# Spatial study of the implementation of ivermectin, diethylcarbamazine citrate, and albendazole in an urban area

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## **ABSTRACT**

Studies on lymphatic filariasis (LF) in Indonesia have mostly focused on the disease determinants with limited focus on spatial-based and the determinants of implementing ivermectin, diethylcarbamazine citrate, and albendazole (IDA). This study aimed to identify the causes of program failure. A cross-sectional survey was conducted from November to December 2022 in nine urban villages with high endemic records and one sentinel village in Pekalongan City, Central Java, Indonesia. The analysis using Quantum Geographical Information System (QGIS) and Pearson correlation. Slum settlements were linked to the presence of open sewers (p=0.000; r=0.974) and overcrowding (p=0.033; r=0.672), while the first round of IDA medication adherence correlated with knowledge of medication (p=0.054; r=-0.623) and willingness to take the medication in the second round (p=0.051, r=0.603). Adverse effects of the treatment are strongly correlated with drug boredom from taking medication (p=0.003; r=0.828) and assistance from health workers (p=0.027; r=0.791). We identified gaps in slum settlements, open sewers, overcrowding, and medication adherence, including low knowledge of medication, unwillingness to take second-round medication, adverse effects, and boredom with taking medication. We recommend effective strategies by engaging health education between health workers, local leaders, and private sectors as key to ensuring elimination program.

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#### 1. INTRODUCTION

Lymphatic filariasis (LF) is one of the neglected tropical diseases (NTDs), which presents chronic disabling and disfiguring pathologies with occasional painful attacks on affected persons [1]. LF is a mosquito-borne infection caused by filarial nematodes: Wuchereria bancrofti, Brugia timori, and Brugia malayi [2]. The disease is transmitted by various mosquito species from several genera including Culex, Anopheles, Aedes, Mansonia, and Armigeres [3]. Indonesia is endemic for many other neglected tropical diseases and an estimated 110 million Indonesians are believed to suffer from at least one NTD, including LF [4]. Currently, the mainstay elimination strategies, which include mass drug administration (MDA) and

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vector control, have significantly interrupted LF transmission in many previously including MDA and vector control, have significantly interrupted LF transmission in many endemic settings [5]. Indonesia is a country that has filariasis endemic areas in most of its territory and follows the MDA program that has been launched by WHO for countries that have microfilariasis rate criteria of >1% [6].

Central Java Province is an area in Indonesia where LF is endemic. Mass filariasis treatment has been implemented for five consecutive years to combat the disease. One of the targets for this treatment is Pekalongan City, where the diethylcarbamazine citrate and albendazole (DA) regiments have been used from 2011 to 2015, with treatment coverage reaching 76.3% [7]. Despite this, the results of the pre-transmission assessment survey (Pre-TAS) in 2016 showed that there were still positive filariasis cases with a microfilaria rate of over 1%. As a result, WHO extended mass treatment with DA in the Pekalongan City area for two consecutive years (in 2017 and 2018) and achieved treatment coverage of 86% in 2017 and 88% in 2018 [3]. However, a re-PreTAS survey conducted in 11 Spot Check villages using FTS still found a microfilaria rate of over 1% [3]. These results encourage the WHO to extend the LF medication into triple-drug therapy, including ivermectin, diethylcarbamazine citrate, and albendazole (IDA).

It has been demonstrated through various studies that the success of MDA implementation can be impacted by issues with drug acceptability. Factors such as the treatment's importance, intrusiveness, characteristics, effectiveness, side effects, and alignment with an individual's values or beliefs are all believed to contribute to their evaluation of its acceptability [8]–[10]. Additionally, the success of MDA in a particular area has been linked to MDA coverage and compliance, as well as perceptions about the treatment and disease [11]. A prior study specifically noted that willingness to consume IDA medication for the second round increased IDA drug-taking behavior in Pekalongan City (PR=5.32; 1.520-18.656). Furthermore, local health workers' assistance (PR=2.690; 1.681-4.306) and knowledge about the disease and treatment (PR=1.030; 0.943-1.125) significantly correlated with the behavior of taking the first round of IDA medication [12]. It is also important to consider other factors that may contribute to filariasis cases, beyond simply the implementation of IDA. Environmental and behavioral factors, such as the ecological requirements of the main mosquito species and local characteristics, have been found to influence transmission [13]. Previous research has identified a number of these factors, including the annual precipitation, wettest quarter, and temperature positively correlated with the LF morbidity prevalence [14].

In 2021, the city of Pekalongan implemented administering triple-drug therapy IDA to the masses. However, the first treatment coverage survey reported less than 65% coverage [15]. This report warns of the urgency of evaluation during the first round of triple therapy to possibly be implemented for the better result of second-round medication. Thus, it's crucial to develop a local understanding of the environmental and behavioral factors that drive transmission which may differ by geography. This will enable the assessment of correlation across different urban villages and identify factors that must be considered based on the site. This paper presents the outcome of our previous study, which compared the correlation between determinant variables while describing the factors of both the disease and medication using spatial-based data. The study aimed to pinpoint potential factors linked to MDA failure by examining compliance with IDA triple-drug therapy, environmental factors, and medication behaviors across urban villages. We also aimed to uncover patterns in one endemic village and nine high-endemic record villages.

## 2. METHOD

#### 2.1. Study design and site

This study was a cross-sectional community-based survey conducted in 10 urban villages with criteria of having a history of high endemic areas: nine villages and one sentinel village with a microfilaria rate of >1% [16] between November and December 2022. The study was conducted after the first round of IDA medication was implemented. All the selected study locations were in Pekalongan City, Central Java, Indonesia, which received an extension of the triple therapy of filariasis mass treatment program (ivermectin, diethylcarbamazine citrate, albendazole). These urban villages include Bandengan Village and Padukuhan Kraton Village (North Pekalongan District), Pasirkratonkramat Village, Tirto Village, Pringrejo Village (West Pekalongan District), Banyurip Village, Buaran Kradenan, Jenggot, Kuripan Yosorejo, Kuripan Kertoharjo (South Pekalongan District) [16].

# 2.2. Population and sample size determination

The scope of our research is focused on the residents, aged between 18 and 65, who are registered in 10 villages known for a history of high endemic filariasis rates in Pekalongan City and live near residents who have a history of positive cases of filariasis. These sub-districts comprise nine villages that have a high endemic history and one sentinel village where IDA antifilariae drugs are distributed. The sample size of 871 participants was determined using the probability proportional to Size method, which possible to select a

representative sample of a population. In this case, the sample size was determined based on the population size of each village. Additionally, 40 clusters were selected through simple random sampling. The cluster in question is the ward level of the total ten urban villages. To select respondents, we visited households in each ward cluster using simple random sampling, with a minimum of 21 respondents per ward. This method of selecting respondents ensures that our sample is representative of the population of interest and our research results are reliable and valid.

#### 2.3. Variable assessment

This study investigated the correlation between several determinants of medication adherence in the first round of filariasis triple therapy, environmental, behavioral determinants, and basic knowledge. Demographic characteristics consisting of age, gender, and address of the participant were assessed. We identified determinants of first-round IDA, such as taking the medication, boredom from taking medication, adverse effects, and getting assistance from health workers during the medication. Basic knowledge was collected by asking whether participants knew the filariasis and IDA. Environmental determinants include open sewers, slum neighborhoods, and occupancy density collected through observation. The behavior of hanging clothes and willingness to take the second round of IDA were also collected.

#### 2.4. Data collection

A structured questionnaire form was developed in Bahasa, it was asked into the Javanese dialect used in the subdivision for interviewing urban village residents. The questionnaire was validated in the same subdivision area of the study. Interviewers helped respondents to appropriately understand the meanings of questions according to the guidelines for interviewers. Interviews were conducted by 6 trained interviewers. Mapping was carried out to see the distribution of people who taking triple therapy (IDA medications), boredom state from taking IDA, and adverse effects, as well as environmental and behavioral determinants based on the area of 10 urban villages. Respondents selected in the household and being interviewed are then mapped based on these variables using the global positioning system (GPS), to get the household coordinates.

#### 2.5. Data analysis

Paper-based questionnaire data is transferred into Microsoft Excel and then entered into the SPPS 20 program to analyze variables univariately, namely respondent characteristics. Distribution data for environmental conditions and adherence to taking IDA anti-filarial drugs were mapped using the quantum geographical information system (QGIS) version 3.28.3. To analyze the correlation relationship of determinants related to adherence to taking the first round of IDA drugs and the correlation between variables, Pearson correlation analysis was used with the unit of analysis being mapped village.

## 2.6. Ethical clearance

This study received ethical approval from the Ethics Committee Faculty of Public Health, Universitas Indonesia (No. Ket- 41/UN2. F10. D11/PPM.00.02/2023). Written informed consent was obtained from all respondents interviewed in this study. No personal identifiers were collected, and the data were restricted to study personnel.

#### 3. RESULTS AND DISCUSSION

Table 1 shows the survey included 871 individuals from 10 selected urban villages in Pekalongan, Central Java, Indonesia. The majority of participants were females (71.9%) and less than or equal to 43 years old (52.5%). Jenggot village had the largest proportional sample (17.7%). The trend of distribution of filariasis determinants was that the risk category of each variable did not exceed 40%, with the lowest being participants who hung clothes no more than 10% of the time. The proportion of participants who did not take IDA medication in the second round (1.6%) was lower than in the first round (3.25%). During medication, 13.9% and 20.3% of participants experienced boredom and side effects, respectively. Only 4.5% of participants claimed to have not received any assistance from local health workers. In terms of basic knowledge of filariasis and medication, 34.1% and 7.3% of participants still did not have a complete understanding.

Figure 1 shows a map of the spatial distribution of environmental factors in Pekalongan City. The map provided displays a breakdown of colors and points for each village. Blue hues indicate higher proportions of factors such as open sewers, occupancy density, and slum neighborhoods. The urban villages with the most prevalent open sewers or puddles near residents' homes are Bandengan, Padukuhan Kraton, and PasirKratonKramat as shown in Figure 1(a). Figure 1(b) shows that PasirKratonKramat, Bandengan, and Padukuhan Kraton have the highest residential densities. PasirKratonKramat, Padukuhan Kraton, and

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Bandengan have the highest proportion of slum environments, while Buaran Kradenan Village has the lowest as shown in Figure 1(c).

Table 1. Demographic characteristics, determinants of filariasis, and behavior of taking IDA medication

among the study participants								
Characteristics	Frequency (N=871)	%						
Demographic characteristics								
Age (years)	457	50.5						
≤ 43	457	52.5						
> 43	414	47.5						
Sex								
Male	245	28.1						
Female	626	71.9						
Urban villages								
Bandengan	61	7.0						
Padukuhan Kraton	63	7.2						
Pasirkratonkramat	79	9.1						
Tirto	67	7.7						
Pringrejo	80	9.2						
Jenggot	154	17.7						
Kuripan Kertoharjo	89	10.2						
Kuripan Yosorejo	103	11.8						
Banyurip	110	12.6						
Buaran Kradenan	65	7.5						
Environmental factors								
Open sewer								
Yes	286	32.8						
No	585	67.2						
Occupancy density								
Yes	332	38.1						
No	539	61.9						
Slum neighborhood								
Yes	290	33.3						
No	581	66.7						
Behavioral factors								
Hanging-clothes behavior								
Yes	76	8.7						
No	795	91.3						
Willingness to take the second round of triple therapy								
No	14	1.6						
Yes	857	98.4						
The first round of triple therapy								
Taking the medication								
No	28	3.2						
Yes	843	96.8						
Boredom state from taking medication								
Yes	121	13.9						
No	750	86.1						
Adverse effect								
Yes	177	20.3						
No	694	79.7						
Medication assistance by health workers								
No	39	4.5						
Yes	832	95.5						
Basic knowledge								
Filariasis								
No	297	34.1						
Yes	574	65.9						
Filariasis medication								
No	64	7.3						
Yes	807	92.7						

Figure 2 is a descriptive spatial of IDA medication determinants. Figures 2 (a)-(c), we see a map displaying the spatial distribution of possible factors influencing the decision to take triple therapy in the first round. The blue color of each urban village indicates the proportion of risk categories in all variables, with darker shades indicating a higher risk. Kuripan Yosorejo had the greatest proportion of respondents not taking IDA drugs in the first rounds, while Padukuhan Kraton, Buaran Kradenan, Pringrejo, and Pedukuhan Kraton Village had 100% population took the medication in the first rounds. Kuripan Kertoharjo and Kuripan

Yosorejo had the highest proportion of respondents recognizing the side effects of drugs, while all respondents living in Buaran, Kradenan, and Pringrejo urban villages did not have the state boredom of taking antifilarial drugs.

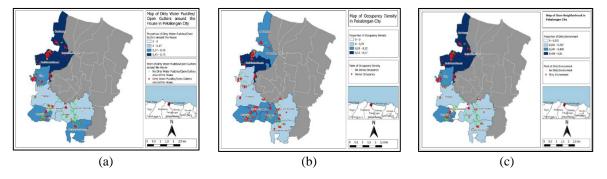


Figure 1. Spatial descriptive of environmental filariasis determinants: (a) open sewers, (b) occupancy density, and (c) slum neighborhood

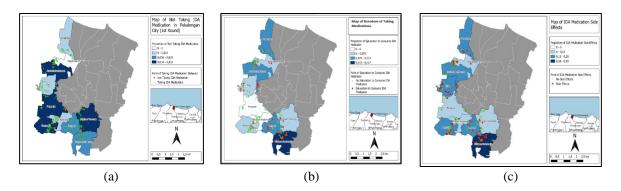


Figure 2. Descriptive spatial of IDA medication determinants: (a) taking the first round of IDA medication, (b) drug-state boredom, and (d) adverse events

Figure 3 presents the behavioral factors of study participants. Figure 3(a) shows the distribution of hanging-clothes behavior while willingness to take a second round of medication is described in Figure 3(b). Kuripan Kertoharjo, PasirKratonKramat, and Pringrejo have the highest proportions of respondents with the behavior of hanging clothes, with Buaran Kradenan having none. The greatest proportion of respondents have no intention to take medication for the second round was Kuripan Yosorejo.

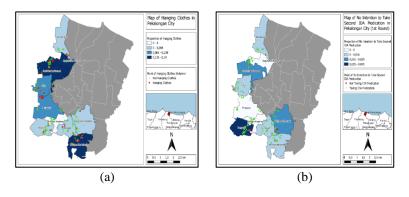


Figure 3. Distribution of behavioral factors: (a) hanging-clothes behavior and (b) willingness to take a second round of medication

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The result of basic knowledge of filariasis and the medications among 10 villages can be seen in Figure 4. Kuripan Yosorejo and Tirto Villages had the most and least findings related to respondents who did not know about filariasis Figure 4(a). Bandengan Village had the highest proportion of participants who did not know about IDA treatment, while Banyurip and Tirto Villages had the largest proportion of respondents with knowledge of IDA treatment Figure 4(b).

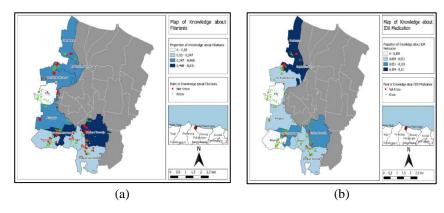


Figure 4. Map of knowledge of filariasis: (a) Basic knowledge regarding filariasis and (b) the medications

Table 2 presents the results of the correlation analysis between variables based on the analysis unit of wards in 10 mapped neighborhoods. The analysis revealed robust positive correlations between the behavior of taking IDA filariasis drugs in the first versus the willingness for the second round, the adverse effect of the IDA versus boredom of taking medications, the adverse effect versus medication assistance from health workers, and between medication boredom versus medication assistance from health workers. Additionally, strong positive correlations were identified in the factors of filariasis, such as the presence of sewers versus occupancy density, the presence of sewers versus slum neighborhoods, and occupancy density versus slum neighborhoods. However, respondents' knowledge of filariasis medication showed a negative correlation with medication adherence in the first round.

Table 2. Aggregate analysis of the correlation between factors of filariasis and behavior of taking IDA medication in ten urban villages

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Variable	Value	1st IDA	Willingness	Boredom	Adverse			Knowledge	Open	Occupancy	Slum	Hanging
			to take 2nd	state of	effects	assistance	of filariasis	of	sewers	density	neighborhood	clothes
			IDA	taking				medication				
				medication								
1st IDA	r coeff.	-	0.603*	-0.022	0.016	0.199	0.137	-0.623	-0.319	0.046	-0.135	-0.066
	p-value	-	0.051	0.952	0.966	0.582	0.706	0.054	0.370	0.899	0.711	0.856
Willingness to take 2 <sup>nd</sup> IDA	r coeff.	0.630*	-	0.065	0.194	0.307	-0.110	-0.393	0.076	0.207	0.229	-0.280
_	p-value	0.051	-	0.858	0.591	0.293	0.763	0.262	0.834	0.567	0.524	0.434
Boredom state of taking	r coeff.	-0.022	0.065	-	0.875*	0.691*	-0.283	-0.130	0.140	-0.004	0.195	0.356
medication												
	p-value	0.952	0.858	-	0.001	0.027	0.429	0.721	0.699	0.991	0.589	0.313
Adverse effects	r coeff.	0.016	0.194	0.875*	-	0.828*	-0.571	-0.389	0.188	-0.174	0.227	0.400
	p-value	0.966	0.591	0.001	-	0.003	0.085	0.267	0.604	0.630	0.528	0.252
Medication assistance	r coeff.	0.199	0.370	0.691*	0.828*	-	-0.386	-0.314	0.110	-0.229	0.181	0.169
	p-value	0.582	0.293	0.027	0.003	-	0.270	0.376	0.762	0.525	0.616	0.640
Knowledge of	r coeff.	0.137	-0.110	-0.283	-0.571	-0.386	-	0.522	-0.131	0.431	-0.155	-0.319
filariasis												
	p-value	0.706	0.763	0.429	0.085	0.270	-	0.121	0.717	0.213	0.670	0.368
Knowledge of medication	r coeff.	-	-0.392	-0.130	-0.389	-0.314	0.522	-	0.431	0.465	0.305	-0.039
		0.623**										
	p-value	0.054	0.262	0.721	0.267	0.376	0.121	-	0.213	0.175	0.392	0.916
Open sewers	r coeff.	-0.319	0.076	0.140	0.188	0.110	-0.131	0.431	-	0.646*	0.974*	0.549
	p-value	0.370	0.834	0.699	0.604	0.762	0.717	0.213	-	0.044	0.000	0.100
Occupancy density	r coeff.	0.046	0.207	-0.004	-0.174	-0.229	0.431	0.465	0.646*	-	0.672*	0.079
	p-value	0.899	0.567	0.991	0.630	0.525	0.213	0.175	0.044	-	0.033	0.829
Slum neighborhood	r coeff.	-0.135	0.229	0.195	0.227	0.181	-0.155	0.305	0.974*	0.672*	-	0.546
	p-value	0.711	0.524	0.589	0.528	0.616	0.670	0.392	0.000	0.033	-	0.103
Hanging clothes	r coeff.	-0.066	-0.280	0.858	0.591	0.293	0.763	0.262	0.549	0.079	0.546	-
	p-value	0.856	0.434	0.356	0.400	0.169	-0.319	-0.039	0.100	0.829	0.103	-

Note: \* strong correlation; \*\* significantly correlated

In the context of eliminating LF, we examined the spatial description of the sentinel village, and nine villages have a history of high endemic. We chose the areas of high infection prevalence of LF and still applied mass drug distribution for two consecutive years (2021 and 2022). Such a setting was also chosen to highlight the relationship between determinant variables between communities, which may differ between villages even though they are geographically located on each other's borders. Understanding the correlation between those potential determinants may make it feasible to use action-based evidence to define similar factors trending in the ongoing transmission of filariasis across the villages. Therefore, it would prove a valuable policy for the filariasis elimination program in those areas. We aim to develop a description and analysis of the correlated factors causing the disease and medication compliance.

#### 3.1. Environmental and behavioral factors

Various environmental and climate factors are suggested to be predictors of the distribution of mosquitoes that transmit filariasis larvae, including the culex mosquito, anopheles, and aedes [17]. This study aims to identify environmental and behavioral factors that may contribute to the spread of filariasis, such as the presence of dirty puddles, open gutters, and slum neighborhoods. The study also measured household occupancy density and behavior, such as hanging clothes, to assess individual exposure.

This study found that the highest presence of open sewers and dirty puddles was found in Bandengan and Pasirkratonkramat villages, which are among the nine villages with a high endemic history and receive mass treatment regiment IDA. These conditions provide a breeding ground for *Culex quinquefasciatus* mosquitoes. A previous field survey reported that this species was the filariasis vector in Pekalongan City [18], which thrives in dirty water and lays its eggs in various locations, including household containers, gutters, tires, ponds, puddles, and creeks [17], [19]. This species of mosquito tends to thrive during the wet season and can be found around the home and yard [20].

As part of the study, an evaluation was conducted to assess the state of each urban village with regard to slum conditions. The results showed that Pasirkratonkramat and Bandengan villages had the largest percentage of slum neighborhoods compared to the other villages. According to previous research, slum environments are the primary contributor to filariasis in most participants (76.8%) [21]. This is because vectors, particularly *C. quinquefasciatus*, breed and thrive excessively in congested areas with inadequate sanitation, sewage, and drainage systems [22]. Therefore, a densely populated slum area with open drains, in which *C. quinquefasciatus* breeds prolifically, can lead to a higher incidence of the disease.

At the household level, the number of people per household room, called occupancy density, has been acknowledged as a risk of LF infection as it favors transmission and may influx new infections. In this study, Pasirkratonkramat village has the highest proportion of residential density, compared to nine other sub-districts Figure 1(c). This high residential density can increase the density of indoor *Culex* mosquitoes, as has been shown in previous entomological studies [23]. It is therefore hypothesized that crowding may lead to a greater density of indoor *Culex* mosquitoes, which can increase the risk of transmission among household members (OR 1.59; 1.31–1.92) [9].

Pasirkratonkramat and Kuripan Kertoharjo stand out with the highest percentage of clothes-hanging behavior, which can pose a risk for filariasis contraction due to the potential for mosquitoes to rest on clothing [24]. Mosquitoes are attracted to sweat or perfume on hanging clothes, and although bed nets, floors, and furniture remain popular resting places, a significant number of mosquitoes were found on hanging clothes. To prevent indoor mosquito resting, it is crucial to implement a behavior change communication program that educates people about the dangers of hanging clothes as a potential mosquito resting place.

#### **3.2.** Factors of medication adherence

A recent study conducted by IDA on medication-taking behavior revealed that in the first rounds, Kuripan Yosorejo had the highest percentage of non-medication takers among the ten villages studied. This is particularly noteworthy as Kuripan Yosorejo is not a sentinel area, but rather part of a village with a high endemic history. While the consumption of IDA among residents in the sub-district has been low overall, state boredom may be a contributing factor, as mass drugs have been distributed since 2011 and the regimen was extended for two consecutive years (2021-2022) [25]. Interestingly, Kuripan Kertoharjo Village had the highest medication-state boredom rate, while Kuripan Yosorejo ranks fifth among the studied villages.

It has been noted that there is a similarity between adherence to medication during the initial round and the inclination to take part in the subsequent round. Notably, Kuripan Yosorejo, which demonstrated the highest rate of non-adherence in the first round, also exhibited the greatest proportion of reluctance to take medication in the following round. This suggests that previous non-adherence to medication can influence the decision to abstain from participation in the next round of medication. Insufficient information and understanding of the medication may contribute to making inadequate decisions [26], as Kuripan Yosorejo identified that most residents did not know about filariasis.

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Pekalongan is an urban area with people who tend not to trust antifilarial medications, because of the side effects of some residents who have taken antifilarial with the DA regimen before the extension of MDA with the triple therapy using IDA regiments [27]. Reports of side effects from previous treatments encourage residents not to want to take drugs with the IDA regimen [28]. Based on the mapping of the village area that has the highest proportion of side effects from anti-filarial drugs, namely Kuripan Yosorejo Village, which is the village with the highest proportion of not taking IDA drugs in Pekalongan in two distribution rounds. A similar trend was found in Indian communities, where 37.5% of individuals refused to consume drugs due to fear of side effects [29]. Those who received medicines sometimes felt symptoms like nausea, and dizziness, over the next few hours. Observing side effects among family members and neighbors, few participants even refused to receive the pills.

While several obstacles to MDA compliance have been identified, our research has revealed further barriers linked to people's comprehension of the disease and the MDA. Our investigation indicates that the greatest number of individuals who are not informed about filariasis can be found in Kuripan Yosorejo, which coincidentally has the lowest rate of medication compliance. Conversely, Bandengan has the lowest awareness of medication, but it's challenging to gauge the extent of their knowledge since our data collection was restricted to ascertaining whether individuals were aware of filariasis and its treatment without delving deeper.

## 3.3. Correlation between environmental, behavioral, and adherence to taking triple therapy

The present study found that two factors are strongly linked to the likelihood of taking the first round of IDA antifilarial drugs. These factors are familiarity with IDA treatment (p=0.054, r=-0.623) and willingness to take the medication in the second round (p=0.051, r=0.603). The latter factor is particularly important, as it has a positive correlation with drug adherence behavior in the first round. This link can be explained by the theory of planned behavior, which posits that attitudes, social norms, and perceived control all play a role in determining behavior [30], [31]. By fostering a positive attitude towards taking IDA drugs and empowering individuals to feel in control of their health decisions, this theory can help encourage interest and participation in the treatment.

A study conducted in Tanzania has shown that one of the key factors that encourage compliance with the MDA program and increase its coverage is having prior knowledge of the program [32]. Conversely, individuals unaware of the MDA or (LF) elimination programs tend to be non-compliant. While knowledge is important, this study demonstrated that it negatively correlated with medication adherence due to uneven socialization regarding the treatment of filariasis. Knowledge mapping results revealed that there are still areas where there is no knowledge at all. Across various studies, knowledge associated with compliance was primarily related to three specific topics: LF transmission, the knowledge that MDA protects against LF, and knowledge of lymphedema management techniques. Misconceptions and misinformation about the treatment can hinder people's uptake of MDA medications. For example, the community in ogun believed that prayer or home remedies are better than getting medical treatment [8].

The fear of negative outcomes after the MDA has led to many individuals not complying with the treatment. Numerous studies have attributed the reluctance of some community members to participate in MDA to the potential side effects of IDA filariasis drugs [33], [34]. This study has demonstrated that the most common adverse effects of the treatment are headache, dizziness, abdominal pain, fever, nausea, and fatigue [34]. As a result, it's crucial for health workers to adequately educate communities about the potential side effects of the drugs to ensure successful MDA implementation. Health workers also have a significant role in socializing the community about side effects to prevent boredom. In some cases, the lack of correct and comprehensive information about negative outcomes led to detrimental consequences in the success of the MDA. Participants have reported that they weren't accompanied by health workers when taking IDA filariasis drugs, which made it possible for people not to swallow the pills. The recognition of side effects of taking filariasis drugs with the previous IDA regimen, such as dizziness and nausea, made people hesitant to retake filariasis drugs with the IDA regimen. The absence of information about MDA and its potential negative effects led to a loss of trust in the community, resulting in the postponement of MDA for three years [35]. This underscores the significance of the support provided by health workers and the need for advanced knowledge to address the possibility of negative outcomes.

Research has established a correlation between the presence of sewers (p=0.000; r=0.974) and high occupancy density (p=0.033; r=0.672) with the emergence of slum environments. Slums typically arise from rapid population growth and urban poverty, resulting in limited access to proper sanitation [36]. Studies show that environment-based diseases are linked to various socioeconomic factors, including population density, water, and the density of squatter/slum dwellers [37], [38]. In the case of Pekalongan, the slum settlement will be related to its potential as a breeding ground for *C. quenquefasciatus* mosquitoes which are identified as filariasis vectors in Pekalongan. This is exacerbated by overcrowding in one house which causes easier transmission of filariasis.

Our findings indicate that certain areas require additional attention to their environmental conditions. For instance, PasirKratonKramat, Padukuhan Kraton, and Bandengan have the highest percentage of slum settlements, which raises the risk of LF transmission in those regions. Therefore, it is essential to implement environmental interventions to eradicate breeding sites of filariasis mosquitoes, particularly *C. quenquefasciatus*. Additionally, education on improving environmental hygiene, like proper waste disposal to avoid accumulation, keeping open gutters clean, and using mosquito repellent or nets when sleeping to prevent mosquito bites, should be provided. By leveraging the distribution mapping, the local government can prioritize environmental policies in the three villages. Our study's evidence indicates that the slum environment in the ten target villages is related to open sewers and overcrowding. This suggests that repeated exposure to unhygienic environments can lead to an increase in the breeding of filariasis-transmitting mosquitoes.

### 4. CONCLUSION

This study highlights the gaps in environmental conditions and medication adherence for IDA treatment, including the factors associated with them. The findings indicate that slum settlements in 10 villages are linked to the presence of open sewers and overcrowding, while medication adherence is influenced by adverse events, drug boredom, and assistance from health workers. Mapping has revealed that many people are still not adhering to IDA drug consumption and live in poor environments.

We have observed that some participants find taking medications for IDA boring and are concerned about adverse effects. To address this, we support the development of new drugs with fewer adverse effects that could improve the success of the filariasis elimination program MDA. It is also essential to promote collaboration among regional healthcare facilities, government bodies, and other relevant parties to enhance the effectiveness of healthcare professionals and raise awareness of the importance of treating IDA filariasis. Health officers and local health cadres with knowledge of the local environmental conditions can play a crucial role in this effort. In future research, integrating location-based analysis could provide valuable insights into the geographical factors associated with the illness and its treatment.

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## REFERENCES

- [1] E. V. S. Kwarteng *et al.*, "Spatial variation in lymphatic filariasis risk factors of hotspot zones in Ghana," *BMC Public Health*, vol. 21, no. 1, p. 230, Dec. 2021, doi: 10.1186/s12889-021-10234-9.
- [2] S. Specht, T. K. Suma, B. Pedrique, and A. Hoerauf, "Elimination of lymphatic filariasis in South East Asia," The BMJ, vol. 364, p. k5198, Jan. 2019, doi: 10.1136/bmj.k5198.
- [3] Indonesian Ministry of Health, "Annual performance report in 2019: Directorate for prevention and control of vector-borne and zoonotic diseases," pp. 1–83, 2020, [Online]. Available: https://e-renggar.kemkes.go.id/file\_performance/1-465842-4tahunan-052.pdf
- [4] WHO, "Indonesia firmly committed to eliminating lymphatic filariasis as a public health problem," WHO, 2020, [Online]. Available: https://www.who.int/news/item/29-04-2020-indonesia-firmly-committed-to-eliminating-lymphatic-filariasis-as-a-public-health-problem
- [5] M. A. Dorkenoo *et al.*, "Molecular xenomonitoring for post-validation surveillance of lymphatic filariasis in Togo: No evidence for active transmission," *Parasites and Vectors*, vol. 11, no. 1, p. 52, Dec. 2018, doi: 10.1186/s13071-017-2611-9.
- [6] A. Deshpande et al., "The global distribution of lymphatic filariasis, 2000–18: a geospatial analysis," The Lancet Global Health, vol. 8, no. 9, pp. e1186–e1194, Sep. 2020, doi: 10.1016/S2214-109X(20)30286-2.
- [7] Pekalongan Health Office, "Health profile of Pekalongan City in 2019," (in Indonesian), pp. 1–226, 2020, [Online]. Available: https://dinkes.pekalongankota.go.id//upload/file/file\_20210629020936.pdf
- [8] A. F. N. Abdul Halim et al., "Factors associated with the acceptability of mass drug administration for filariasis: a systematic review," *International Journal of Environmental Research and Public Health*, vol. 19, no. 19, p. 12971, Oct. 2022, doi: 10.3390/ijerph191912971.
- B. F. R. Dickson et al., "Risk factors for lymphatic filariasis and mass drug administration non-participation in Mandalay Region, Myanmar," Parasites and Vectors, vol. 14, no. 1, 2021, doi: 10.1186/s13071-021-04583-y.
- [10] Z. D. Schneider et al., "Mass Drug Administration: Contextual Factor Considerations," American Journal of Tropical Medicine and Hygiene, vol. 110, no. 4, pp. 30–37, Apr. 2024, doi: 10.4269/ajtmh.22-0767.
- [11] R. A. Niles et al., "Assessing factors influencing communities' acceptability of mass drug administration for the elimination of lymphatic filariasis in guyana," PLoS Neglected Tropical Diseases, vol. 15, no. 9, p. e0009596, Sep. 2021, doi: 10.1371/journal.pntd.0009596.

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[12] I. Nafilata, T. Yunis, M. Wahyono, and T. Supali, "Determinant factors of taking anti-filarial medication behavior in the first round of the mass drug administration program with ivermectin, diethylcarbamazine citrate, albendazole: A cross-sectional study," vol. 2023, pp. 7–14, 2023, doi: 10.11594/nstp.2023.3501.

- [13] A. P. Ora, S. Landi, T. A. Patmawati, N. T. Kambuno, and S. Poddar, "Lack of changes in community behavior and environmental factors after filariasis elimination program in Kodi Balaghar district, Southwest Sumba regency: A qualitative study," *Malaysian Journal of Medicine and Health Sciences*, vol. 17, pp. 92–97, 2021.
- [14] T. Williams et al., "Socio-economic and environmental factors associated with high lymphatic filariasis morbidity prevalence distribution in Bangladesh," PLoS Neglected Tropical Diseases, vol. 17, no. 7 July, p. e0011457, Jul. 2023, doi: 10.1371/journal.pntd.0011457.
- [15] Indonesian Ministry of Health, "POPM filariasis data in Pekalongan City 2021 in Indonesian: data POPM Filariasis Kota Pekalongan Tahun 2021," 2021, [Online]. Available: https://dinkes.pekalongankota.go.id//upload/file/file\_20210629020936.pdf.
- [16] Pekalongan Health Office, "Draft assessment of post-Mass Drug Administration (MDA) filariasis transmission in Pekalongan City, Central Java," pp. 1–12, 2020. Accessed: Apr. 30, 2024. [Online]. Available: https://dinkes.pekalongankota.go.id//upload/file/file\_20210629020936.pdf
- [17] C. Ekedo, E. C. Mathias, O. Oghale O'woma, U. V. Chidiebere, and O. P. Igwe, "Habitat preference of mosquito larvae in Habitat preference of mosquito larvae in Michael Okpara University of agriculture, Umudike, Nigeria," *Article in International Journal of Mosquito Research*, vol. 7, no. 4, pp. 6–09, 2020.
- [18] N. Nurjazuli and N. A. Y. Dewanti, "Culex quinquefasciatus as the filariasis vector and environment condition in Pekalongan City," (in Indonesia), ASPIRATOR Journal of Vector-borne Disease Studies, vol. 13, no. 2, pp. 79–88, 2021.
- [19] WHO, "Lymphatic filariasis," WHO. Accessed: May 30, 2024. [Online]. Available: https://www.who.int/news-room/fact-sheets/detail/lymphatic-filariasis
- [20] D. McNaughton, E. R. Miller, and G. Tsourtos, "The importance of water typologies in lay entomologies of Aedes aegypti habitat, breeding and dengue risk: a study from northern Australia," *Tropical Medicine and Infectious Disease*, vol. 3, no. 2, p. 67, Jun. 2018, doi: 10.3390/tropicalmed3020067.
- [21] C. S. Ahorlu et al., "A comparative study of lymphatic filariasis-related perceptions among treated and non-treated individuals in the Ahanta West Municipality of Ghana," *Tropical Medicine and Infectious Disease*, vol. 7, no. 10, p. 273, Sep. 2022, doi: 10.3390/tropicalmed7100273.
- [22] T. V. Ha et al., "Spatial distribution of culex mosquito abundance and associated risk factors in hanoi, vietnam," PLoS Neglected Tropical Diseases, vol. 15, no. 6, p. e0009497, Jun. 2021, doi: 10.1371/journal.pntd.0009497.
- [23] P. M. Graves, S. Sheridan, S. Fuimaono, and C. L. Lau, "Demographic, socioeconomic and disease knowledge factors, but not population mobility, associated with lymphatic filariasis infection in adult workers in American Samoa in 2014," *Parasites and Vectors*, vol. 13, no. 1, 2020, doi: 10.1186/s13071-020-3996-4.
- [24] B. J. Msugupakulya et al., "Preferred resting surfaces of dominant malaria vectors inside different house types in rural south-eastern Tanzania," Malaria Journal, vol. 19, no. 1, p. 22, Dec. 2020, doi: 10.1186/s12936-020-3108-0.
- [25] Indonesia Health Ministerial, "Health Ministerial Regulation No. 94/2014," *Indonesia Ministry of Health*, pp. 1–118, 2014, [Online]. Available: https://rskgm.ui.ac.id/wp-content/uploads/2021/03/148.-pmk942014.pdf
- [26] K. Kvarnström, A. Westerholm, M. Airaksinen, and H. Liira, "Factors contributing to medication adherence in patients with a chronic condition: A scoping review of qualitative research," *Pharmaceutics*, vol. 13, no. 7, 2021, doi: 10.3390/pharmaceutics13071100.
- [27] Indonesian Ministry of Health, "Regulation of the Minister of Health of the Republic of Indonesia Number 94 of 2014 concerning Filariasis Management," (in Indonesia), *Kementerian Kesehatan RI*, pp. 1–118, 2013, [Online]. Available: https://peraturan.bpk.go.id/Home/Download/164801/Kepmenkes HK.01.07-Menkes-445-2021.pdf
- [28] Indonesian Ministry of Health, "Decree of the Minister of Health of the Republic of Indonesia No. HK.01.07/MENKES/445/2021 on the Implementation of Mass Drug Administration of Filariasis Regimen Ivermectin, Diethyl Carbamazine Citrate, and Albendazole in Mamuju District, Biak Numfor District, Sorong City, and Pekalongan City," (in Indonesia), *Indonesia Ministry of Health*, pp. 1–4, 2021, [Online]. Available: https://peraturan.bpk.go.id/Home/Download/164801/Kepmenkes HK.01.07-Menkes-445-2021.pdf
- [29] S. Banerjee et al., "Coverage of mass drug administration for elimination of lymphatic filariasis in urban Nagpur, Central India: A mixed method study," Journal of Family Medicine and Primary Care, vol. 8, no. 9, p. 3009, 2019, doi: 10.4103/jfmpc.jfmpc\_503\_19.
- [30] A. Ghasemian, K. Sargeran, M. R. Khami, and A. R. Shamshiri, "Effects of educational interventions based on the theory of planned behavior on oral cancer-related knowledge and tobacco smoking in adults: a cluster randomized controlled trial," BMC Cancer, vol. 24, no. 1, 2024, doi: 10.1186/s12885-024-11845-2.
- [31] X. Xu, P. Li, and S. Ampon-Wireko, "The willingness and influencing factors to choose institutional elder care among rural elderly: an empirical analysis based on the survey data of Shandong Province," BMC Geriatrics, vol. 24, no. 1, p. 17, Jan. 2024, doi: 10.1186/s12877-023-04615-5.
- [32] D. A. Ngunyali et al., "Knowledge and participation in mass drug administration against lymphatic filariasis and soil-transmitted helminth infections among the community members in Dar es Salaam, Tanzania," Transactions of the Royal Society of Tropical Medicine and Hygiene, vol. 117, no. 5, pp. 358–364, May 2023, doi: 10.1093/trstmh/trac119.
- [33] I. F. Aboagye and Y. A. A. Addison, "The impact of mass drug administration on lymphatic filariasis," Genetics Research, vol. 2022, 2022, doi: 10.1155/2022/7504871.
- [34] G. J. Weil et al., "The safety of double-and triple-drug community mass drug administration for lymphatic filariasis: A multicenter, open-label, cluster-randomized study," PLoS Medicine, vol. 16, no. 6, p. e1002839, Jun. 2019, doi: 10.1371/journal.pmed.1002839.
- [35] R. Dellar et al., "Knowledge, attitudes and practices of health professionals towards people living with lymphoedema caused by lymphatic filariasis, podoconiosis and leprosy in northern Ethiopia," *International Health*, vol. 14, no. 5, pp. 530–536, Sep. 2022, doi: 10.1093/inthealth/ihab067.
- [36] N. Uddin, "Assessing urban sustainability of slum settlements in Bangladesh: Evidence from Chittagong city," *Journal of Urban Management*, vol. 7, no. 1, pp. 32–42, 2018, doi: 10.1016/j.jum.2018.03.002.
- [37] S. J. Campbell et al., "Water, sanitation and hygiene (WASH) and environmental risk factors for soil-transmitted helminth intensity of infection in Timor-Leste, using real time PCR," PLoS Neglected Tropical Diseases, vol. 11, no. 3, p. e0005393, Mar. 2017, doi: 10.1371/journal.pntd.0005393.
- [38] F. R. S. Prakoeswa *et al.*, "Correlation analysis between household hygiene and sanitation and nutritional status and female leprosy in gresik regency," *Dermatology Research and Practice*, vol. 2020, pp. 1–7, Sep. 2020, doi: 10.1155/2020/4379825

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