, vomiting - Medical history: Ovarian cyst since 2021
O (*Objective*)	- Initial vital signs: Blood pressure 110/70 mmHg (normal), Pulse 105x/minute (high), Temperature: 38.5°C (high), Leukocyte: 13,800/µL (elevated) - Platelet: 371,000/mm³ (normal) Limphocyte: 6% (low count) - Random blood glucose: 158 mg/dL (normal) - Erithrocyte: 3,88 million/µL (normal)
A (*Assessment*)	- Diagnosis: Abdominal colic + acute bacterial infection + clinical anemia - DRP Identification: Antibiotic duplication (Ceftriaxone + Fiocilas®) - Rationality of Ceftriaxone use according to the 5T principle - Fiocilas was deemed unnecessary (no therapy failure or culture results)
P (*Planning*)	a. Pharmacology: - Omeprazole IV 2x1 - Ondansetron IV 3x1 - Antrain IV 3x1 - Ceftriaxone IV 2x1 (continue) - Fiocilas IV 3x1 (Stopped) - Paracetamol drip (if the temperature is ≥ 38.5^0C) - NaCl 0.9% infusion + Ketorolac - Sucralfate syrup 3x1

- Paracetamol tablet 3x1
- Dulcolax syrup 2x1
- Santramol 3x1
- Ferro sulfat 1x1
- VIP albumin 3x2
- Mefenamic acid 3x1

b. Non- pharmacology:

- Avoid spicy, sour, fatty foods
- Drink enough fluids 2–2.5 litres/day
- Teach relaxation techniques (deep breathing, meditation)
- High fiber, low fat diet

DRP: Drug-related problem, IV: Intravenous

Table 2. Patient vital signs examination results.

Inspection	Results	Literature	Interpretation
Blood pressure	110/70 mmHg	<120/80 mmHg	Normal
Pulse	105 x/menit	60-100 x/minute	High
Temperature	38.5^{0}C	36.5^{o}C -37.5^{o}C	High
Respiratory rate	20 x/m	12-20 x/minute	Normal

Table 3. Laboratory data of presented case.

Type of Examination	Results	Normal Value	Remarks
Haemoglobin	8.8 g/dL	11.00-16.00 g/dL	Abnormal
Leukocytes	13,800/uL	5,000-10,000/uL	Abnormal
Platelet	371.000/mm^3	150.000-450.000/mm^3	Normal
Random blood glucose	158 mg/dL	<200 mg/dL	Normal
Erythrocytes	3.88 million/uL	3.5-5.5 million/uL	Normal
Lymphocytes	6%	20-40%	Abnormal

Discussion

Mrs. x aged 43 years, was admitted and hospitalized in class I of Regional General Hospital on February 11, 2025 and was treated for seven days with the chief complaint of frequent abdominal pain that often comes and goes suddenly, fever, conjunctivitis, and pain in the lower left quadrant area. The patient also had a history of ovarian cysts since 2021. The physical examination obtained BP 110/70 mmHg, Pulse 105x per minute and body temperature

38.5^{0}C and further laboratory examinations were immediately carried out. This patient was diagnosed with abdominal colic, acute bacterial infection (main diagnosis) and clinical anemia by the doctor. On the first day of admission the patient was given Omeprazole intravenous, Antrain intravenous, and Ondansetron intravenous.

Table 4. Drug administration of presented case.

No	Drug Name	Dose	Route	Dosage Regimen	Date of admission (February 2025)							
					11	12	13	14	15	16	17	18
1.	Sucralfat syrup	500 mg/5mL	Oral	3x1		✓	✓	✓	✓	✓	✓	✓
2.	Santramol®	500 mg	Oral	3x1					✓	✓	✓	✓
3.	Ferrous Sulfate	200 mg	Oral	1x1						✓	✓	✓
4.	VIP albumin	500 mg	Oral	3x2							✓	✓
5.	Paracetamol	500 mg	Oral	3x1		✓	✓					
6.	Dulcolax syrup	15 ml	Oral	3x1					✓			
7.	Omeprazole		IV	2x1	✓	✓	✓	✓	✓	✓	✓	✓
8.	Ondansentron		IV	3x1	✓	✓	✓	✓	✓	✓	✓	✓
9.	Antrain®		IV	3x1	✓	✓	✓					
10.	Paracetamol drips		IV	If body temperature ≥38,5°C					✓		✓	
11.	Ceftriaxone		IV	2x1		✓	✓	✓	✓			
12.	Fiocilas®	500 mg/6 hours	IV					✓	✓	✓	✓	✓
13.	NaCl 0.9% + Ketorolac 3%	8 tpm	IV								✓	

On February 11, 2025, the patient was given Omeprazole injection 1 ampoule two times daily to protect the gastric mucosa from the risk of irritation due to stress and the use of pain medication. Omeprazole works by inhibiting the H^+/K^+-ATPase enzyme in gastric parietal cells, which is a proton pump as the final pathway for gastric acid production. This is in line with the dose of omeprazole injection, which is 40 mg 1–2 times/day IV.[5] In addition, the

patient was also given Antrain® 1 ampoule three times daily injection, which functions as an analgesic and antispasmodic to reduce pain due to spasm of the smooth muscles of the gastrointestinal tract, which is a characteristic of abdominal colic. According to MIMS literature the correct dose for the use of Antrain® is 1 ampoule three times a day intramuscular or intravenous.[6] The patient also complained of nausea and vomiting, thus Ondansetron injection 1 ampoule three timed daily was given. Ondansetron is an antiemetic that works by inhibiting the 5-HT3 type serotonin receptor in the central nervous system and digestive tract. According to MIMS literature, the Ondansentron dose is 4–8 mg every 8–12 hours intramuscular or intravenous.[7]

From February 12, 2025, to February 17, 2025, the patient began receiving Ceftriaxone injection, 1 gram twice daily, as the primary antibiotic therapy. Ceftriaxone is a third-generation cephalosporin that works by inhibiting bacterial cell wall synthesis. The usual dose of Ceftriaxone is 1–2 grams per day, divided into 1–2 doses. This antibiotic was chosen because it is able to treat systemic infections indicated by an increase in leukocytes and fever symptoms experienced by the patient.[8] After several days of administration, the patient's leukocyte levels showed a decrease, indicating a positive response to therapy.

In addition to antibiotic therapy, the patient was given 500 mg Paracetamol tablets three times daily to reduce fever. The dosage given is in line with the dosage listed in the literature, namely 500–1000 mg every 4–6 hours, a maximum of 4 grams/day. Paracetamol works by inhibiting the cyclooxygenase enzyme in the central nervous system, thereby reducing the production of prostaglandins that trigger an increase in body temperature.[9] Paracetamol also has a mild analgesic effect that helps relieve discomfort due to fever and abdominal pain. To overcome persistent colic pain, the patient was also given centramol® tablets three times daily. The dosage in this case is in line with the dosage listed in the MIMS, namely 3x1 tablet per day. Centramol contains a combination of analgesic and antispasmodic substances that work by reducing pain impulses and relaxing the smooth muscles of the gastrointestinal tract, making it very suitable for use in patients with complaints of spasmodic abdominal colic.[10] In addition, patients are also given Sucralfate syrup three times daily, which works locally by coating the stomach wall and forming a barrier against stomach acid, thus helping the healing process of gastric mucosa that may be irritated due to illness or medication use. According to Dipiro, the correct dosage for sucralfate is 1 gram (10 mL) four times daily (1 hour before meals and before bedtime).[9]

Patients were also given a daily infusion of 0.9% sodium chloride (NaCl) during treatment as part of fluid therapy. NaCl 0.9% is an isotonic crystalloid solution containing

sodium and potassium. This solution is used to maintain electrolyte balance and fluid volume, particularly in patients experiencing fever, vomiting, or signs of mild dehydration.[10]

Midway through treatment, the patient was given an injectable antibiotic containing a combination of imipenem 500 mg and cilastatin 500 mg. Imipenem is a carbapenem antibiotic, a broad-spectrum antibiotic that is highly effective against a wide range of Gram-positive and Gram-negative bacteria, including beta-lactamase-producing bacteria. Cilastatin itself is not an antibiotic, but it inhibits the dehydropeptidase-I enzyme in the kidneys that breaks down imipenem. Therefore, cilastatin's presence is crucial for maintaining imipenem levels and effectiveness in the body. The addition of Fiocilas® was presumably intended to broaden antimicrobial coverage in response to suspected severe infection. However, there was no clinical deterioration, no worsening of symptoms, and no laboratory evidence indicating treatment failure with ceftriaxone at the time of antibiotic escalation.

The use of Ceftriaxone was deemed clinically appropriate because the patient exhibited symptoms of systemic infection, namely fever and leukocytosis. A few days after administration, a decrease in leukocyte count was observed, indicating that the patient responded well to Ceftriaxone therapy. However, midway through the treatment period, Ceftriaxone therapy was discontinued and replaced with a combination of imipenem-cilastatin, which belongs to the carbapenem class and is commonly used for severe or resistant infections. This change raised the suspicion that the physician considered a decrease in the effectiveness of Ceftriaxone. However, objectively, no clinical or laboratory evidence indicated therapeutic failure.

The administration of this antibiotic raised the potential for a DRP in the form of antibiotic therapy duplication, as the patient had already been receiving Ceftriaxone consistently since February 12, 2025. Objectively, the patient showed a favorable clinical response to ceftriaxone therapy, as indicated by decreased leukocyte levels and improvement of clinical symptoms. Therefore, the use of an additional broad-spectrum antibiotic without microbiological evidence was considered unnecessary. Laboratory results showed a decrease in leukocyte count, meaning that infection therapy with Ceftriaxone had been effective. According to Brunton et al.,[10] the administration of two broad-spectrum antibiotics simultaneously without clear indication falls into the DRP category of “unnecessary drug therapy.” This not only adds a metabolic burden to the body but also increases the risk of adverse effects such as kidney damage, disruption of normal microbiota, and bacterial resistance. Billstein-Leber et al. also state that the use of additional antibiotics should be based on culture and sensitivity data or in cases of prior therapeutic failure, which in this case did not

occur.[8]

Therefore, the administration of the Imipenem and Cilastatin combination was deemed unnecessary and potentially harmful. The recommended pharmaceutical intervention is to discontinue Fiocilas and continue Ceftriaxone therapy with periodic monitoring of the patient's clinical condition and laboratory parameters.

In addition to pharmacological therapy, the patient was also advised on non-pharmacological measures. The patient was encouraged to consume a diet high in fiber and low in fat to support the healing process and maintain digestive health. According to Thompson, examples of foods that are high in fiber but low in fat include fresh vegetables such as spinach, broccoli, carrots, and green beans. Fruits such as apples (with skin), pears, strawberries, and papayas are also highly recommended as they are rich in soluble fiber, which helps maintain intestinal mucosa health.[11] Additionally, whole grains such as oatmeal, quinoa, brown rice, and whole wheat bread are sources of complex fiber that promote optimal bowel function. Legumes such as lentils and chickpeas are also good options, if they are consumed in appropriate portions to keep fat content low. Tubers such as sweet potatoes and cassava, when prepared without frying, can also be part of a healthy high-fiber diet.

It is important to avoid spicy, acidic, and high-fat foods as they may worsen symptoms or delay recovery. According to Zhao et al., examples of spicy foods include chili sauce, spicy curry, and chili-seasoned dishes such as *ayam rica-rica*. Acidic foods include citrus fruits (such as lemon, lime), tomato sauce, pickles, and carbonated beverages.[12] Examples of high-fat foods include fried snacks (such as fried bananas, vegetable fritters), fast-food burgers, pizza, French fries, sausages, and foods with concentrated coconut milk. It is also essential to ensure adequate fluid intake by drinking 2 to 2.5 liters of water per day. Adequate hydration is particularly important if the patient has fever or diarrhea, to prevent dehydration. The patient was also taught simple relaxation techniques such as deep breathing or light meditation to help naturally reduce pain.

Rationality of antibiotic use

In this case, the rationality of antibiotic use was evaluated based on the 5T principles: right indication, right patient, right drug, right dose, and right duration. According to right indication aspect, the administration of Ceftriaxone was deemed rational because the patient exhibited signs of acute bacterial infection: fever (38.5°C), leukocytosis (13,800/µL), and lymphopenia. Severe infections with systemic manifestations require broad-spectrum antibiotics such as Ceftriaxone to prevent serious complications.[8] According to right patient aspect, patient was 43 years old with no history of allergy to cephalosporins and had an active

infection, making them an appropriate candidate for Ceftriaxone therapy. According to right drug aspect, Ceftriaxone, a third-generation cephalosporin antibiotic, is effective against many gram-negative bacteria and some gram-positive bacteria. In the absence of culture results, the use of a broad-spectrum empiric antibiotic can be justified in cases of severe infection.[10] According to right dose and route of administration, a dose of 1 gram intravenous two times daily is in accordance with recommendations for the treatment of severe infections.[9] According to right duration, Ceftriaxone therapy was maintained as long as the patient remained in an active infectious state, with plans to switch to oral antibiotics (Cefixime) once the condition improved, in line with the principle of antibiotic de-escalation.[8]

Identification of inappropriateness

In the middle of the treatment period, the patient received an additional antibiotic, Fiocilas® (combination of Imipenem and Cilastatin). This additional antibiotic administration was considered irrational because there was no evidence of Ceftriaxone treatment failure. In addition, it was not based on culture results. Moreover, it increased the risk of side effects and bacterial resistance. According to previous study, the use of additional antibiotics without a clear indication falls under the category of *unnecessary drug therapy* and should be avoided to preserve long-term antibiotic effectiveness.[8] Therefore, a recommendation was made by discontinue Fiocilas® and continue intravenous Ceftriaxone with close clinical and laboratory monitoring. Finally, DRP in the present case is summarized in Table 5.

Table 5. Drug related problem of presented case.

No	Category	Description
1	Indication Without Therapy	No
2	Therapy Without Indication	No
3	Dose Too Low	No
4	Dose Too High	No
5	Adverse Reaction	No
6	Drug Interaction	No
7	Patients Not Using Medication	No
8	No Indication	Yes
9	Polypharmacy	Yes

This case has limitations due to its single-patient case study design, which limits the generalizability of the findings. However, this case provides valuable insight into the importance of drug therapy monitoring and rational antibiotic use in clinical practice.

Conclusion

Ceftriaxone therapy in this patient was rational and consistent with the 5T principles of appropriate antibiotic use. However, the addition of imipenem–cilastatin without documented clinical indication constituted a drug-related problem in the form of unnecessary drug therapy and potential polypharmacy. This case underscores the essential role of pharmacists in antimicrobial stewardship, ensuring rational drug use, minimizing resistance risk, and enhancing patient safety.

Conflict of Interest

The authors declare no conflicts of interest.

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Ethics and Patient Consent

This retrospective case report used anonymized patient data. Written informed consent for publication was obtained from the patient. Ethical approval was waived due to the non-interventional and retrospective nature of the study.

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