

The Burden of Malaria Incidence in Subaim, East Halmahera, North Maluku, Indonesia in 2016

Novyan Lusiyana^{1*}, Anggia Fitria Agustin¹, Asril Abdul Sa'ad²

¹Department of Parasitology, Faculty of Medicine, Universitas Islam Indonesia, Yogyakarta, Indonesia; ²Subaim Primary Health Care, East Halmahera, North Maluku, Indonesia

Abstract

Citation: Lusiyana N, Agustin AF, Sa'ad AA. The Burden of Malaria Incidence in Subaim, East Halmahera, North Maluku, Indonesia, in 2016. Open Access Maced J Med Sci. https://doi.org/10.3889/camims.2019.434

Keywords: Malaria; Plasmodium vivax; Plasmodium falciparum; Severe malaria; Incidence; Indonesia

*Correspondence: Novyan Lusiyana. Department of Parasitology, Faculty of Medicine, Universitas Islam, Indonesia, Yogyakarta, Indonesia. E-mail: 107110411@uii.ac.id

Received: 14-Aug-2019; Revised: 15-Sep-2019; Accepted: 16-Sep-2019; Online first: 14-Oct-2019

Copyright: © 2019 Novyan Lusiyana, Anggia Fitria Agustin, Asril Abdul Sa'ad. This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (CC BY-NC 4.0)

Funding: This research did not receive any financial support

Competing Interests: The authors have declared that no competing interests exist

AIM: This study investigated the distribution, characteristics, clinical manifestation and severity of Malaria in East Halmahera, North Maluku.

METHODS: A retrospective and an observational method were used in this study. Data were obtained through analysing medical records of malaria patients from January to December 2016.

RESULTS: There were 89 malaria patients enrolled in the study. The cases infected by *P. vivax* only were 75 cases (84.3%), by *P. falciparum* only (7, 7.8%), and by both infections (7, 7.8%). The incidence of malaria was higher in July and August 2016 in Cemara Jaya district (18, 20.2%) and Baturaja district (17, 19.1%). While severe malaria was higher in children (4, 28.6%) and pregnant women 2 (100%) by *P. vivax* infection.

CONCLUSION: *Plasmodium vivax* infection was higher than *P. falciparum*. Severe *P. vivax* infection was higher than *P. falciparum*, and most of the cases were in children and pregnant women.

Introduction

WHO stated that there are 91 endemic countries for malaria with 212 millions of new cases and 429.000 death. Half of the world's population was at risk for malaria in 2016 included South East region is that still endemic for malaria [1].

Malaria is caused by blood protozoa which is *Plasmodium* spp., transmitted to human through *Anopheles* spp mosquitoes bite [2]. Malaria is an endemic disease, mainly in tropical and subtropical countries [1], [2], [3]. The majority of South-East Asian countries are endemic for malaria [2], [3]. However, there is a decline in incidence and mortality in those countries for 54% and 46%, respectively, between

2010 and 2015 [1], [3]. Indonesia is one of the South-East Asian countries with high endemicity of malaria. This high endemicity is concentrated in East Indonesia. The 5 provinces with high endemicity of malaria are Papua, West Papua, South East Nusa, Maluku and North Maluku [2], [3].

North Maluku was ranked number 5 for malaria burden in 2015 with medium cumulative incident API 1-5. Malaria incidence in an area with medium endemicity tend to increase in 2012-2015, and it reached its peak in 2016 [4]. This study aims to investigate the distribution and characteristics of malaria patients, the clinical manifestation of malaria, as well as its complications.

Material and Methods

The study was approved by the research and an ethical review committee of the Faculty of Medicine, Universitas Islam Indonesia. Inclusion criteria included inpatients who had been diagnosed with malaria that had been proved by laboratory test result in 2016. Exclusion criteria included inpatients who had been diagnosed with malaria without a laboratory test and those who had been diagnosed by RDT only.

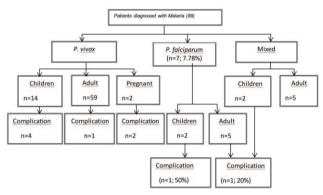


Figure 1: Flow chart of the study

This study assessed some parameters such as age, sex, address, admission month, occupation, clinical symptoms, blood smear examination results, malaria history, malaria treatment, and severe malaria event. Classification of malaria with complications was based on WHO criteria such as haemoglobin < 5 gr/dl. seizure, hyperpyrexia, and hemoglobinuria [5]. Patients were then categorised into age groups < 1y.o; 1-5 y.o; 6-10 y.o; 11-15 y.o; 16-25 y.o; and > 25 groups, occupation groups, bodv y.o; sex temperature, symptoms, previous history, previous treatment, and haemoglobin levels. The data obtained such as clinical manifestations, demographic, and parasitology data were analysed using descriptive analysis method.

Results

Distribution, population characteristics & transmission of Plasmodium sp.

The data were taken from January to December 2016. There were 90 in patients who had been diagnosed with malaria, but 1 patient was excluded as s/he did not meet the inclusion criteria (Figure 1). The monthly incidence of malaria occurred throughout the year 2016 and reached its peak in July and August 2016 for 22 patients (24.72 %) (Figure 2).

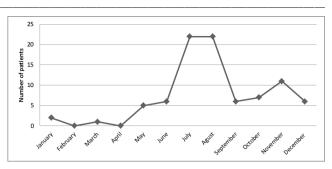


Figure 2: Malaria prevalence in Subaim Primary Health Care, East Halmahera in 2016

The increase of malaria incidence was associated with the transmission factors, including the presence of vectors and gametocyte stage within malaria patients. Gametocyte stage of *P. vivax* and *P. falciparum* in the Subaim region were found in 1% of the total population (Table 1).

Table 1: The distribution of Plasmodium sp. in Subaim Primary Health Care, East Halmahera (n = 89)

Location	Number of the patient, n (%)	Type of Plasmodium			
		P. f		<i>P. v</i>	
		Т	G	Т	G
Baturaja	17 (19.1)	+	-	+	-
Buli	1 (1.12)	-	-	+	-
Bumirestu	7 (7.78)	+	-	+	-
Cemara jaya	18(20.2)	+	-	+	-
Dakaino	2 (2.25)	-	-	+	-
Volly	1 (1.12)	+	-	-	-
Dodaga	1 (1.12)	+	-	+	-
Fayaul	5 (5.62)	-	-	+	-
Gulapapo	4 (4.49)	+	-	+	-
Mekarsari	10 (11.2)	+	-	+	-
Rawamangun	3 (3.37)	-	-	+	-
Subaim	11 (12.3)	+	+	+	+
Ternate	1 (1.12)	-	-	+	-
Toboino	1 (1.12)	-	-	+	-
Tutulingjaya	2 (2.25)	+	-	+	-
Waisuba	4 (4.49)	+	-	+	-
Wasile	1 (1.12)	-	-	+	-

P. f: Plasmodium falciparum; P. v: Plasmodium vivax; T: Trophozoit; G: Gametocyte.

Clinical manifestation & malaria complications

Amongst 89 total patients, there were 40 (44.9%) women and 49 (5.1%) men. Sociodemographic and clinical manifestation data of malaria patients are shown in Table 3.

Severe malaria symptoms amongst patients infected by Plasmodium sp.

There were 9 patients diagnosed with severe malaria. Table 3 describes severe malaria caused by *Plasmodium vivax* infection. Five patients (6.7%) had seizure, 1 patient (1.1%) with hemoglobinuria, 1 patient (1.1%) had hyperpyrexia, and 2 patients (2.25%) got severe anemia (Table 2). The seizure occurred in 4 of 5 patients, and all of them were children under 5 years old, while 1 patient was 17 years old. Severe malaria characterised by hemoglobinuria occurred on a 23-year-old patient, whereas hyperpyrexia (body temperature > 40°C) was found in a patient aged 7 months old.

Table 2: Clinical manifestation of malaria by different Plasmodium sp. in Subaim Primary Health Care, East Halmahera

Characteristic	<i>P. v</i> (n = 75) %	<i>P. f</i> (n = 7) %	<i>P. mix</i> (n = 7) %		
Febrile	55 (73.3)	7 (100)	5 (71.4)		
Chills	19 (23.3)	3 (42.9)	1 (14.3)		
Nausea	31(41.3)	3 (42.9)	4 (57.1)		
Vomiting	40 (53.3)	4 (57.1)	2 (28.6)		
Diarrhea	9 (12.0)	0	1 (14.3)		
Abdominal pain	17 (22.7)	1 (14.3)	2 (28.6)		
Headache	37 (49.3)	2 (28.6)	4 (57.1)		
Seizure	5 (6.7)	1 (14.3)	1 (14.3)		
Hemoglobinuria	1 (1.3)	ÌO Í	`O ´		
Temperature (°C)	38.0 ± 1.1	38.4 ± 0.8	38.2 ± 0.9		
P. f = Plasmodium falciparum; P. v = Plasmodium vivax; Mix = mixed infection.					

It can be seen in Table 3; there was a 1-yearold malaria patient with complications caused by *P. falciparum* infection and characterised by a seizure. Similarly, there was a 4-month-old patient who suffered from a mixed infection and had a seizure.

 Table 3: Sociodemographic and clinical manifestation of malaria in Subaim Primary Health Care, East Halmahera

Characteristics	Proportion		
Age			
< 1 y	6 (6.7%)		
1-5 y	4 (4.5%)		
6-10 y	8 (8.9%)		
11-15 y	7 (7.9%)		
16-25 y	17 (19.1%)		
> 25 y	46 (51.5%)		
Sex	. ,		
Male	49 (55.1 %)		
Female	40 (44.9 %)		
Occupation			
Carpenter	20 (22.5%)		
Employee	17 (19.1%)		
Student	38 (42.7%)		
Housewife	14 (15.7%)		
Body temperature (°C)	38.09 ± 1.1		
Febris	67 (75.3 %)		
Chills	23 (25.8 %)		
Nausea	38 (42.7 %)		
Vomiting	46 (42.7 %)		
Seizure	7 (7.9 %)		
Diarrhoea	10 (11.2 %)		
Abdominal pain	20 (22.5 %)		
Headache	43 (48.3 %)		
Currently on Malaria medication	6 (6.7 %)		
Having malaria history	3 (3.4 %)		
Mean Hb level (g/dl)	7.1 ± 2.3		

Discussion

The Indonesia Government, through the Ministry of Health, has continuously tried to control the incidence of malaria [6]. The decreasing malaria incidence indicates this from year to year [4]. This study described the incidence of malaria at Subaim Primary Health Care, East Halmahera, North Maluku in the year 2016. Malaria remains an endemic disease in East Halmahera and needs to be controlled, especially in East Indonesia [3], [4].

The highest case of malaria in this study was caused by *P. vivax* infection, and this is similar to other studies [3], [7], [8]. The result of this study suggested that the incidence of malaria increased in July and August 2016 (Figure 2) with the highest

incidence of malaria occurred in Cemara Jaya Village in 18 cases and Baturaja in 17 cases. The malaria transmission factor supports this in the presence of gametocytes in the patients' blood [9]. The presence of gametocytes in the bloodstream is also linked with seasonality prevalence at the local state, submicroscopic and asymptomatic infection [10]. Other factors that also affect the emergence of malaria outbreaks are the climate factor from local regions such as La Nina, rainy season, and human population dynamic [8], [11], [12].

The presence of gametocyte phase in the patients' bloodstream is a key factor influencing the transmission of malaria disease. Further, this is also enhanced by several factors, such as the presence of *Anopheles* spp. as a vector, occupational factor, as well as outdoor activities [13]. This study discovered that malaria attacks mostly students and farmers. This might be due to both occupations are owned by the productive age group, which most of their activities are outdoor. Therefore, the possibility to be bitten by *Anopheles* spp. is higher than the other age group [2], [12].

Plasmodium vivax and *P. falciparum* are the most common malaria-causing species in Indonesia [2], [3], [14]. Likewise, *P. vivax* was the most common cause of malaria disease (82.3%) found in this study [3].

Malaria is one of the most common infectious diseases with high morbidity and mortality in Indonesia [4], [14]. In this study, the elements such as age, occupation, especially students and pregnant women are important to be noted as the predisposing factors for severe malaria [14], [15]. Based on this study, the incidence of malaria in Subaim Primary Health Care was mostly suffered by the working-age group and in children aged 15 years or less. This is in line with a previous study [13].

This study described that 25 people were children, likewise to other studies which clarified that malaria cases were found in young age groups [8], [16], [17]. In this study, 6 patients were diagnosed with malaria in the age under 1 year old and the youngest age was 4 months old (1 baby), this is similar to another study [8], [16]. The previous study reported out of 18 malaria-infected children, 7 of them were diagnosed with severe malaria, which characterized by seizures [16]. Therefore, all malaria patients < 1-year-old were diagnosed with severe malaria patient is 17 years-old. Additionally, a study in Ethiopia also showed similar results where children were at higher risk for severe malaria [15], [18], [16].

There are approximately 11.6-28.4% of infected pediatric patients that progress to severe malaria [15], [18] and most of them were infected by *P. vivax*. Our study also found that pediatric patients who were diagnosed with malaria accounted for 16%, and they were infants, preschoolers, and school-aged

children.

Further, this study also discovered pregnant malaria patients was accounted for 2.3%, which is similar to the previous study [19]. It should be noted that all pregnant women in this study were in their first trimester of pregnancy and were diagnosed with severe malaria as they suffered from severe malaria. This is important to note as it has also been reported in previous studies [19], [20]. The results of this study prove that *P. vivax* causes malaria with complications [15]. This suggests that a condition in the endemic area is associated with the disease's pathway.

Some studies suggest that pregnant women with malaria may have a complication with a Hb level < 9.3 g/dl [21], [22]. This complication was not affected by age, parity, gestational age as well as education level [20], [21]. The previous study stated that pregnant women are at high risk for *P. vivax* infection, which causes severe malaria conditions [23]. Immunity status is believed to be the underlying factor that causes severity in pregnant women [24]. In addition, malaria in pregnancy may pose a risk to abortion, prematurity, low birth weight, malaria congenital, intrauterine fetal death or stillbirth [25].

Most of the children with malaria had a complication [15], [18] as were seen in our study. In Africa, where the diseases have a higher prevalence, a study of 263 patients showed that 17.5% were diagnosed with severe malaria [15].

Mixed-infection of Plasmodium spp. was found for 7.8% patients in our study. This number was range from 1.2% to 22.5% worldwide [15], [26]. It is important to be understood that mixed infection can cause severe illness than a single infection. However, based on the current theory, P. falciparum infection is the most common cause of severe malaria [27]. Yet, this study discovered that the incidence of severe malaria is triggered by age, pregnancy and P. vivax infection. The incidence of malaria with complications infants and children that occurred in were characterized by anemia, and seizures [18], [28]. Severe malaria in children is commonly occurred due to the episode of Plasmodium spp. infection, parasitemia degree, parasitic virulence, and immune response [18], [28].

The result of this study supports the results of the previous study, where *P. vivax* is responsible to the incidence of malaria complications [28], [29]. Some metabolites products such as heme and lipid in the patients' blood can be used as a marker of severe malaria which is caused by *P. vivax* infection [29]. Another study proved that in *P. vivax* infection, there is phosphatidylserine, a cytoadherence factor that could be found on the surface of the Plasmodiuminfected erythrocytes [30].

We conclude that *P. vivax* infection was higher than *P. falciparum* and was associated with severe malaria. Severe malaria was higher in children

and pregnant women and was caused by *P. vivax.* Further study needs to find malaria risk factors in East Halmahera, East Maluku.

Acknowledgement

We would like to thank to the Faculty of Medicine Universitas Islam Indonesia for providing this study.

References

1. World Health Organization. World Malaria Report 2016. 2016.

2. Elyazar IRF, Gething PW, Patil AP, Rogayah H, Kusriastuti R, Wismarini DM, Tarmizi SN, Baird JK, Hay SI. Plasmodium falciparum malaria endemicity in indonesia in 2010. PLoS One. 2011; 6(6):e21315. <u>https://doi.org/10.1371/journal.pone.0021315</u>

3. Surjadjaja C, Surya A, Baird JK. Epidemiology of Plasmodium vivax in Indonesia. Am J Trop Med Hyg. 2016; 95(6):121-132. https://doi.org/10.4269/ajtmh.16-0093

4. Kementrian Kesehatan Republik Indonesia. Pusat Data Dan Informasi Penyakit Malaria, 2016.

5. Direktorat Jenderal Pengendalian Penyakit dan Penyehatan Lingkungan Departemen Kesehatan RI. Pedoman tatalaksana malaria, 2008.

6. Kusriastuti R, Surya A. New treatment policy of malaria as a part of malaria control program in Indonesia. Acta Med Indones. 2012; 44(3):265-9.

7. Anvikar AR, Shah N, Dhariwal AC, Sonal GS, Pradhan MM, Ghosh SK, Valencha N. Epidemiology of Plasmodium vivax malaria in India. Am J Trop Med Hyg. 2016; 95(6):108-120. https://doi.org/10.4269/ajtmh.16-0163

8. Woyessa A, Deressa W, Ali A, Lindtjørn B. Prevalence of malaria infection in Butajira area. Malar J. 2012; 11(1);84. https://doi.org/10.1186/1475-2875-11-84

9. Diallo A, Sié A, Sirima S, Sylla K, Ndiaye M, Bountogo M, Ouedraogo E, Tine R, Ndiaye A, Coulibaly B, Ouedraogo A. An epidemiological study to assess Plasmodium falciparum parasite prevalence and malaria control measures in Burkina Faso and Senegal. Malaria journal. 2017; 16(1):1-12. https://doi.org/10.1186/s12936-017-1715-1

10. Rovira-Vallbona E, Contreras-Mancilla JJ, Ramirez R, Guzmán-Guzmán M, Carrasco-Escobar G, Llanos-Cuentas A, Vinetz JM, Gamboa D, Rosanas-Urgell A. Predominance of asymptomatic and sub-microscopic infections characterizes the Plasmodium gametocyte reservoir in the Peruvian Amazon. PLoS Negl Trop Dis. 2017; 11(7):1-18.

https://doi.org/10.1371/journal.pntd.0005674

11. Ikeda T, Behera SK, Morioka Y, Minakawa N, Hashizume M, Tsuzuki A, Maharaj R, Kruger P. Seasonally lagged effects of climatic factors on malaria incidence in South Africa. Sci Rep. 2017; 7(1):1-9. <u>https://doi.org/10.1038/s41598-017-02680-6</u>

12. Vajda E, Webb C. Assessing the Risk Factors Associated with Malaria in the Highlands of Ethiopia: What Do We Need to Know? Trop Med Infect Dis. 2017; 2(1):4. https://doi.org/10.3390/tropicalmed2010004

13. Chirebvu E, Chimbari MJ, Ngwenya BN. Assessment of Risk Factors Associated with Malaria Transmission in Tubu Village,

Northern Botswana. Malar Res Treat. 2014; 2014:1-10. https://doi.org/10.1155/2014/403069

14. Karyana M, Burdarm L, Yeung S, Kenangalem E, Wariker N, Maristela R, Umana KG, Vemuri R, Okoseray MJ, Penttinen PM. Malaria morbidity in Papua Indonesia, an area with multidrug resistant Plasmodium vivax and Plasmodium falciparum. Malar J. 2008; 7:1-10. <u>https://doi.org/10.1186/1475-2875-7-148</u>

15. Geleta G, Ketema T. Severe Malaria Associated with Plasmodium falciparum and P. vivax among Children in Pawe Hospital, Northwest Ethiopia. Malar Res Treat. 2016; 2016:1-7. https://doi.org/10.1155/2016/1240962

16. D'Acremont V, Kilowoko M, Kyungu E, Philipina S, Sangu W, Kahama-Maro J, Lengeler C, Cherpillod P, Kaiser L, Genton B. Beyond Malaria - Causes of Fever in Outpatient Tanzanian Children. N Engl J Med. 2014; 370(9):809-817. https://doi.org/10.1056/NEJMoa1214482

17. Patricia D, Mboumba M, Bouyou-akotet MK, Mawili-mboumba DP, Akotet MKB, Kendjo E, Nzamba J, Medang MO. Increase in malaria prevalence and age of at risk population in different areas of Gabon Increase in malaria prevalence and age of at risk population in different areas of Gabon. Malar J. 2013; 12(1):1-7. https://doi.org/10.1186/1475-2875-12-3

18. Gonçalves BP, Huang C, Morrison R, Holte S, Kabyemela E, Prevots DR, Fried M, Duffy PE. Parasite Burden and Severity of Malaria in Tanzanian Children. N Engl J Med. 2014; 370(19):1799-1808. <u>https://doi.org/10.1056/NEJMoa1303944</u>

19. Fana SA, Bunza MDA, Anka SA, Imam AU, Nataala SU. Prevalence and risk factors associated with malaria infection among pregnant women in a semi-urban community of northwestern Nigeria. Infect Dis Poverty. 2015; 4(1):4-8. https://doi.org/10.1186/s40249-015-0054-0

20. Oladeinde BH, Omoregie R, Odia I, Oladeinde OB. Prevalence of malaria and anemia among pregnant women attending a traditional birth home in Benin city, Nigeria. Oman Med J. 2012; 27(3):232-236. <u>https://doi.org/10.5001/omj.2012.52</u>

21. Ishag A, Amar H, Mustafa I. Prevalence and risk factors for Plasmodium falciparum malaria in pregnant women of eastern Sudan Malar. J. 2005; 4(18):1475-2875.

22. Tonga C, Kimbi HK, Anchang-Kimbi JK, Nyabeyeu HN, Bissemou ZB, Lehman LG. Malaria Risk Factors in Women on Intermittent Preventive Treatment at Delivery and Their Effects on Pregnancy Outcome in Sanaga-Maritime, Cameroon. PLoS One. 2013; 8(6):E65876. <u>https://doi.org/10.1371/journal.pone.0065876</u>

23. McLean ARD, Ataide R, Simpson JA, Beeson JG, Fowkes FJI. Malaria and immunity during pregnancy and postpartum: A tale of two species. Parasitology. 2015; 142(8):999-1015. https://doi.org/10.1017/S0031182015000074

24. Chandrasiri UP, Fowkes FJI, Beeson JG, Richards JS, Kamiza S, Maleta K, Ashorn P, Rogerson SJ. Association between malaria immunity and pregnancy outcomes among Malawian pregnant women receiving nutrient supplementation. Malar J. 2016; 15(1):1-9. https://doi.org/10.1186/s12936-016-1597-7

25. Moya-Alvarez V, Abellana R, Cot M. Pregnancy-associated malaria and malaria in infants: An old problem with present consequences. Malar J. 2014; 13(1):1-10. https://doi.org/10.1186/1475-2875-13-271

26. Addimas T, Gabriel M, Mulugeta A, Francis K. Detection of mixed infection level of Plasmodium falciparum and Plasmodium vivax by SYBR green I-based real-time PCR in North Gondar, north-west Ethiopia. Malar J. 2014; 13:1-8. https://doi.org/10.1186/1475-2875-13-411

27. Mankhambo L, Phiri A, Mallewa M, Molyneux M, Management of severe malaria. 2010; 7(1):27-38. https://doi.org/10.2217/thy.09.81

28. Im JH, Kwon HY, Baek J, Park SW, Durey A, Lee KH, Chung MH, Lee JS. Severe Plasmodium vivax infection in Korea. Malar J. 2017; 16(1):1-8. <u>https://doi.org/10.1186/s12936-017-1684-4</u>

29. Gardinassi LG, Cordy RJ, Lacerda MVG, Salinas JL, Monteiroet WM, Melo GC, Siqueira AM, Val FF, Tran FL. Metabolome-wide association study of peripheral parasitemia in Plasmodium vivax malaria. Int J Med Microbiol. 2017; 307(8):533-541. <u>https://doi.org/10.1016/j.ijmm.2017.09.002</u>

30. Totino PR, Lopes SC. Insights into the cytoadherence phenomenon of Plasmodium vivax: The putative role of phosphatidylserine. Front Immunol. 2017; 8:1-6. https://doi.org/10.3389/fimmu.2017.01148