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FACTORS RELATED TO THE CLINICAL DEGREE OF MALARIA IN ELIMINATION AREAS IN INDONESIA

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ABSTRAK

Pengobatan malaria bergantung pada derajat klinis penyakit dan dapat menyebabkan kematian jika tidak ditangani dengan tepat. Penelitian ini bertujuan untuk melihat faktor-faktor yang berhubungan dengan derajat klinis malaria pada daerah eliminasi di Indonesia. Desain penelitian menggunakan studi kuantitatif cross-sectional dari data sekunder aplikasi Sistem Informasi Surveilans Malaria (Sismal) pada tahun 2023 di seluruh kabupaten/kota yang telah eliminasi di Indonesia sebanyak 9435 orang. Analisis dilakukan pada masing-masing variabel untuk melihat gambaran distribusi frekuensi dan persentase dari setiap variabel. Data diolah dengan program SPSS. Pada analisis multivariat diperoleh bahwa anemia (p=0,000; OR=11,748; CI 95% =7,833-17,620) dan status pengobatan (p=0,000; OR=8,554; CI 95% = 5,694-12,851) mempunyai p<0,05. Dapat disimpulkan bahwa anemia dan status pengobatan berhubungan secara bermakna dengan derajat klinis malaria. Pada daerah eliminasi karena sudah jarang kasus ditemukan perlu dilakukan pelatihan bagi tenaga kesehatan agar dapat memberikan diagnosis dan pengobatan yang tepat dan cepat sehingga tidak terjadi infeksi atau kekambuhan yang berulang menyebabkan anemia berat dan kematian. Banyak faktor yang mempengaruhi derajat klinis malaria namun variabel yang digunakan terbatas sehingga perlu dilakukan penelitian lebih lanjut terkait faktor-faktor yang lebih lengkap yang mempengaruhi derajat klinis malaria.

ABSTRACT

Factors Related to The Clinical Degree of Malaria in Elimination Areas in Indonesia. Malaria treatment depends on the clinical degree of the disease and can cause death if not treated appropriately. This study looks at factors associated with the clinical degree of malaria in elimination areas in Indonesia. The research design used a cross-sectional quantitative study of secondary data from the Malaria Surveillance Information System (Sismal) application in 2023 in all 9435 elimination districts in Indonesia. Analysis was conducted on each variable to see the frequency distribution and percentage of each variable. Data was processed with the SPSS program. Multivariate analysis showed that anemia (p=0.000; OR=11.748; CI 95% =7.833-17.620) and treatment status (p=0.000; OR=8.554; CI 95% =5.694-12.851) had p<0.05. It can be concluded that anemia and treatment status are significantly associated with the clinical degree of malaria. In elimination areas, because cases are rare, training is needed for health workers to provide appropriate and rapid diagnosis and treatment so that no infection or recurrence causes severe anemia and death. Many factors affect the clinical degree of malaria. However, the variables employed are constrained, necessitating further investigation into a comprehensive array of factors influencing the clinical severity of malaria.

INTRODUCTION

Malaria is contagious and deadly in tropical countries.[1] According to the WHO World Report 2022, malaria cases increased by 247 million in 2021 compared to 245 million in 2020. In 2021, more malaria cases were reported in African countries, accounting for 95% of all cases caused by COVID-19 interference.[2] Malaria remains a public health issue in Indonesia.[3] Malaria raises the risk of mortality and morbidity in newborns, toddlers, and pregnant women and reduces job productivity. Reaching regions without local malaria transmission is a national and worldwide objective for malaria initiatives. [4] Malaria cases dropped to 443,530 in 2022, a slight decrease from 20 years earlier. Malaria cases have stagnated over a decade. The topic under consideration forms the basis for implementing interventions to reduce malaria incidence rates significantly. Several regions reported 71 deaths. [3]

Two methods used for parasitological diagnosis are inspection with a microscope and RDT *(Rapid Diagnostic Test).* Anti-malarial treatment was administered when inspection test results with a microscope or RDT were positive.[4,5] In areas lacking quality microscope[6]s, RDT (Rapid Diagnostic Tests) is necessary for effective diagnosis. Patients who have partially completed anti-malarial treatment may exhibit negative results in blood examinations, thus necessitating RDT to detect ha/HRP2. Should the initial blood smear examination yield negative results in patients exhibiting symptoms consistent with severe malaria, subsequent blood smear examinations must be conducted at 6-12 hours. Five species of Plasmodium cause malaria in humans: P. falciparum, P. vivax, *P. ovale*, *P. malariae*, and the recently identified *P. knowlesi*, predominantly found in forested areas of Southeast Asia, with several reported cases in Indonesia [6]as well.[5]

Current malaria treatments are Artemisinin Combination Therapy (ACT) and Primaquin. Giving combination drugs increases effectiveness and prevention resistance to malaria. Malaria treatment is based on clinical degrees given in malaria without complications and severe malaria or malaria with complications. Malaria without complications has the same symptoms as a mild viral infection from a Sick head, the body that feels weak and lethargic as well as pain, frequent joints followed by fever Then, shivering, and sweating. Patients with severe malaria will come with very complex pathophysiology involving lots of organ systems. Seizures and anemia generally occur in children, whereas hyperparasitemia, kidney failure, and acute jaundice generally occur in adults, as Cerebral malaria (with shock), and acidosis. The treatment of uncomplicated malaria aims to cure the infection, prevent the progression to severe disease, reduce morbidity, minimize transmission to others, and prevent the emergence of drug-resistant strains. The primary objective of anti-malarial treatment for severe malaria is to prevent fatalities. Administering treatment for all degrees of uncomplicated malaria keeps the fatality rate low, approximately 0.1% for P. falciparum, whereas other parasite species rarely result in fatalities if promptly and effectively treated. However, if severe malaria progresses untreated, the mortality rate can rise to 15-20%.[5]

Research conducted in Rwanda by G. Gakinahe et al. identified a need for more medicine availability and other essential malaria logistics.[7] Similarly, a study in Spain by M. Linares-Rufo et al. revealed that only 5.7% of doctors demonstrated a high level of knowledge about malaria, leading to deficiencies in patient compliance with medication due to insufficient understanding of the disease.[8] Another investigation in Iran by H. Azizi et al., conducted in the East Azerbaijan Province, observed no new malaria cases since 2018 and no local transmission in the past 14 years. However, identifying suspected malaria cases was found inadequate, resulting in malaria cases not being treated without using anti-malarial drugs.[9] Additionally, a study in Ecuador, an area with low malaria

transmission, reported an average of 6.4 ± 0.88 months for the lack of availability of anti-malarial drugs at the primary healthcare level. Moreover, the assessment of doctors' knowledge regarding the treatment of uncomplicated malaria and severe malaria according to national guidelines revealed that only 29% had adequate knowledge, and only 10% had sufficient knowledge about the management of severe and maternal malaria in pregnant women. Consequently, 95.7% of malaria cases were treated and managed at home due to the inability to access primary healthcare services and the unavailability of drugs at that level.[10]

In contrast, a study conducted in Bulu Kumba, South Sulawesi Province, in 2015 reported only imported malaria cases since 2012, with treatments administered according to national standard guidelines.[11] To prevent fatalities, malaria re-transmission, and incidents outside the normal range, researchers undertook a study to investigate the factors related to the clinical degrees of malaria in elimination areas in Indonesia.

METHOD

The research design employed an observational analytic method. In 2023, researchers undertook a study to explore the factors associated with the clinical manifestations of malaria in regions where the disease has been eliminated in Indonesia. The dependent variable was the severity of malaria (categorized into malaria without complications and malaria with complications/severe malaria). In contrast, the independent variables included age, gender, weight, parasite species, anemia, and treatment status. The data utilized in this study were secondary data obtained from the Malaria Surveillance Information System (Sismal), which collects reports directly from malaria control programs. These reports are provided by trained malaria surveillance officers who input data into the application and oversee the monitoring and evaluation processes overseen by the Directorate of Prevention and Control of Infectious Diseases.

The study participants were individuals who tested positive for malaria across 389 districts/cities certified as malaria elimination areas. These confirmed cases were diagnosed through microscopic examination or Rapid Diagnostic Test (RDT) from January to December 2023, totaling 9435 individuals. Univariate analysis was conducted for each variable to describe the frequency distribution and percentage of each variable. Bivariate and multivariate analyses were utilized to investigate the relationship between the dependent (or outcome) variable and the independent (or predictor) variables, with a significance level of $p<0.05$. The data were analyzed using the Statistical Program SPSS.

RESULTS

The research results indicate that a total of 9435 malaria cases were confirmed through laboratory inspections using both microscopy and RDT in the elimination regions of Indonesia in 2023. Regarding demographic characteristics, the cases were distributed across different age groups, with the highest number of malaria cases observed in individuals aged between 18 and 89 years, accounting for 87.59% of the total cases. This was followed by individuals aged 6 to 17 years, constituting 10.41% of the cases, and those aged 1 to 5 years, comprising 2%. Regarding gender distribution, males accounted for a more significant proportion (78.04%) than females (21.96%). Occupationally, the cases were diverse, with individuals engaged in gardening (1.64%), mining (13.06%), household chores (13.16%), fishing (7.68%), police personnel (2.8%), various occupations

(4.26%), students (11.20%), forest exploration (4.25%), farming (10.1%), military personnel (8.35%), and others (workers, employees, self-employed, and miscellaneous) constituting 23.5% of the cases.

Physically, 94.71% of the cases were found to be non-anemic, while 5.29% exhibited signs of anemia. Treatment adherence to standard protocols was observed in 83.96% of the cases, while 16.04% did not adhere to the standard guidelines. Microscopic examination revealed the predominance of Plasmodium vivax parasites, accounting for 73.83% of the cases, followed by P. falciparum at 19.62%, mixed infections at 4.92%, probable *P. knowlesi* at 1.09%, P. malariae at 0.43%, and *P. ovale* at 0.11%. The demographic characteristics of the participants and the clinical examination of malaria cases in the elimination areas of Indonesia are summarized in Table 1.

Table 1. Description Characteristics Demographics Participant Research and Examination Clinical

Variable	Category	Amount	Percentage
Age	0-5 years	189	2%
	6-17 years	982	10.41%
	18-89 years	8264	87.59%
Gender	Man	7363	78.04%
	Woman	2072	21.96%
Work	Gardening	150	1.64%
	Laborer mine	1195	13.06%
	Housewife	1204	13.16%
	Fisherman	703	7.68%
	POLRI	256	2.8 %
	Employee	390	4.26%
	Student	1025	11.20%
	Browser forest	389	4.25%
	Farmer	916	10.1%
	TNI	764	8.35%
	Other	3207	23.5%
Anemia	Anemia	499	5.29%
	Not Anemic	8936	94.71%
Treatment Status	Not standard	1513	16.04%
	Standard	7922	83.96%
Parasite	Falciparum	1851	19.62%
	Vivax	6966	73.83%
	Malaria	41	0.43%
	Mix	464	4.92%
	oval	10	0.11%
	Probable Knowles	103	1.09%

The analysis reveals that the predominant age group affected by malaria is individuals aged between 18 and 89 years, with a higher proportion of males than females. Regarding occupation, laborers in mining, professionals, and homemakers are the most affected. These findings are consistent with a study conducted in China by L. Jia et al., which found that most cases were between 30 to 50 years old, predominantly males engaged in farming and other professions. In areas where malaria has been eliminated, no local transmission and most cases are imported cases. Therefore, it is essential to inquire about the travel history of individuals presenting with malaria symptoms. Adult individuals, particularly those engaged in work in malaria-endemic areas, are more

likely to have a history of travel to these regions, leading to a higher incidence of malaria among productive-age adults. Males are more commonly affected than females.[12]

The most prevalent parasite species identified in malaria cases is *Plasmodium vivax*. This corresponds with previous studies and WHO guidelines indicating that regions free from *P. falciparum* often have endemic *P. vivax* infections. Treatment of *P. vivax* malaria requires radical measures to prevent relapses and potential outbreaks. Additionally, it is crucial to improve the quality of microscopy techniques to detect low parasite densities and prevent severe anemia and further transmission. Studies, such as those by Cindy S. Chu, emphasize the importance of preventing and treating *P. vivax* infections, especially in areas with reduced *P. falciparum* prevalence, where it cases may increase.

Types of parasites Amount Parasite the most is vivax. This matter is the same as several studies, as stated in the WHO Guideline on Elimination of residual foci in Europe, Southwest Asia, and North Africa, where accessible areas from P. falciparum find P. vivax endemic . In malaria caused by *P. Vivax*, treatment must be radical so that no possible relapse causes an outbreak.[13] Cindy S. Chu's journal regarding the Prevention and Treatment of *P.vivax* also mentioned that with a reduced number of *P. falciparum*, the amount of p. viva will increase. *Plasmodium vivax* infection density of the parasite is low, so it is often not detected. Quality from slides and skills microscopy is necessary to prevent severe anemia and determine how not to prevent source transmission.[14]

Standard Treatment

The adherence to established standards in treatment administration underscores the commitment of healthcare professionals, particularly physicians, to follow national guidelines. This observation is consistent with findings from a study conducted in Bulu Kumba, South Sulawesi, Indonesia. However, it contrasts with other studies conducted in Rwanda, Spain, Iran, and Ecuador, focusing on malaria elimination efforts. Sporadic cases often arise in these areas due to logistical constraints and healthcare system capabilities. Consequently, many malaria cases must be treated according to established standards, leading patients to seek treatment at home or resort to alternative medications. Moreover, there needs to be proper identification of suspected malaria cases, resulting in the administration of inappropriate drugs. Additionally, research indicates a decline in diagnostic capabilities for malaria, exacerbating the problem. Furthermore, poor public knowledge about malaria contributes to non-compliance with treatment guidelines. Given the rarity of malaria cases, there is a pressing need for enhanced education and health promotion efforts to ensure timely and accurate diagnosis and treatment.[7–10]

In cases of malaria, anemia is not more prevalent among individuals who are not anemic, indicating the effectiveness of the diagnosis and treatment of malaria cases. The low density of parasites contributes to the absence of clinical symptom s, thereby preventing the occurrence of anemia. Furthermore, the absence of anemia indicates the administration of radical treatment. Anemia typically arises from recurrent infections and repeated recurrences of *P. vivax* malaria, often resulting from non-standard treatment protocols.[14,15]

Table 2. **Description Characteristics Participant Study Based on Activity Invention**[16]

Variable	Category	Amount	Percent
Checking type	Microscope	6365	67.46
	RDT	3070	32.54
Activity Invention	FUP (Follow up Treatment)	36	0.38
	Home Visits	273	2.89
	IMCI	2	0.02
	PCD	8874	94.05
	Integrated Healthcare Center	6	0.06
	Public Health Center Around	1	0.01
	Screening Mother Pregnant	4	0.04
	Contact Survey	84	0.80
	Surveillance Migration	133	1.41
	MBS	22	0.23
Type of Health Facility	Public health center	5535	58.66
	TNI/POLRI Hospital	730	7.74
	Hospital	316	33.57
	Practice Private	73	0.03

Regarding participant characteristics, most inspections were conducted using a microscope, accounting for 67.46%, while 32.54% were performed using Rapid Diagnostic Tests (RDTs). The most common method for detecting malaria cases was passive case detection (PCD), comprising 94.05% of the activities. Other activities included house visits (2.89%), migration surveillance (1.41%), contact surveys (0.80%), follow-up treatments (0.38%), mass blood surveys (MBS) (0.23%), Posyandu (0.06%), screening of pregnant mothers (0.04%), Integrated Management of Childhood Illness (IMCI) (0.02%), and peripheral community health centers (0.01%). The primary facilities utilized for inspections were public health centers (58.66%), followed by home visits (33.57%), military and police hospitals (7.74%), and private practices (0.03%). Participant characteristics based on inspection activities are summarized in Table 2.

Checking type

A microscope, considered the gold standard for examination, was utilized during the observation. Good quality assurance is required for microscopic activity inspection. Vivax, who has density, is the main case. A minor clinical requirement for excellent microscopic ability with symptoms.[13,14]

Activity Invention

The predominant method of case detection is passive case detection, which indicates a potentially high level of awareness and knowledge among individuals. This contrasts with studies conducted in regions with low malaria cases, where inadequate knowledge results in self-diagnosis and lack of adherence to malaria medication. Therefore, it is necessary to enhance active case detection activities to prevent the resurgence of transmission.

Type of Health facility

Invention case detection bypasses most of the time. This demonstrates that cognizance and, conceivably, exceptional knowledge are both feasible. Cases are shallow compared to research in other fields due to a lack of knowledge. No, check yourself and abstain from consuming malaria

medication. However, active case detection efforts must be increased to prevent the spread of appearance return contagion.

Table 3. Analysis results bivariate related factors with degrees of clinical malaria

Variable	Category	Degrees of Malaria				Statistic test
		With complications		Without Complication		
		Amount	Percen	Amount	Percent	
Age	0-5 yrs	3	1,59	186	98,41%	P=0,062
	6-17 yrs	4	0,41	978	99,59%	
	18-66 yrs	102	1,23%	8167	98,77%	
Gender	Man	89	8,20%	7274	91,80%	P=0,36
	Woman	20	5,13%	2052	94,87%	
Anemia	Anemia	47	2,20%	452	4,8%	P=0,000
	Not Anemia	62	7,01%	8874	95,2%	
Parasite	Faciparum	45	2,43%	1806	97,57%	P=0,000
	Vivax	45	0,65%	6921	99,35%	
	Malaria	0	0%	41	100%	
	Ovale	0	0%	10	100%	
	Mix	16	3,45%	448	96,55%	
	Probable knowledge	3	2,91%	100	97,09%	
Treaatment status	Not standart	71	4,7%	1442	95,3%	P=0,000
	Standart	38	0,5%	7884	99,5%	

Variables with p-values less than 0.25 were included in the multivariate analysis of the research (Table 2). Four variables met this criterion: age, type of parasites, anemia, and treatment status. The subsequent step involved modeling, where all variables were analyzed collectively. Model selection was performed by gradually entering independent variables meeting the inclusion criteria. Variables with nonsignificant p-values were gradually excluded, starting with the variable with the most significant p-value. The multivariate analysis revealed that anemia (p=0.000; OR=11.748; 95% CI =7.833-17.620) and treatment status (p=0.000; OR=8.554; 95% CI = 5.694-12.851) exhibited p-values less than 0.05, indicating their significant association with the degree of malaria (Table 3). The statistical tests indicated that the other independent variables were not significantly associated with the degree of malaria (p-value > 0.05).

Table 4. Analysis results Multivariate influencing factors to degrees clinical malaria

Variable	B	P	OR	95%CI
Gender	0,523	0,76	1,868	0,948-3,002
Parasit	-0,177	0,16	0,838	0,726-0,968
Anemia	2,448	0,000	11,560	7,694-17,371
Treatment status	2,230	0,000	9,298	6,154-14,047

Table 5. Final model influencing factors to degrees clinical malaria

Variable	B	P	OR	95%CI
Anemia	2,448	0,000	11,748	7,833-17,620
Treatment Staus	2,230	0,000	8,554	5,694-12,851

From the results, the multivariate analysis shows which variables relate to degrees of clinical malaria: anemia (p=0.000) and treatment status (p=0.000). At the same time, variable age (p=0.76) and parasites (0.16) did not have connection with degrees clinical malaria (Table 5).

DISCUSSION

The study was conducted in districts/cities certified as malaria elimination areas. In these elimination areas, local transmission of malaria was not detected. The absence of local transmission implies the absence of indigenous malaria cases; instead, malaria cases are attributed to transmission from external sources, termed imported cases. Therefore, in areas certified as malaria-free, it is crucial to inquire about individuals' travel histories to ascertain potential exposure to malaria-endemic regions. In regions where malaria remains endemic, the presence of malaria cases necessitates vigilant surveillance, particularly in locales conducive to breeding Anopheles mosquitoes, the vectors responsible for malaria transmission. The displacement of residents and inadequate malaria prevention and control services can lead to malaria outbreaks, posing significant mortality risks across all age groups. The study findings underscore the association between standard treatment protocols and the presence of anemia with the clinical severity of malaria cases.

Timely and appropriate treatment for malaria cases without complications or vital organ dysfunction results in a fatality rate of only 0.1% when caused by P. falciparum. However, fatalities are rare if caused by other malaria parasite species. In cases where treatment is administered during the severe stage of malaria, the mortality rate ranges between 15-20%, and untreated malaria inevitably leads to death. [5] The journal defines severe malaria as cases with a heightened risk of mortality. Mortality rates for uncomplicated falciparum malaria are meager when treated with effective anti-malarial drugs (OAM). Severe malaria is characterized by a mortality rate exceeding 5%, particularly in individuals with compromised immunity, such as those residing in areas with low malaria transmission or malaria-free zones. Globally, mortality rates have declined following the adoption of artemisinin-based combination therapies (ACTs) as first-line parenteral treatments, replacing quinine. Studies conducted in Asia and Africa have demonstrated that replacing quinine with artesunate therapy reduces mortality rates by up to one-third among severe malaria patients.[7–10]

Some research conducted in the area of elimination treatment in accordance with no standard. This caused by several matters, among other things because lack of knowledge power health about malaria because at least existing cases, no availability of OAM, late medication, and drinking drug No in accordance rule Because lack of knowledge public about malaria and access treatment that is difficult to reach. In areas that have elimination, If malaria prevention and control is not done well, it can cause very rapid -re-transmission of malaria. This matter because it is in an existing area seldom Malaria cases are very vulnerable for contracting malaria due to no own immunity body against malaria from imported malaria cases brought in from area endemic malaria by people who come from outside the region. For prevention and control of malaria, the officer's existing health must still provide appropriate malaria services standards with methods to improve

and maintain existing knowledge related to malaria treatment and institutions' health at the central level until the area ensures the availability of malaria drugs and logistics.[7–10]

In regions characterized by low transmission levels of malaria, anemia can manifest across all age groups, with children and pregnant women being particularly susceptible due to their heightened vulnerability to malaria infection. Despite considerable strides in malaria elimination efforts in Indonesia, malaria cases stemming from *P. vivax* remain prevalent, alongside instances attributed to P.falciparum and other Plasmodium species. Notably, untreated *P. vivax* infections can lead to recurrent relapses, often serving as a significant contributor to malaria-induced anemia in children. Conversely, inadequate management of P. falciparum infections, compounded by frequent reinfections, contributes significantly to malaria-related anemia in various regions. Implementation of appropriate treatment regimens aimed at averting recurrent episodes or reinfections represents a pivotal strategy in preventing anemia. Despite the low transmission intensity characteristic of elimination areas, the constrained resource base poses a challenge, particularly concerning the risk of severe anemia. Each sporozoite inoculation potentially sets the stage for recurrent relapses, underscoring the persistent threat of severe anemia. Left untreated, severe anemia carries a grave risk of mortality, emphasizing the imperative of prompt intervention. [15]

Indonesia still has endemic malaria areas with an *Annual Parasite Index (API)* ranging from 1 to 5 and above 5. Individuals migrating from areas with endemic malaria to regions designated as elimination areas need to exercise caution to prevent becoming sources of transmission.[17] Research conducted in endemic malaria areas has identified a high prevalence of severe malaria cases among children lacking their immune defenses. Conversely, adults in endemic malaria regions often possess natural immunity. Primary healthcare services in endemic malaria areas demonstrate proficiency in diagnosing suspected cases due to the frequent occurrence of malaria. Furthermore, communities with sufficient knowledge about malaria promptly seek healthcare services upon experiencing symptoms, facilitating timely treatment. In contrast, various parasite species, notably *P. falciparum*, are frequently encountered in regions transitioning to malaria elimination status.[18]

A study conducted by N. Kayiba et al. in the Congo, a region endemic to malaria, revealed that the predominant species causing infections is *Plasmodium falciparum*, with no instances of *Plasmodium vivax* detected. Furthermore, the study noted a higher incidence of malaria among females, although the comparison with males did not reveal statistical significance.[19] The researchers noted similar findings in another study conducted in Kenya, where a higher prevalence of Plasmodium falciparum was observed among women. Researchers attributed the increased susceptibility of children to severe malaria to their lack of prior immunity compared to adults who have been exposed to the disease multiple times. [20] Additionally, research conducted in Turkey's rural areas focused on the local population's behavioral patterns and knowledge regarding malaria. The study found that most respondents were aware of the classic symptoms of malaria and were knowledgeable about preventive measures. Approximately half of the respondents were familiar with the administration of Primaquine medication for 14 days. Furthermore, the study highlighted that most individuals would seek malaria treatment upon experiencing symptoms. These findings contribute to understanding malaria epidemiology and public health practices in diverse geographic regions. [21]

The study has inherent limitations due to its reliance on secondary data, resulting in a restricted set of variables about factors associated with the clinical degrees of malaria. Additional factors, such as those highlighted in WHO guidelines, including immunity factors, comorbidities, and other diseases influencing malaria clinical outcomes, must be fully explored. Moreover, research

indicates that parasite density significantly influences clinical conditions. These limitations pose a risk of bias, necessitating further analysis to explore additional factors. It is advisable to conduct thorough data collection using primary sources to augment comprehension of the variables associated with the clinical severity of malaria.

CONCLUSION

A region attains elimination status when its *Annual Parasite Incidence (API)* falls below 1 per thousand residents (< 1 per thousand population), the Positivity Rate (PR) is less than 5%, and no local transmission cases occur for three consecutive years. However, sustained vigilance is necessary in elimination areas due to the ongoing importation of cases, which could trigger local transmission resurgence. Despite the absence of local cases, imported cases from outside the region persist, warranting continuous vigilance to prevent the re-establishment of local transmission. Addressing these challenges requires strengthening healthcare capacity, fostering intersectoral collaboration, and securing governmental commitments to achieve the elimination goal by 2030.

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