

# The Characteristic of Recurrent Malaria Episode: An Observational Study in Timika Papua

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## ABSTRACT

**Background:** People living in malaria endemic areas are at risk of suffering from the recurrent malaria episodes. The recurrent episode of malaria can be determined by various factors and will bring some serious impacts on all life aspects. This study aims to identify malaria demographics and factors associated with the recurrent episodes of malaria in Timika, Papua. **Methods:** This observational study used medical record data from the Naena Muktipura Sub-District Health Center, Timika Papua in 2020. Plasmodium infection was identified based upon microscopic examination. Subjects were then categorized into positive and negative malaria followed by the determination of the positivity rate. Each case of malaria was traced regarding frequency, time, and type of Plasmodium. The recurrent episodes of malaria were defined as Plasmodium infections occurred more than once in a year. Demographic data including age, sex, and ethnicity were then analyzed using Chi square. **Results:** The incidence of recurrent malaria in Timika Papua was 16% with the highest positivity rate occurred in June. The most recurrent episodes of malaria were 2 episodes (77.2%) in which men were more at risk (OR 2.512). Meanwhile, ethnicity and age were not associated with recurrent episodes. Most of recurrent episodes of malaria are caused by the similar plasmodium species, particularly Plasmodium falciparum (82.25%) with the shortest interval between episodes of 14 days. **Conclusion:** Malaria is mostly experienced by men, of productive age and Javanese ethnicity. Men were found more at risk of experiencing recurrent episodes of malaria. The identification of these demographic factors is important to issue the policies on malaria elimination and malaria transmission termination in Timika, Papua.

**Keywords:** Malaria, epidemiological characteristic, recurrent episode, Timika Papua.

## INTRODUCTION

Malaria still becomes a global health issue as proven by the 87 countries with malaria endemic status. Southeast Asia Region is one of the regions with the highest number of malaria cases in the world in which Indonesia becomes the country with the highest number of cases in that region.<sup>1</sup> The high morbidity of malaria leads to the increasing health cost both for treatment and for prevention.<sup>2</sup> One of the malaria endemic areas in Indonesia is Timika Regency, Papua Province.<sup>3</sup> Timika consists of forests, beaches, swamps

and has high rainfall throughout the year.<sup>4</sup> Regional characteristics and sociodemographic factors of the community have caused the local transmission of malaria to occur continuously; as a consequence, the residents in endemic areas are at risk of being infected with Plasmodium more than one episode.<sup>5-7</sup>

The prevalence of recurrent episodes of malaria reaches 16%, in which the average within 5 years can reach 5-16 episodes.<sup>8,7</sup> Recurrent episodes are determined by age, sex, ethnicity, occupation and history of malaria in the family.<sup>7</sup>

Previous study stated that the episode of malaria is not associated with an inadequate immune system, but more associated with recurrent *Plasmodium* infection.<sup>8</sup> This condition is mainly experienced by children and then decreases along with aging.<sup>9</sup> Children are the potential reservoir in malaria transmission.<sup>10</sup> In which the parasitemia of children is higher than that of adult.<sup>11</sup> It has been suggested that epidemiological characteristic could lead to caused recurrent of malaria episode, but there are yet no published data.

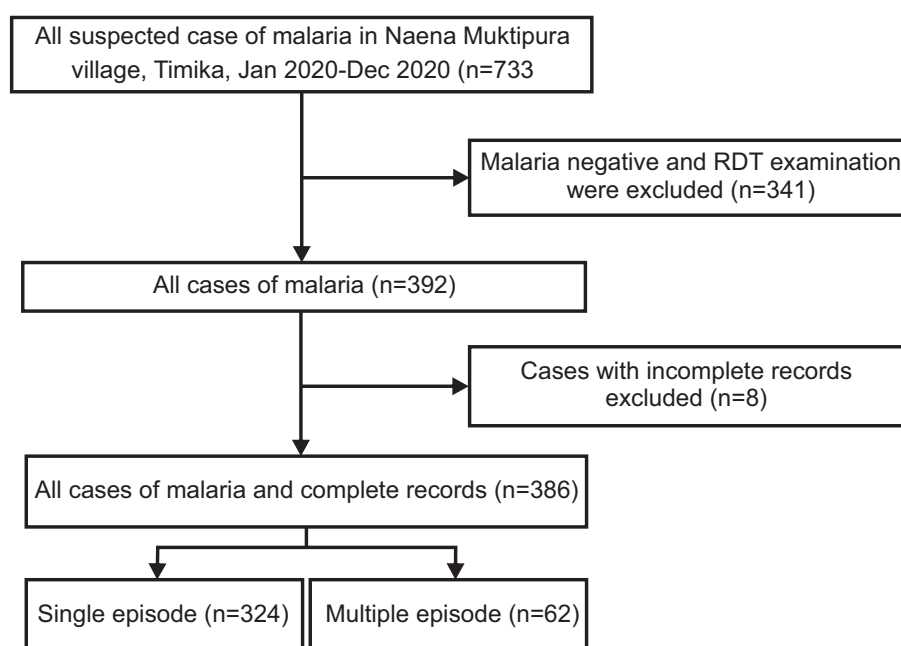
The recurrent malaria episode can be caused by failure of malaria treatment that caused recrudescence, reinfection from mosquito bite, or reactivation of hypnozoite stadium in liver called relaps.<sup>3</sup> This recurrent malaria can impose severe burdens not only for the people but also governments. The impact on malaria patients also varies, such as decreases work productivity and cognitive decline in school children. Far, little is known about the condition of recurrent malaria episode especially in Timika as a high endemic area in Indonesia.<sup>3</sup> Identifying factors associated with recurrent episode of malaria, which is core indicator of this study, can give valuable information. All these factors need to be studied in depth to formulate the policies on malaria prevention efficiently.

## METHODS

This observational study used medical record data at the Sub-District Health Center of Naena Muktipura, Timika, Papua. It has received approval from the health research ethics committee of the Faculty of Medicine, Islamic University of Indonesia with number 2/Ka.Kom. Et/70/KE/VI/2021.

### Data Collection

Malaria cases were found by tracing malaria examination data carried out by officers during 2020 that met the inclusion and exclusion criteria. All malaria cases between 1 January 2020 and 31 December 2020 in sub-district health center of Naena Muktipura, were enrolled (**Figure 1**). Totality sampling is used to determine the sample size. Based on observational sample size, only 246 samples were needed, while the sample on this study was 386. The research was conducted in Naena Muktipura Village. This village is one of the high endemic villages for malaria and there is a sub-district health center to facilitate the residents to have medical treatment. Malaria cases in the sub-health center were obtained through passive case detection (PCD). Malaria negative and RDT examination for diagnosis malaria, incomplete medical record was also excluded. Patients who examined with RDTs



**Figure 1.** Flowchart of patients included and excluded.

were excluded, so bias could result from it. The diagnosis by RDT was not analyzed because the type of RDTs that used could not identify the plasmodium species.

### Research Variables

The subjects of this study were all villagers showing symptoms related to malaria and were examined for malaria at the Naena Muktipura Sub-District Health Center. The diagnosis of malaria was done when *Plasmodium sp.* was found on microscopic examination as a gold standard for diagnose malaria. From the results of microscopic examination, Plasmodium species (*Plasmodium falciparum* and *Plasmodium vivax*) can be identified. The number of malaria incidents in the same person during 2020 was defined as the recurrent episode of malaria. The incidence of malaria in one month was also recorded to calculate the positivity rate.

Each malaria case was continued by recording demographic data including age, sex, ethnicity, Plasmodium type, and number of malaria episodes. The recurrent episodes of malaria were defined as *Plasmodium* infections occurred more than once throughout 2020. Each incident of recurrent episodes of malaria was recorded in the form of the month of infection, type of *Plasmodium* and the distance between episodes. The interval between episodes was defined as the average number of days between recurrent episodes.

### Statistical Analysis

We analyzed the data using SPSS and the demographic characteristics of the subject were presented in a descriptive form. The positivity rate for malaria was obtained by adding up the malaria cases in one month divided by all malaria examinations within one month in percent units.<sup>12</sup> The correlation of the demographic characteristics of the subjects and recurrent episodes of malaria was analyzed using the Chi Square test.

## RESULTS

### Patients' Characteristic and Positivity Rate of Malaria in Naena Muktipura Village

In 2020 Naena Muktipura Village was populated by 1492 people. During this year, a

total of 733 people were examined related to malaria and 386 (52.66%) of them confirmed malaria. The incidence of malaria in Naena Muktipura Village in 2020 reached 25.87%. As shown in **Table 1**, malaria in Naena Muktipura Village was dominated by men (60.88%), in the range of 15-64 years old (64.25%) and were those as the ethnic Javanese (42.49%). The highest positivity rate occurred in June, i.e., 65 cases (60.18%) and the lowest one occurred in May with 13 cases (38.23%) (**Table 2**).

**Table 1.** Characteristics of malaria demography in Naena Muktipura Village.

Variables	Total
Gender, n (%)	
Male	235 (60.88)
Female	151 (39.12)
Age (years), n (%)	
0-11	4 (1.03)
1-4	31 (8.03)
5-9	36 (9.33)
10-14	55 (14.25)
15-64	248 (64.25)
>64	12 (3.11)
Ethnic, n (%)	
Timika	65 (16.84)
Java	164 (42.49)
East Nusa	123 (31.86)
Papua	9 (2.33)
Sulawesi	23 (5.95)
Sumatra	2 (0.53)

**Table 2.** Positivity Rate Malaria in pada 2020.

Month	Malaria Examination, n (%)		Total
	Positive	Negative	
January	39 (52)	36 (48)	75
February	9 (47.4)	10 (52.6)	19
March	6 (54.54)	5 (45.45)	11
April	17 (42.5)	23 (57.5)	40
Mei	13 (38.23)	21 (61.77)	34
June	65 (60.18)	43 (39.82)	108
July	54 (64.28)	30 (35.72)	84
August	56 (64.36)	31 (35.64)	87
September	48 (46.6)	55 (53.39)	103
October	30 (46.15)	35 (53.85)	65
November	23 (40.35)	34 (59.65)	57
December	26 (52)	24 (48)	50
Total	386 (52.66)	347 (47.34)	733

### Correlation of Risk Factor and Recurrent Malaria in Timika

Episodes of malaria in 2020 were dominated by single episodes of malaria by 324/386 people (83.93%), while 62 people (16.06%) experienced

the recurrent episodes of malaria dominated by men (12.43%), aged 15-64 years (66.1%), and Javanese ethnic (17.7%). As shown in **Table 3**, the recurrent episodes of malaria in sequence from the highest number included 2-episodes (48 people; 77.42%), 3-episodes (12 people; 19.35%) and 4-episodes (2 people; 3.23%). A total of 48 people experienced 2 recurrent episodes, and the most recurrent episodes were 4 episodes within one year. A total of 21/62 children (33.87%) were children  $\leq 15$  years old, and one of them experienced 4-episodes within one year. The results of the Chi Square test showed that age and ethnicity were not associated with malaria episodes ( $p > 0.05$ ), while sex was associated with malaria episodes ( $p = 0.004$ ). The proportion of recurrent episodes of malaria in males was 2.51 times higher than that of females.

### Plasmodium Type in Multiple Episode

Subsequently, it was continued to analyze the types of plasmodium and multiple malaria. The Plasmodium species identified in Naena Muktipura Village were *Plasmodium falciparum* and *Plasmodium vivax*. *Plasmodium falciparum* was the most common type (82.25%;  $n = 51/62$ ) (**Table 4**). Recurrent infections caused by the similar Plasmodium species were experienced by 50% of people, most of which were caused by *P. falciparum* (32.26%;  $n = 20/62$ ), followed by *P. vivax* (17.74%;  $n = 11/62$ ), while 31/62 people (50%) experienced recurrent infections by 2 Plasmodium species. The mean time between the nearest malaria episodes was from episode 2 to episode 3 (72 days) and the shortest distance between episodes was 14 days (**Table 4**).

**Table 3.** Correlation of risk factors and recurrent malaria in Timika.

Characteristic	Single Episode	Multiple Episode			Total	p
		2 <sup>nd</sup>	3 <sup>th</sup>	4 <sup>th</sup>		
Sex, n (%)						
Male	187 (48.45)	34 (54.84)	12 (19.35)	2 (3.22)	235 (60.88)	0.004 <sup>*</sup> ; OR 2.512 (1.331-4.739)
Female	137 (35.5)	14 (22.58)	0	0	151 (39.12)	
Age (year), n (%)						
0-0,11	3 (0.9)	0	0	0	4 (1.03)	0.763
1-4	26 (8)	5 (8.06)	0	1 (1.62)	31 (8.03)	
5-9	30 (9.3)	5 (8.06)	1 (1.62)	0	36 (9.33)	
10-14	46 (14.2)	5 (8.06)	4 (6.45)	0	55 (14.25)	
15-64	207 (63.9)	33 (53.23)	7 (11.29)	1 (1.62)	248 (64.25)	
>64	12 (3.7)	0	0	0	12 (3.11)	
Ethnic, n (%)						
Timika	55 (84.6)	8 (12.9)	1 (1.62)	1 (1.62)	65 (16.84)	0.287
Java	135 (82.3)	21 (33.87)	7 (11.29)	0	164 (42.49)	
Nusa Tenggara	102 (82.9)	19 (30.65)	3 (4.84)	1 (1.62)	123 (31.86)	
Papua	9 (100)	0	0	0	9 (2.33)	
Sulawesi	22 (95.7)	0	0	0	23 (5.95)	
Sumatra	1 (50)	0	1 (1.62)	0	2 (0.53)	

**Table 4.** Plasmodium types and distance in malaria episodes.

Characteristics of malaria episode	Number
Type of <i>Plasmodium</i>	
<i>P.f</i> - <i>P.f</i>	18 (29.03)
<i>P.f</i> - <i>P.f</i> - <i>P.f</i>	2 (3.23)
<i>P.v</i> - <i>P.v</i>	7 (11.29)
<i>P.v</i> - <i>P.v</i> - <i>P.v</i>	4 (6.45)
Mix	31 (50)
Time transition of malaria episodes (day)	
Episode 1 to 2	94 $\pm$ 64.46 (14-328)
Episode 2 to 3	72.14 $\pm$ 56.19 (14-214)
Episode 3 to 4	96.5 $\pm$ 101.11 (25-168)

*Plasmodium falciparum* (*P. f*); *Plasmodium vivax* (*P. v*); mix (*P.f* + *P.v*)

## DISCUSSION

The results of this study indicated that more males suffered from recurrent episodes of malaria compared to females. Men were more at risk of suffering from malaria i.e. 2.51 times compared to women, as also shown in other studies.<sup>7,12,13</sup> This might be caused by the occupation of males as a farmer in which this occupation became one of predisposition factors of the malaria incidence.<sup>14</sup> Working as a farmer has made them to work outside leading them to be more potential to have a contact with the malaria vector (*Anopheles sp*),<sup>15</sup> as the due to *Anopheles sp.* activity was outdoor in nature, and exophagic feeding.<sup>16,17</sup> This is supported with information showing that malaria transmission occurs outdoors more.<sup>16</sup>

In Timika, malaria was dominated by those at productive age (64.25%) and this finding was found the same with other studies.<sup>12</sup> Most of the productive age population in endemic areas work as farmers. Agricultural land in malaria endemic area is new land resulted from the forest clearing.<sup>4</sup> The work located near forests and living near forests are one of the risks of malaria.<sup>7,18</sup> This phenomenon was similar to what has occurred in the border of Myanmar-Thailand where land clearing and staying in huts near fields can increase the risk of Plasmodium infection.<sup>18</sup>

Interestingly, the recurrent episodes of malaria were mostly experienced by people with ethnic Javanese living in Timika (42.49%). The results of this study are similar to those of previous studies stating that malaria was found in the immigrants more compared to the natives of Iran and Uganda.<sup>19,20</sup> This might be due to the fact that most of ethnics of the immigrants have been living in Timika for so long, thus they have been acculturated with the local environment and culture in Timika. The population of Timika consists of the natives of Timika and the migrants. The indigenous Timika tribe consists of Kamoro and Amume tribes, while the immigrant are mostly those coming from various regions in Indonesia, one of which is Javanese tribe.<sup>21-24</sup>

The prevalence of recurrent episodes of malaria in this study was found similar to a study in Thailand where 16% of malaria cases

were the recurrent episodes of malaria.<sup>7</sup> 33.87% of cases of the recurrent episodes of malaria in this study occurred in children. The results of this study are in line with other studies showing that children aged  $\leq 10$  years are at risk of experiencing the recurrent episodes of malaria. The risk of recurrent episodes of malaria in children will decrease along with the aging.<sup>25</sup> This risk will recur until the 4<sup>th</sup> year after birth, while other studies mentioned at the age of 7 years.<sup>25,26</sup> The recurrent episodes of malaria in children might be related to the modifications of the immune system, where children who often experience recurrent malaria are more at risk of again experiencing the episodes of malaria.<sup>26,27</sup>

In this study, the distance between malaria episodes was in the range of 72 to 94 days and it was more related to the type of infecting *Plasmodium* and repeated exposure to *Plasmodium sp.* - not caused by the failure of immune system.<sup>7,8</sup> In endemic areas, the recurrent episode of malaria might be associated with the relapse, recrudescence and reinfection condition of *Plasmodium sp.*<sup>28</sup> Also, in endemic areas might occur up to 16 episodes, and the average episode per person per year might reach 5 episodes.<sup>29</sup>

Plasmodium species identified in this study included *P. falciparum* and *P. vivax*. 32% of cases of recurrent episodes of malaria were caused by *Plasmodium falciparum*. These findings were similar to those as reported by previous studies where recurrent infection of *P. falciparum* occurred in 64.51% cases. Meanwhile, other studies have shown that recurrent episodes of malaria can also be caused by different *Plasmodium*.<sup>7,25,30</sup> The results of this study revealed that 50% of cases were the mixed infections that might be associated with the incidence of cerebral malaria, although in mixed infections the proportion of organ failure will be more apparent.<sup>31,32</sup>

In Timika, Malaria cases can be found throughout the year, but an increase in cases occurs from June to September. The increasing cases was accompanied by an increase in rainfall from June to September with the highest rainfall of 819 mm<sup>3</sup> in June.<sup>21</sup> High rainfall will cause areas dominated by swamps, sago forests



and shallow ponds inundated by rainwater. These characteristics are consistent with the characteristics of the Papua region where there are many stagnant waters in swamps, sago forests, shallow pools exposed to direct sunlight.<sup>4</sup> This location is a breeding place for mosquito *Anopheles sp.*<sup>22,23</sup> Also the existence of breeding place of *Anopheles sp.* near forests and agricultural land, and the activity of *Anopheles* mosquitoes, which are more active at night to suck the blood, makes malaria transmission continual.<sup>24</sup>

This research, nevertheless, also has some weaknesses. First, in this study there was no information regarding clinical manifestations of malaria cases due to limited information in medical records. This study also did not look at parasitemia as the examination carried out at the sub-district health center of Naena Muktipura only looked at *Plasmodium* species followed by calculating parasitemia. Patients diagnosed with malaria were also not subjected to re-evaluation of post-treatment microscopic examination. As a consequence, its relation to recurrent episodes and treatment success could not be evaluated. Further research also needs to identify the conditions of submicroscopic malaria and the incidence of recurrent episodes of malaria in Timika, Papua. This is necessary to be able to develop malaria control policies in Timika, Papua. This is in line with the endeavor to break the chain of malaria transmission to reduce the morbidity will decrease and to realize the malaria elimination immediately.

## CONCLUSION

Men are more at risk of suffering from the recurrent episodes of malaria. Moreover, the incidence of recurrent malaria was more found in productive age and migrants, particularly those from Javanese ethnic. These results can be of particular concern to related agencies considering that the residents suffering from the recurrent episodes might become a reservoir of malaria transmission. Also, it is necessary to evaluate malaria examination to ensure the *Plasmodium* elimination in the patient's blood to prevent recurrence and break the chain of malaria transmission, especially in endemic areas.

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## CONFLICT OF INTEREST

The researcher declared that there will be no conflict of interest in this research

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