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Knowledge and Attitudes of Indonesian General Practitioners Towards the Isoniazid Preventive Therapy Program in Indonesia

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Objectives: The Indonesian Ministry of Health launched isoniazid preventive therapy (IPT) in 2016, with general practitioners (GPs) at the frontline of this program. However, the extent to which GPs have internalized this program remains uncertain. The aim of this study was to identify the knowledge and attitudes of GPs towards the IPT program in Indonesia.

Methods: This study used an online, self-administered questionnaire distributed via e-mail and social messaging services. A logistic regression model was employed to identify the explanatory variables influencing the level of knowledge and attitudes toward IPT among GPs in Indonesia. An empirical analysis was conducted separately for each response variable (knowledge and attitudes).

Results: Of the 418 respondents, 128 (30.6%) had a good knowledge of IPT. Working at a public hospital was the only variable associated with good knowledge, with an adjusted odds ratio (aOR) of 1.69 (95% confidence interval [CI], 1.02 to 2.81). Furthermore, 279 respondents (66.7%) had favorable attitudes toward IPT. In the adjusted logistic regression analysis, good knowledge (aOR, 0.55; 95% CI, 0.34 to 0.89), 1-5 years of work experience (aOR, 2.09; 95% CI, 1.21 to 3.60), and having experienced IPT training (aOR, 0.48; 95% CI, 0.25 to 0.93), were significantly associated with favorable attitudes.

Conclusions: In general, GPs in Indonesia had favorable attitudes toward IPT. However, their knowledge of IPT was limited. GPs are an essential element of the IPT program in the country, and therefore, adequate information dissemination to improve their understanding is critical for the long-term viability and quality of the IPT program in Indonesia.

Key words: Tuberculosis, Isoniazid, Latent tuberculosis, General practitioner

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INTRODUCTION

Tuberculosis (TB) is one of the top global public health burdens. In 2018, approximately 10 million people were infected, with more than 1.5 million deaths worldwide [1]. Asia and Africa contributed to nearly 44% of global TB cases [1,2]. During the past decades, the incidence and mortality have persistently declined due to the use of new anti-TB drug regimens, the

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increasing number of cases identified, and the improvement of anti-TB treatment coverage [3-6].

The declared end TB strategy at the 67th World Health Assembly has set an ambitious target of reducing TB incidence by 90% and TB mortality by 95% by 2035 [7,8]. A recent study estimated that almost a quarter of the world population was latently infected with *Mycobacterium tuberculosis* [9]. One of the vital strategies to achieve the end-TB goals is implementing TB preventive therapy. The World Health Organization (WHO) has stated that an essential intervention to prevent TB transmission is using isoniazid for 6 months to 12 months [10]. Therefore, implementing prevention therapy using isoniazid is vital to end TB, particularly in high-TB-burden countries [11].

A growing number of studies have reported the benefits of isoniazid preventive therapy (IPT) in preventing TB in human immunodeficiency virus (HIV)-positive or non-HIV-positive individuals [12,13]. A meta-analysis revealed a TB risk reduction of 35% in HIV-infected adults using IPT [10]. Another study reported that ITP reduced TB-associated deaths by 65% among adults living with HIV [14]. The effectiveness of IPT in non-HIV-infected persons has also been reported [15].

Indonesia is among the top 3 countries with the highest TB prevalence globally [16]. In concurrence with WHO guidelines, Indonesia started integrating the IPT strategy into the Indonesian National TB Program in 2016 [17]. The government has passed a law requiring all healthcare facilities to report TB cases [18]. Consequently, the Indonesian health ministry has implemented the directly observed treatment, short-course (DOTS) program in hospitals, considering DOTS to be a quality indicator of both public and private hospital service standards implementation [19]. More importantly, in Indonesia, general practitioners (GPs) are vital in the National TB Program, including IPT treatment [20]. However, there have been no reports on knowledge and attitudes toward IPT among GPs since the program began, although this information would be essential for evaluating the program. We sought to assess GPs' knowledge and attitudes towards IPT treatment in Indonesia. This paper is the first report on knowledge and attitudes towards IPT treatment among Indonesian GPs.

METHODS

Study Setting

This study was a cross-sectional survey using an online, self-administered questionnaire to assess the knowledge and attitudes of GPs towards IPT treatment. The survey was conducted from January to April 2021. GPs who had worked for at least the past year were eligible to be included in this survey.

Study Instrument and Study Variables

An expert panel designed the questionnaire (including the authors WW, HH, and AY) following the Indonesian guideline for IPT implementation and a previous study [21]. GPs' knowledge about IPT was assessed using 7 fixed-response multiple-choice questions. These questions covered IPT screening criteria, treatment dose, and contraindications for IPT. A score of 1 was given for a correct answer and 0 for an incorrect answer. Participants who had a score equal to and above 70% were considered to have a good knowledge of IPT, and those with a score below 70% were considered to have poor knowledge.

Five questions on 5-point Likert scales were used to assess attitudes, including: (1) whether IPT is effective in reducing TB incidence and death due to TB in people living with HIV/acquired immunodeficiency syndrome (PLWHA); (2) whether the respondent recommends children who are in close contact with active TB patients to take the IPT treatment; (3) whether the respondent recommends PLWHA who do not have active TB to take the IPT treatment; (4) whether the IPT program will increase resistance to isoniazid in the community; and (5) whether the respondent is reluctant to convey information about IPT to patients who ought to receive IPT due to uncertainty regarding whether the patient would comply with taking medication. The participants' attitudes were categorized as favorable or unfavorable using a 70% cut-off value.

Several explanatory variables that might affect knowledge and attitudes were collected and assessed, such as socio-demographics, data related to workplaces and work locations, and IPT-related training experience. For work-related data, respondents were asked about the type of health service facilities they worked in, the location of the workplace, and the length of the work period. Workplaces were divided into 5 types: government hospitals, private hospitals, community health centers (*puskesmas*), private clinics, and independent practice. The workplace locations were divided into the 5 major islands in Indonesia: Java and Bali, Sumatra, Sulawesi, Kalimantan, and Papua. Questions were also asked about IPT-related training experiences, such as collaborative TB-HIV training, TB training for children, and IPT treatment training.

Data Collection

Participation in this study was voluntary and anonymous. The participants were selected on a convenience sample basis. The survey link was distributed online via e-mail and WhatsApp, the most used messaging application in Indonesia, and written consent was obtained prior to data collection.

Statistical Analysis

A logistic regression model was employed to identify the explanatory variables influencing knowledge and attitudes toward IPT among GPs in Indonesia. A two-step analysis was carried out to model each response variable. In the first step, univariate logistic regression was conducted between the ex-

Table 1. Unadjusted and adjusted logistic regression analyses showing factors associated with good knowledge

Variables	n (%)	Good knowledge, n (%)	Unadjusted	*p*-value	Adjusted	*p*-value
Gender						
Men	154 (36.8)	56 (36.4)	1.00 (reference)	-	1.00 (reference)	-
Women	264 (63.2)	72 (27.3)	0.66 (0.43, 1.00)	0.052	0.69 (0.44, 1.08)	0.102
Age (y)						
18-24	14 (3.3)	6 (42.9)	1.88 (0.64, 5.59)	0.254	-	-
25-34	302 (72.2)	86 (28.5)	1.00 (reference)	-	-	-
35-44	74 (17.7)	26 (35.1)	1.36 (0.79, 2.33)	0.263	-	-
45-54	21 (5.0)	7 (33.3)	1.26 (0.49, 3.22)	0.635	-	-
>54	7 (1.7)	3 (42.9)	1.88 (0.41, 8.59)	0.413	-	-
Work experience (y)						
1-5	275 (65.8)	86 (31.3)	1.10 (0.67, 1.82)	0.714	-	-
6-10	99 (23.7)	29 (29.3)	1.00 (reference)	-	-	-
11-15	22 (5.3)	5 (22.7)	0.71 (0.24, 2.11)	0.537	-	-
16-20	11 (2.6)	3 (27.3)	0.91 (0.22, 3.66)	0.889	-	-
>20	11 (2.6)	5 (45.5)	2.01 (0.57, 7.12)	0.278	-	-
Type of workplace						
Public hospital	149 (35.6)	63 (42.3)	1.77 (1.08, 2.92)	0.024	1.69 (1.02, 2.81)	0.043
Private hospital	47 (11.2)	10 (21.3)	0.65 (0.30, 1.45)	0.295	0.62 (0.28, 1.39)	0.249
Puskesmas	130 (31.1)	38 (29.2)	1.00 (reference)	-	1.00 (reference)	-
Private clinic	66 (15.8)	12 (18.2)	0.54 (0.26, 1.12)	0.096	0.55 (0.26, 1.16)	0.115
Individual practice	26 (6.2)	5 (19.2)	0.58 (0.20, 1.64)	0.302	0.58 (0.20, 1.66)	0.307
Workplace current location						
Java and Bali	166 (39.7)	56 (33.7)	1.00 (reference)	-	-	-
Outside of Java and Bali	252 (60.3)	72 (28.6)	0.79 (0.52, 1.20)	0.263	-	-
Working area						
The capital city of the province	142 (34.0)	41 (28.9)	1.00 (reference)	-	-	-
Municipality	44 (10.5)	13 (29.5)	1.03 (0.49, 2.17)	0.932	-	-
Regency	232 (55.5)	74 (31.9)	1.15 (0.73, 1.82)	0.539	-	-
TB-HIV training experience						
Yes	136 (32.5)	50 (36.8)	1.00 (reference)	-	1.00 (reference)	-
No	282 (67.5)	78 (27.7)	0.66 (0.43, 1.02)	0.059	0.73 (0.44, 1.21)	0.220
Pediatric TB training experience						
Yes	130 (31.1)	43 (33.1)	1.00 (reference)	-	-	-
No	288 (68.9)	85 (29.5)	0.85 (0.54, 1.32)	0.465	-	-
IPT training experience						
Yes	109 (26.1)	40 (36.7)	1.00 (reference)	-	1.00 (reference)	-
No	309 (73.9)	88 (28.5)	0.69 (0.43, 1.09)	0.110	0.83 (0.48, 1.42)	0.494

Values are presented as odds ratio (95% confidence interval).
TB, tuberculosis; HIV, human immunodeficiency virus; IPT, isoniazid preventive therapy.

planatory and response variables. All explanatory variables with *p*-value ≤0.25 in the univariate analysis were included in the multivariate analysis in the second step. The crude odds ratio (OR) in univariate analyses and the adjusted OR (aOR) in multivariate analyses were calculated and considered significant if there was a *p*-value <0.05. All analyses were performed using SPSS version 20.0 (IBM Corp., Armonk, NY, USA).

Ethics Statement

The study was conducted in compliance with the principles of the Declaration of Helsinki. The protocol of the study was approved by the Institutional Review Board of the School of Medicine, Universitas Syiah Kuala, Banda Aceh (041/EA/FK-RSUDZA/2020), and the National Health Research and Development Ethics Commission (KEPPKN) of the Ministry of Health of the Republic of Indonesia (#1171012P).

RESULTS

A total of 484 GPs were contacted, of whom 418 agreed to participate, resulting in a 75% response rate. Table 1 lists the characteristics of the study participants. Among the total participants, 264 (63.2%) were women. Most of the respondents (72.2%) were 25-34 years old, and most respondents worked at public hospitals and *puskesmas* (35.6 and 31.1%, respectively). The majority of the respondents (60.3%) resided outside Java and Bali. More than 55% of the respondents worked in regency areas. Only small proportions of respondents reported having experienced training in TB-HIV collaboration (32.5%) or pediatric TB (31.1%),

IPT was well-known by 128 (30.6%) of the respondents. The frequency and duration of IPT had the highest rate of correctly answered questions, with 60% of the questions being correct. Contraindications of IPT administration had the lowest number of correctly answered questions, with 39% of respondents answering correctly. Around 50% of the responders answered that pregnancy is a contraindication for IPT (Figure 1). The adjusted logistic regression analysis showed that working in a public hospital was the sole predictor linked to good knowledge (aOR, 1.69; 95% confidence interval [CI], 1.02 to 2.81) (Table 1).

IPT was seen favorably by 279 of 418 respondents (66.7%). The adjusted logistic regression analysis showed that good knowledge, having 1-5 years of work experience, and having experienced IPT training were significantly associated with positive attitudes, with aORs of 0.55 (94% CI, 0.34 to 0.89), 2.09 (95% CI, 1.21 to 3.60), and 0.48 (95% CI, 0.25 to 0.93) (Table 2). IPT effectively reduces TB incidence and death in PLWHA, according to most respondents (72.8%). The majority of respondents also encouraged those eligible to receive IPT to do so. However, some respondents (19.2%) were concerned that IPT would lead to isoniazid resistance (Table 3).

DISCUSSION

The implementation of IPT, as reported in several studies, gives more benefit to children and PLWHA in preventing these groups at risk of getting TB and is recommended by the WHO [21]. The Indonesian Ministry of Health launched the IPT program in 2016. However, the extent to which this program has been internalized in daily practice at Indonesian health care centers remains uncertain. To the best of our knowledge, this is the first study to evaluate the knowledge and attitudes of

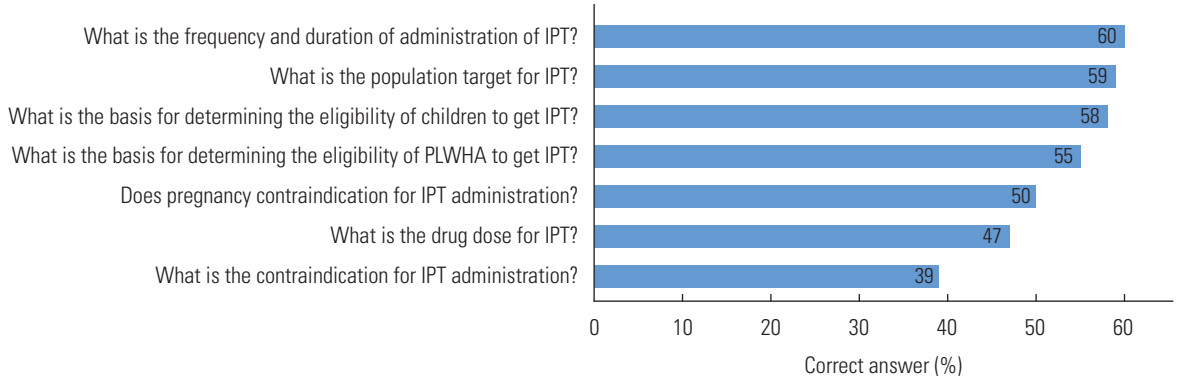

Figure 1. Percentages of correct responses for each question used to measure the knowledge of IPT among general practitioners in Indonesia (n=418). IPT, isoniazid preventive therapy; PLWHA, people living with human immunodeficiency virus/acquired immunodeficiency syndrome.

Table 2. Unadjusted and adjusted logistic regression analyses showing factors associated with favorable attitudes

Variables	n (%)	Favorable attitudes, n (%)	Unadjusted	*p*-value	Adjusted	*p*-value
Knowledge						
Good	128 (30.6)	97 (75.8)	1.00 (reference)	-	1.00 (reference)	-
Poor	290 (69.4)	182 (62.8)	0.54 (0.34, 0.86)	0.010	0.55 (0.34, 0.89)	0.016
Gender						
Men	154 (36.8)	104 (67.5)	1.00 (reference)	-	-	-
Women	264 (63.2)	175 (66.3)	0.95 (0.62, 1.44)	0.794	-	-
Age (y)						
18-24	14 (3.3)	9 (64.3)	0.97 (0.32, 2.98)	0.962	0.53 (0.16, 1.74)	0.294
25-34	302 (72.2)	196 (64.9)	1.00 (reference)	-	1.00 (reference)	-
35-44	74 (17.7)	52 (70.3)	1.28 (0.74, 2.22)	0.383	1.32 (0.66, 2.62)	0.429
45-54	21 (5.0)	17 (81.0)	2.30 (0.75, 7.01)	0.143	1.79 (0.34, 9.40)	0.491
>54	7 (1.7)	5 (71.4)	1.36 (0.26, 7.09)	0.721	1.08 (0.07, 17.55)	0.957
Work experience (y)						
1-5	275 (65.8)	187 (68.0)	1.50 (0.94, 2.41)	0.092	2.09 (1.21, 3.60)	0.009
6-10	99 (23.7)	58 (58.6)	1.00 (reference)	-	1.00 (reference)	-
11-15	22 (5.3)	16 (72.7)	1.89 (0.68, 5.23)	0.223	1.54 (0.50, 4.79)	0.453
16-20	11 (2.6)	10 (90.9)	7.07 (0.87, 57.39)	0.067	5.38 (0.41, 71.38)	0.202
>20	11 (2.6)	8 (72.7)	1.89 (0.47, 7.54)	0.370	1.34 (0.13, 14.22)	0.810
Type of workplace						
Public hospital	149 (35.6)	105 (70.5)	1.31 (0.79, 2.16)	0.297	-	-
Private hospital	47 (11.2)	29 (61.7)	0.88 (0.44, 1.76)	0.722	-	-
Puskesmas	130 (31.1)	84 (64.6)	1.00 (reference)	-	-	-
Private clinic	66 (15.8)	43 (65.2)	1.02 (0.55, 1.91)	0.941	-	-
Individual practice	26 (6.2)	18 (69.2)	1.23 (0.50, 3.05)	0.652	-	-
Workplace current location						
Java and Bali	166 (39.7)	114 (68.7)	1.00 (reference)	-	-	-
Outside of Java and Bali	252 (60.3)	165 (65.5)	0.87 (0.57, 1.31)	0.497	-	-
Working area						
The capital city of the province	142 (34.0)	92 (64.8)	1.00 (reference)	-	-	-
Municipality	44 (10.5)	29 (65.9)	1.05 (0.52, 2.14)	0.892	-	-
Regency	232 (55.5)	158 (68.1)	1.16 (0.75, 1.80)	0.509	-	-
TB-HIV training experience						
Yes	136 (32.5)	98 (72.1)	1.00 (reference)	-	1.00 (reference)	-
No	282 (67.5)	181 (64.2)	0.70 (0.45, 1.09)	0.110	1.09 (0.63, 1.89)	0.752
Pediatric TB training experience						
Yes	130 (31.1)	98 (75.4)	1.00 (reference)	-	1.00 (reference)	-
No	288 (68.9)	181 (62.8)	0.55 (0.35, 0.88)	0.012	0.70 (0.39, 1.27)	0.242
IPT training experience						
Yes	109 (26.1)	86 (78.9)	1.00 (reference)	-	1.00 (reference)	-
No	309 (73.9)	193 (62.5)	0.45 (0.27, 0.74)	0.002	0.48 (0.25, 0.93)	0.029

Values are presented as odds ratio (95% confidence interval).
TB, tuberculosis; HIV, human immunodeficiency virus; IPT, isoniazid preventive therapy.

Indonesian GPs toward IPT.

GPs are at the frontline in TB care in Indonesia, including IPT administration. However, this study revealed that the overall knowledge of IPT among Indonesian GPs was low. This result is different from a study in a district hospital in Gauteng Province, South Africa, which reported a high percentage of good knowledge among GPs. The difference may be because our study setting was broader and encompassed doctors from dif-

Table 3. General practitioners' attitudes towards IPT in Indonesia (n=418)

Variables	n (%)
IPT is effective in reducing TB incidence and death due to TB in PLWHA	
Strongly disagree	26 (6.2)
Disagree	8 (1.9)
Neutral	80 (19.1)
Agree	218 (52.2)
Strongly agree	86 (20.6)
I recommend that children who are in close contact with active TB patients to complete the IPT program	
Strongly disagree	12 (2.9)
Disagree	19 (4.5)
Neutral	88 (21.1)
Agree	195 (46.7)
Strongly agree	104 (24.9)
I recommend PLWHA who do not have active TB to complete the IPT program	
Strongly disagree	10 (2.4)
Disagree	36 (8.6)
Neutral	107 (25.6)
Agree	191 (45.7)
Strongly agree	74 (17.7)
The IPT program will increase resistance to isoniazid in the community	
Strongly disagree	26 (6.2)
Disagree	156 (37.3)
Neutral	156 (37.3)
Agree	71 (17.0)
Strongly agree	9 (2.2)
I am reluctant to convey the information about IPT to patients who deserve it because I am worried that the patient will not comply with taking medication	
Strongly disagree	68 (16.3)
Disagree	213 (51.0)
Neutral	93 (22.2)
Agree	38 (9.1)
Strongly agree	6 (1.4)

IPT, isoniazid preventive therapy; TB, tuberculosis; PLWHA, people living with human immunodeficiency virus/acquired immunodeficiency syndrome.

ferent places and types of healthcare facilities. By contrast, the study in South Africa was conducted at only 1 provincial hospital only [22].

Our study also revealed that only working at a public hospital variable was associated with good knowledge of IPT. A reason for this may be that doctors working at public hospitals have better access to information regarding IPT programs than those working at other healthcare facilities since public hospitals are usually located in the center of the city or regency and have widely implemented TB care. Additionally, even though Indonesia has adopted the public-private mix (PPM) strategy in its national TB program, our results showed that the level of knowledge among GPs who worked at private hospitals was low. This result is concerning and suggests that the PPM strategy should be strengthened, especially in IPT. Other variables such as gender, age, work experience, location, working area, and IPT-related training were not associated with knowledge. We noted that training experience did not affect the respondents' knowledge level, but instead impacted their attitudes. These results contrast with studies in South Africa and Brazil, where training improved the knowledge of IPT [22,23]. This result suggests that the national IPT program cannot rely solely on IPT training to improve GPs' knowledge. There must be massive and continued dissemination of IPT-related information for healthcare workers, especially GPs.

This study demonstrated that the knowledge of IPT among GPs who worked at *puskesmas* was low. This might be explained by the limited dissemination of the IPT program at the district levels. Another possible explanation is that the program is considered newly established and integrated into Indonesian TB care. As a result, most respondents have not yet become knowledgeable about IPT. *Puskesmas* have long been the frontline healthcare facilities for TB care in the Indonesian health system [24]. The services provided in *puskesmas* include diagnosis, drug-sensitive TB treatment, contact tracing, and IPT. Considering that those facilities are available in almost all districts across Indonesia, up-to-date knowledge of TB-related programs, especially IPT, among doctors in *puskesmas* is vital to reducing the TB burden [25]. Thus, failure to implement IPT in the community might bring significant consequences that hamper the National TB program [26].

This study revealed that most respondents had favorable attitudes towards IPT. Most respondents believed that IPT effectively reduces TB incidents and mortality in PWLHA and would recommend PWLHA who do not have TB and children under 5 years who are contact with TB patients to complete IPT. Even though participants' attitudes toward IPT tended to be positive, a high percentage of respondents remained "neutral" in the attitude-related questions. Almost a quarter of respondents answered "neutral" on the recommendation of IPT to children in close contact with active TB patients and PLWHA who do not have active TB. Thirty-seven percent of respondents responded "neutral" to the question asking whether the

IPT program will increase resistance to isoniazid. High percentages of neutral answers were found in other attitude-related questions. These findings are concerning and suggest that GPs may have a lack of confidence in implementing the IPT program. Another possible explanation is that some respondents might never encounter TB patients in their workplaces.

This study also demonstrated that 19,2% of respondents were concerned that IPT implementation might cause drug resistance in the future. The same results were also reported in a study in Ethiopia [27]. Fear of drug resistance development might be a severe obstacle for GPs to implement IPT, although current evidence shows no correlation between IPT implementation and the development of isoniazid resistance in the community [28].

This study encompassed GPs from multiple locations and workplace types, with different lengths of work experience, representing the heterogeneity of the population. However, since the questionnaire was disseminated through the internet and social messaging accounts, there is a possibility that some respondents were GPs who were not responsible for TB care or never had experienced treating TB patients.

In conclusion, the surveyed GPs had favorable attitudes towards IPT in general. However, their knowledge about IPT was inadequate. Some knowledge gaps were found, including eligibility criteria, drug dose, and contraindications for IPT. The study also revealed that some participants were concerned about the development of isoniazid resistance following the IPT program in the community. GPs are at the forefront of TB care, including the IPT program. Adequate information dissemination to improve GPs' understanding is essential to ensure the sustainability and the quality of the IPT program in Indonesia.

CONFLICT OF INTEREST

The authors have no conflicts of interest associated with the material presented in this paper.

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AUTHOR CONTRIBUTIONS

Conceptualization: Winardi W, Harapan H. Data curation: Anwar S. Formal analysis: Winardi W, Yanifitri DB, Arliny Y, Yufika A, Zulfikar T. Funding acquisition: None. Methodology: Winardi W, Nalapraya WY, Fadhil I, Wahyuni MSH. Wibowo A. Project administration: Fadhil I. Visualization: Anwar S, Wibowo A. Writing – original draft: Winardi W, Harapan H, Yufika A, Sarifuddin S, Anwar S, Nalapraya WY. Writing – review & editing: Winardi W, Harapan H, Yufika A,Yanifitri DB, Zulfikar T, Arliny Y, Wibowo A, Wahyuni MSH, Fadhil I.

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