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Research Article

Rationality of Tuberculosis Treatment for Drug-Susceptible Pulmonary Tuberculosis at a Primary Care in Bandung

Alfi Nurul Islamiyah [1*]
Syarifuddin [1]
Morsalina Akhsa [1]
Iis Rukmawati [2]
Eni Margayani [1]
Linda Purnamawati Suherman [1]
Vina Septiani [1]
Robby Ramdani [1]

[1] Department of Pharmacy, Universitas Jenderal Achmad Yani, Cimahi, West Java, Indonesia
[2] Pharmacy Installation, Ibrahim Adjie Primary Care, Bandung, West Java, Indonesia

*email: alfi.nurul@lecture.unjani.ac.id; phone: +6281220542445

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Abstract

Tuberculosis (TB) remains a significant global health concern, particularly in Indonesia. Ensuring rational TB treatment is crucial for effective disease control and preventing the emergence of drug resistance. This study aimed to evaluate the rationality of TB treatment among newly diagnosed drug-susceptible pulmonary TB patients in a primary care center in Bandung. A descriptive-analytical study was conducted on 56 patients who met the inclusion and exclusion criteria. Treatment rationality was assessed based on the Indonesian Society of Respirology 2021 and the National Guidelines for Medical Services 2020. While 100% of patients received the correct medication for the right indication and dose, the duration of therapy was suboptimal for most patients (83.93%) due to drug unavailability. This resulted in a lower-than-ideal treatment regimen, potentially compromising treatment outcomes and increasing the risk of drug resistance. These findings highlight the need for improved drug supply management and adherence to treatment guidelines to optimize TB treatment outcomes and reduce the burden of TB in Indonesia.

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INTRODUCTION

Tuberculosis (TB) is an ancient and enduring global health challenge. Despite decades of treatment efforts, TB remains a significant public health concern, particularly in countries like Indonesia. With a 9.2% global burden, Indonesia ranks second globally in TB cases, following India (28%) and China (7.4%). This persistent burden underscores the urgent need for continued research and innovative approaches to combat this devastating disease[1].

The World Health Organization (WHO) Global Tuberculosis Report 2022 highlights a concerning global trend. In 2021, an estimated 10.6 million people were affected by TB, reflecting a 4.5% increase compared to 2020. This global increase was driven by factors such as the COVID-19 pandemic, which disrupted TB prevention and care services. Notably, Indonesia significantly contributed to this rise, with a 13% increase in TB incidence rates between 2020 and 2021. Geographically, the Southeast Asia region bore the heaviest burden, accounting for 45% of global TB cases in 2021. Indonesia, classified as a high TB burden country, faces significant challenges in TB control, with treatment coverage rates remaining alarmingly low, estimated to be below 50% in 2021. These alarming statistics underscore the urgent need for intensified efforts to combat TB in Indonesia and improve access to effective diagnosis and treatment[2].

Tuberculosis remains a significant public health challenge globally, including in Indonesia. According to the WHO, an estimated 969,000 TB cases were reported in Indonesia in 2021, representing an alarming 17% increase compared to the previous year. This translates to one person being infected with TB every 33 seconds[3]. In West Java province, the number of

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TB cases also showed a concerning trend, rising from 85,681 in 2021 to 106,661 in 2022[4]. Within West Java, Bogor Regency, Bandung City, and Bekasi City reported the highest burden of TB, collectively accounting for 6-14% of the total cases in the province. Specifically, Bandung City witnessed a substantial increase in TB cases, rising from 8,504 in 2021 to 14,541 in 2022[5]. These figures underscore the urgent need for effective interventions to control the ongoing TB epidemic in Indonesia, particularly in high-burden areas such as West Java.

Rational drug use is paramount for successful TB treatment, ensuring optimal therapeutic outcomes and minimizing the emergence of drug-resistant strains[6,7]. This necessitates accurate and timely diagnosis, appropriate drug selection, and adherence to prescribed regimens. A key factor influencing treatment success is the correct dosing and duration of therapy. However, studies have shown that inappropriate dosing and treatment durations are prevalent in certain settings. For instance, a study conducted at the Sikumana Primary Care clinic found that among 65 sputum smear-positive pulmonary TB patients, 8 received inappropriate doses, and 11 received treatment for an incorrect duration. Treatment outcomes in this study were varied, with 47.7% of patients achieving treatment success, 36.9% completing treatment, and a combined 13.8% experiencing treatment failure, discontinuation, or death[8]. These findings underscore the critical need for improved TB treatment practices, emphasizing the importance of adherence to standardized treatment guidelines and regular monitoring of patient outcomes. Understanding the factors that contribute to inappropriate prescribing practices is crucial for developing effective interventions to improve TB treatment outcomes and ultimately combat this global health threat[9].

This study aimed to evaluate the rationality of TB treatment regimens in patients with drug-susceptible pulmonary TB. Rational TB treatment involves administering appropriate medications at correct dosages based on well-established guidelines. This study was conducted at a Primary Care center in Bandung, Indonesia, to investigate various aspects of TB treatment utilization, including prescribing patterns, medication quality, and treatment outcomes. To assess the quality of TB treatment, this study employed an audit methodology, comparing actual treatment practices to the national TB treatment guidelines[7,10]. This approach provides valuable insights into the current state of TB treatment adherence and identifies areas for improvement in TB care delivery.

MATERIALS AND METHODS

Materials

This study utilized data from a Primary Care clinic in Bandung, Indonesia, to investigate specific aspects of TB treatment. Data were collected from patient card sheets and medical records of outpatients newly diagnosed with drug-susceptible pulmonary TB who received treatment at the clinic between January 2021 and December 2022. A non-probability purposive sampling technique was employed to select patients who met the inclusion criteria:

1. Age ≥15 years
2. Completed 6 months of TB treatment
3. Complete patient card sheets and medical records

Patients with co-morbidities and those who died, discontinued treatment, or were transferred to other facilities were excluded from the study. Data collected included patient demographics (initials, gender, age, and weight), diagnosis, laboratory examination results, and dispensing data (prescribed drug, dose, and quantity dispensed).

Methods

This retrospective cohort study aimed to describe drug use patterns, identify treatment outcomes, and assess the standard of care in drug-susceptible pulmonary TB patients. The study included 67 adult patients (≥15 years) diagnosed with pulmonary TB who received treatment at a Primary Care Center in Bandung, Indonesia, between 2021 and 2022. Eleven patients were excluded from the analysis: two due to comorbid diabetes mellitus, four due to death during treatment, two due to loss to follow-up, and three due to transfer to another facility. Thus, a total of 56 patients were research subjects, as presented in **Figure 1**. This study focused on both the processes and outcomes of drug use in patients with drug-susceptible pulmonary TB. The analysis centered on patient-level data, providing insights into drug utilization patterns, including drug selection, dosage, duration of therapy, and adherence to national guidelines. This study received ethical exemption from the Research Ethics Committee of Universitas Padjadjaran Bandung (No. 381/UN6.KEP/EC/2023).

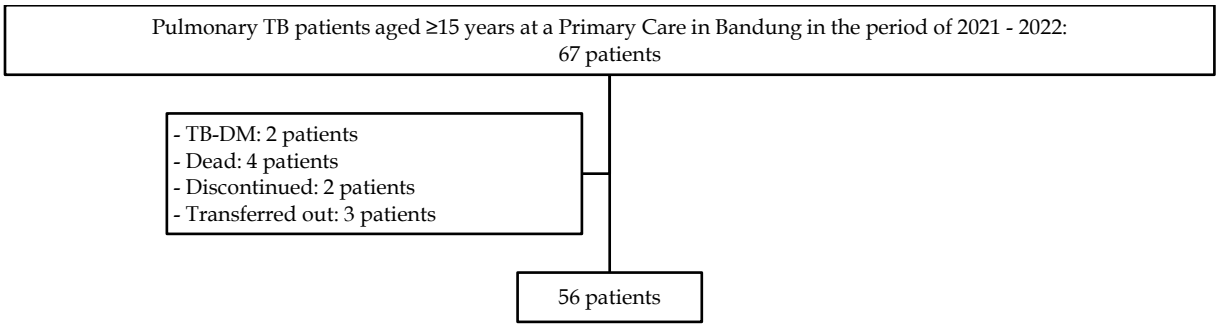

Figure 1. Research sample.

Data analysis

To assess the quality of TB treatment, drug use practices were compared against established national standards. These standards included the *Perhimpunan Dokter Paru Indonesia* (PDPI; Indonesian Society of Respirology) 2021 guidelines[6] and the *Pedoman Nasional Pelayanan Kedokteran* (PNPK; National Guidelines for Medical Services) 2020[8]. These indicators encompassed several key aspects:

1. Medication Indication: Evaluation of the appropriateness of drug prescription for the diagnosed condition.
2. Medication Selection: Assessment of adherence to recommended drug formularies and guidelines.
3. Medication Dosage: Analysis of whether prescribed dosages were appropriate for individual patients, considering factors such as age, weight, and renal/hepatic function.
4. Duration of Therapy: Evaluation of the appropriateness of the prescribed treatment duration based on clinical guidelines and patient-specific factors.
5. Treatment Outcomes: Assessment of the effectiveness of the prescribed medications in achieving desired clinical outcomes, such as symptom reduction, disease control, or cure.

RESULTS AND DISCUSSION

This study included 56 of 67 pulmonary TB patients aged ≥15 years diagnosed at a Primary Care facility in Bandung, Indonesia, between 2021 and 2022 (**Table I**). This sample size aligns with the recommended minimum of 50-75 patient records per healthcare facility for meaningful analysis of drug use and treatment evaluation[11]. The study population exhibited a female predominance, with 34 (60.71%) female patients and 22 (39.29%) male patients. This finding is partially consistent with previous research. For instance, a study in China reported a marginally higher risk of pulmonary TB in females under 40 years of age and a significantly higher risk in males over 40[12]. This disparity may be influenced by factors such as hormonal differences, occupational exposures, and social determinants of health. However, gender disparities in TB incidence are not well-documented, and further research is needed to fully understand their underlying mechanisms. A study conducted in Harare, Zimbabwe, also highlighted the nuanced role of gender in TB, demonstrating that women were more likely to develop severe forms of the disease[13]. These findings emphasize the importance of considering gender-specific factors in TB prevention and treatment strategies.

Table I. Patient demographic information.

Patient information	n (56)	%
Age (years)		
15-24 (adolescence)	19	33.93
25-34 (young adults)	10	17.86
35-44 (adults)	10	17.86
45-54 (older adults)	10	17.86
55-64 (elderly)	4	7.14
≥65 (old)	3	5.36
Gender		
Male	22	39.29
Female	34	60.71

This study found that the highest prevalence of pulmonary TB was observed in the adolescent age group (15-24 years), comprising 33.93% of the patient population. Adults aged 35-44 years and young adults aged 25-34 years followed, accounting for 17.86% and 17.86% of cases, respectively. These findings align with previous research conducted at the Oebobo Health Center in 2020, which reported a high prevalence of pulmonary TB among late adolescents (18-24 years) and young adults (25-43 years)[13]. The elevated risk of pulmonary TB across all age groups above 15 years is likely attributable to several factors, including cumulative exposure to *Mycobacterium tuberculosis*, smoking, air pollution, and other age-related conditions. Adolescents are particularly vulnerable due to factors such as increased social interactions, frequent community transmission, and potential for school-based outbreaks, all of which increase their exposure risk[15].

The cornerstone of TB management lies in the adherence to recommended treatment regimens, which are crucial for effective disease control and minimizing transmission. The WHO recommends a 6-month regimen for new pulmonary TB cases, consisting of 2 months of intensive phase treatment with rifampicin followed by 4 months of continuation phase treatment with rifampicin and isoniazid. Daily dosing is the preferred regimen for optimal treatment outcomes, as it ensures consistent drug levels and enhances treatment adherence[14]. However, this study revealed that 38 out of 53 patients (67.86%) received thrice-weekly dosing due to the unavailability of daily dose medications (**Table II**). This deviation from the recommended regimen may compromise treatment efficacy and increase the risk of treatment failure and drug resistance.

Table II. TB treatment patterns.

Regimen	n (56)	%
2HRZE/4HR*	18	33.93
2HRZE/4H3R3**	38	67.86

Note: *2HRZE/4HR regimen: isoniazid, rifampicin, pyrazinamide, and ethambutol daily for the first 2 months in the intensive phase, followed by isoniazid and rifampicin daily for the next 4 months in the continuation phase. **2HRZE/4H3R3 regimen: isoniazid, rifampicin, pyrazinamide, and ethambutol daily for the first 2 months in the intensive phase, followed by isoniazid and rifampicin three times a week for the next 4 months in the continuation phase.

The use of thrice-weekly regimens, while not the preferred option, is permissible under specific circumstances and requires close patient monitoring to ensure adherence. However, the lack of availability of daily dose medications highlights a critical gap in the current TB treatment program. The government needs to address this issue by ensuring consistent and adequate supply of all recommended medications, particularly daily dose regimens. This is crucial for optimizing treatment outcomes, preventing drug resistance, and achieving the goal of TB elimination[16].

For the treatment of drug-susceptible TB, fixed-dose combination (FDC) tablets are generally preferred over separate drug formulations. It is widely believed that FDCs enhance patient adherence by simplifying the treatment regimen, reducing pill burden, and minimizing the risk of medication omissions. This, in turn, can contribute to improved treatment outcomes and a reduced risk of drug resistance[17].

In this study, we employed two standard TB treatment regimens: 2HRZE/4HR and 2HRZE/4H3R3. The intensive phase of both regimens utilizes a daily FDC containing isoniazid 75 mg, rifampicin 150 mg, pyrazinamide 400 mg, and ethambutol 275 mg (HRZE). The continuation phase differs between the two regimens: 2HRZE/4HR utilizes a daily FDC containing isoniazid 75 mg and rifampicin 150 mg (HR), while 2HRZE/4H3R3 employs a thrice-weekly FDC containing isoniazid 150 mg and rifampicin 150 mg (H3R3). The specific dosage adjustments for each regimen, based on patient body weight, are outlined in **Table III** for 2HRZE/4HR and **Table IV** for 2HRZE/4H3R3.

Table III. 2HRZE/4HR regimen pattern.

	n (18)	%
Daily doses prescribed (tablets)		
2	11	61.11
3	3	16.67
4	4	22.22
Duration of therapy		
Intensive phase (days)		
56	16	88.89
58	1*	5.56
59	1*	5.56
Continuation phase (days)		
112	16	88.89
115	2*	11.11

Note: *inappropriate

Table IV. 2HRZE/4H3R3 regimen pattern.

	n (38)	%
Daily doses prescribed (tablets)		
2	3	7.90
3	25	65.79
4	10	26.32
Duration of therapy		
Intensive phase (days)		
56	31	81.58
57	1*	2.63
58	2*	5.26
59	2*	5.26
61	1*	2.63
66	1*	2.63
Continuation phase (weeks)		
16	38	100

Note: *inappropriate

Table V presents the results of the TB treatment use evaluation. The findings demonstrate that the indication for TB treatment and the selection of anti-TB drugs in all patients were in accordance with current treatment guidelines (100%). However, adherence to the recommended duration of therapy was observed in only 83.93% of patients. These findings are generally consistent with previous studies. For instance, a study conducted at RSUD Dr. Soedarso reported that while 100% of patients received appropriate indications and drug selections, only 85% adhered to the recommended duration of therapy[18]. Similarly, a study conducted in Oebobo Primary Care in Kupang found that while 100% of patients received the correct drug dosage, only 94.11% adhered to the recommended treatment duration[13]. These studies collectively suggest that adherence to the recommended duration of anti-TB therapy remains a significant challenge in clinical practice.

Table V. Rational use of drugs.

Criteria reviewed	n	%
Indication	56	100
Drug selection	56	100
Doses prescribed	56	100
Duration of therapy	47	83.93

The standard treatment regimen for drug-susceptible pulmonary TB typically consists of a 6-month course, divided into an intensive phase of 2 months (8 weeks or 56 days) followed by a continuation phase of 4 months (16 weeks or 112 days)[6,8]. However, our analysis revealed that 9 out of 56 patients (16.07%) received inappropriate treatment durations. Among patients receiving the 2HRZE/4HR regimen, two patients (11.11%) experienced discrepancies in both the intensive and continuation phases. Conversely, seven patients (18.42%) receiving the 2HRZE/4H3R3 regimen had inappropriate treatment durations specifically within the intensive phase. These findings highlight a significant concern regarding adherence to recommended treatment guidelines for drug-susceptible pulmonary TB within our study population.

Effective TB treatment requires a meticulously planned and consistently administered regimen, encompassing both the intensive and continuation phases. The primary objective of the intensive phase is to rapidly diminish the bacterial load within the patient's body, thereby minimizing the risk of disease transmission. This is achieved through the concurrent administration of multiple anti-TB drugs, which synergistically target and eliminate the actively multiplying bacteria[19]. Adherence to the prescribed medication regimen, including the correct dosage and frequency, is crucial. Typically, within the first two weeks of the intensive phase, the risk of transmission significantly decreases. Furthermore, this phase aims to mitigate the impact of pre-existing drug-resistant strains, ensuring that a comprehensive range of anti-TB drugs are employed from the outset. The continuation phase serves as a crucial follow-up, targeting the remaining dormant or slow-growing bacteria that may have survived the initial intensive treatment. This sequential approach is essential to prevent relapse and ensure a complete eradication of the infection[20].

Drug utilization studies play a crucial role in promoting the rational use of medications within a population. This study revealed an early signal of irrational drug use, namely inappropriate therapy duration, among TB patients. This finding underscores the critical need for pharmacist interventions to optimize TB treatment adherence and improve overall treatment outcomes. The results highlight the importance of continuing medical education programs specifically designed

for healthcare practitioners involved in TB treatment. These programs should emphasize appropriate treatment durations and address common prescribing errors. Furthermore, the implementation of regular drug utilization reviews as part of a quality improvement cycle is essential for continuous monitoring and evaluation of TB treatment practices, ultimately leading to better patient outcomes and improved public health[21].

Patient evaluation in TB treatment encompasses a multifaceted approach, including clinical assessment, bacteriologic evaluation, radiologic evaluation, monitoring of drug side effects, and assessment of treatment adherence. Among these, bacteriologic evaluation is crucial for determining the presence and clearance of *M. tuberculosis* in sputum[22]. In this study, sputum smear microscopy was performed at key intervals: at baseline (before treatment initiation), after two months of intensive phase treatment, at the end of the intensive phase if the two-month smear was positive, and at the end of the six-month treatment course (**Figure 2**). At baseline, 37 patients presented with sputum smear-positive results, while 13 patients were smear-negative. Following two months of treatment, a significant reduction in bacterial load was observed, with only two patients remaining sputum smear-positive. In the third month of treatment, these two patients achieved sputum smear negativity. By the end of the six-month treatment course, all 39 patients evaluated at this stage exhibited negative sputum smear results.

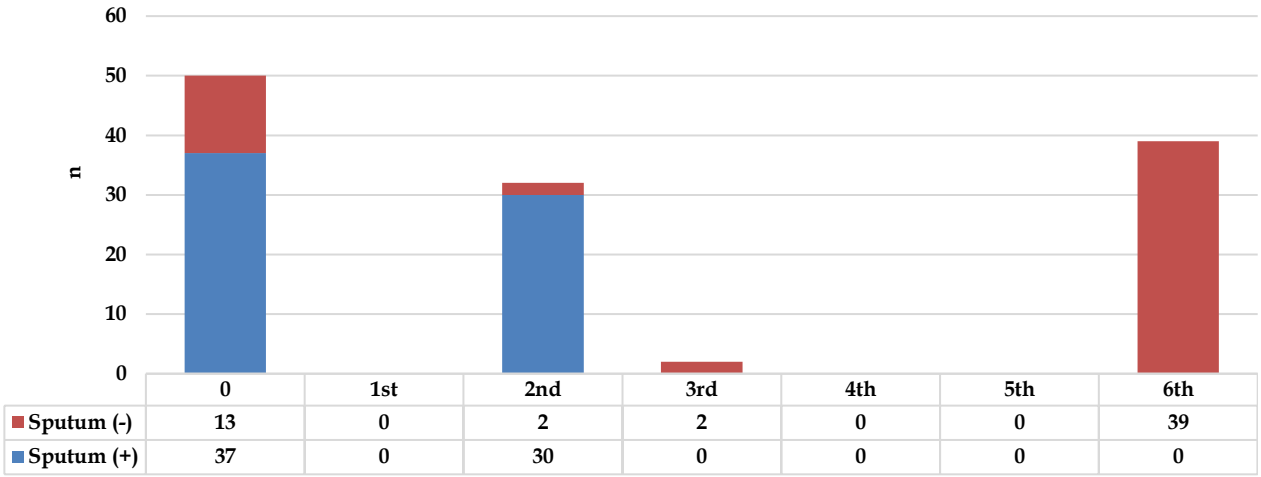

Figure 2. Bacteriological evaluation of TB treatment.

Several barriers have been identified that hinder effective TB evaluation. A study conducted in Uganda among 22 health center staff highlighted key impediments, including insufficient training for healthcare workers, heavy workloads, low staff motivation, poor coordination among healthcare services, and significant challenges faced by patients, such as time constraints, financial burdens associated with seeking and completing TB evaluations, limited health knowledge, and the stigma associated with TB[18]. Furthermore, a cohort study involving 456 participants in Ethiopia underscored the critical role of nutritional assessment, counseling, and management within TB treatment programs. This study demonstrated that incorporating these components into the treatment regimen has the potential to significantly improve treatment outcomes[23].

This study evaluated the effectiveness of anti-tuberculosis therapy by analyzing patient outcomes as presented in **Table VI**. A patient was considered "recovered" if they had a positive bacteriological test at the initiation of treatment and subsequently converted to negative at the end of the treatment course. "Complete treatment" was defined as patients who had undergone the full course of therapy with a negative bacteriological test at a previous examination but without a subsequent bacteriological evaluation at the end of treatment. Among the 56 pulmonary tuberculosis patients aged 15 years and older treated at a Primary Care Center in Bandung between 2021 and 2022, 39 patients (69.64%) were declared recovered, while 17 patients (30.36%) completed treatment. These findings are comparable to a similar study conducted at the Oebobo Primary Care Center in Kupang, which reported a treatment success rate of 57.35% and a completion rate of 36.79%[13]. However, that study also reported mortality (4.41%) and patients with no evaluation (1.47%), indicating potential gaps in patient follow-up.

Table VI. Rational use of drugs.

Outcomes of treatment	Regimen (n (%))		Total (n (%))
	2HRZE/4HR	2HRZE/4H3R3	
Recovered	11 (61.11)	28 (73.68)	39 (69.64)
Complete treatment	7 (38.89)	10 (26.32)	17 (30.36)

This study highlights a crucial observation: not all patients in the Bandung cohort underwent the recommended evaluation procedures. This underscores the critical need for enhanced education and training programs for healthcare providers to emphasize the importance of adhering to standardized treatment guidelines and conducting thorough patient evaluations for all tuberculosis cases. This will ensure accurate assessment of treatment outcomes and facilitate timely identification of patients requiring additional support or alternative treatment strategies[24,25].

CONCLUSION

This study revealed several critical shortcomings in the management of drug-susceptible pulmonary TB patients. Firstly, due to limited availability of the recommended thrice-weekly dosing regimen, a significant proportion of patients likely received suboptimal treatment. Secondly, the quality of drug use was suboptimal, characterized by irrational treatment decisions, including inappropriate durations of therapy. Finally, a concerning observation was the lack of adherence to standardized patient evaluation protocols. These findings underscore the urgent need for improvements in the management of drug-susceptible pulmonary TB, including ensuring access to recommended treatment regimens, optimizing treatment durations, and strengthening patient monitoring and evaluation systems.

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AUTHORS' CONTRIBUTION

Conceptualization: Alfi Nurul Islamiyah, Syarifuddin, Morsalina Aksha, Iis Rukmawati
Data curation: Morsalina Aksha, Iis Rukmawati
Formal analysis: Alfi Nurul Islamiyah, Syarifuddin, Morsalina Aksha, Iis Rukmawati, Eni Margayani, Linda Purnamawati Suherman, Vina Septiani, Robby Ramdani
Funding acquisition: Alfi Nurul Islamiyah, Eni Margayani
Investigation: Alfi Nurul Islamiyah, Syarifuddin, Morsalina Aksha, Iis Rukmawati
Methodology: Alfi Nurul Islamiyah, Syarifuddin, Morsalina Aksha, Iis Rukmawati
Project administration: Alfi Nurul Islamiyah, Syarifuddin, Morsalina Aksha
Resources: Alfi Nurul Islamiyah, Syarifuddin, Morsalina Aksha, Iis Rukmawati, Eni Margayani, Linda Purnamawati Suherman, Vina Septiani, Robby Ramdani
Software: -
Supervision: Alfi Nurul Islamiyah, Syarifuddin, Iis Rukmawati
Validation: Eni Margayani, Linda Purnamawati Suherman, Vina Septiani, Robby Ramdani
Visualization: -
Writing - original draft: Alfi Nurul Islamiyah, Morsalina Aksha, Iis Rukmawati
Writing - review & editing: Eni Margayani, Linda Purnamawati Suherman, Vina Septiani, Robby Ramdani

DATA AVAILABILITY

None.

CONFLICT OF INTEREST

The authors declare no conflicts of interest related to this study.

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