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Original Article

Clinical and Hemoglobin Profile of Malaria Patients in Karitas Hospital, Southwest Sumba District, Indonesia during 2017

Alvin Johan[1*], Audrey Natalia[2], William Djauhari[3], Rambu Farah Effendi[4]
[1] Watu Kawula Healthcare Center, Southwest Sumba
[2] Karitas Hospital, Southwest Sumba
[3] Amahai Healthcare Center, Central Maluku
[4] Department of Internal Medicine, Waikabubak Regional General Hospital, West Sumba

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ABSTRACT

Malaria infections in high endemic areas are not pathognomonic and often show non-specific symptoms. The Southwest Sumba district is a high endemic area of malaria with the annual parasite incidence (API) of 14.48‰. The research conducted in this area was to identify the clinical and hemoglobin profile of malaria patients and to obtain comprehensive information on the clinical characteristics of malaria in a high endemic area of Southwest Sumba district. This is a descriptive cross-sectional study. The data was obtained from the medical record of malaria patients between January 1st and December 31st, 2017 in Karitas Hospital, Southwest Sumba district. Inclusion criteria were patients with asexual stages of Plasmodium spp. on their Giemsa-stained thick and thin peripheral blood smears examination. Exclusion criteria were malaria patients with coexisting diseases and who had taken medication before admitted to the hospital. The total number of patients was 322 patients, 50.6% of the subjects were ≥ 15 years old and 59.3% were male. Among 322 patients, 133 subjects were treated as inpatients. The result shows that most infection was caused by a single infection of P. falciparum. The most common clinical symptom was fever (98.4%), followed by headache, vomiting, cough, and nausea. The most common physical finding was the axillary temperature of > 37.5°C (87.6%) followed by anemic conjunctiva and hepatomegaly, which was mostly found in pediatric patients. The number of patients with hemoglobin level ≤ 10 g/dL was 129. The MCV <80 fL was found in 79% of patients with anemia. Severe malaria was found in 116 subjects in this study according to severe malaria criteria set by the Indonesian Ministry of Health. Study results were consistent with other existing studies from other high endemic areas in East Nusa Tenggara province.

Keywords: *Malaria, Plasmodium, Clinical profile, Hemoglobin, East Nusa Tenggara*

ABSTRAK

Infeksi malaria di daerah endemis tinggi seringkali tidak khas dengan keluhan klinis tidak spesifik. Kabupaten Sumba Barat Daya merupakan daerah endemis tinggi malaria dengan annual parasite incidence (API) sebesar 14.48‰. Penelitian yang dilakukan pada daerah ini untuk mengidentifikasi profil klinis dan hemoglobin pasien malaria dan memperoleh informasi komprehensif mengenai karakteristik klinis malaria di kabupaten Sumba Barat Daya yang merupakan daerah endemis tinggi. Penelitian ini adalah penelitian deskriptif dengan metode potong lintang. Data diambil dari rekam medis pasien malaria dari tanggal 1 Januari sampai dengan 31 Desember 2017 di rumah sakit Karitas, kabupaten Sumba Barat Daya. Kriteria inklusi adalah pasien yang melakukan pemeriksaan hapus darah tepi tebal tipis dengan pewarnaan Giemsa dan ditemukan stadium aseksual Plasmodium spp. Kriteria eksklusi adalah pasien malaria dengan penyakit penyerta dan pasien yang sudah meminum obat sebelum datang ke rumah sakit. Total pasien berjumlah 322 pasien, 50.6% termasuk dalam kelompok usia ≥ 15 tahun dan 59.3% berjenis kelamin laki-laki. Dari 322 pasien, 133 pasien dirawat inap. Hasil penelitian menunjukkan kebanyakan infeksi malaria disebabkan oleh infeksi tunggal P. falciparum. Gejala klinis yang paling sering ditemukan adalah demam (98.4%), diikuti oleh sakit kepala, muntah, batuk, dan mual. Hasil pemeriksaan fisik

Corresponding Author.
E-mail: alvinjohanmd@gmail.com

yang paling banyak ditemukan adalah suhu aksila > 37.5°C (87.6%) diikuti oleh konjungtiva anemis dan hepatomegali yang kebanyakan ditemukan pada pasien pediatrik. Sebanyak 129 pasien memiliki kadar hemoglobin ≤ 10 g/dL. Kadar MCV < 80 fL ditemukan pada 79% pasien dengan anemia. Malaria berat ditemukan pada 116 subjek dalam penelitian ini berdasarkan kriteria dari Kementerian Kesehatan Indonesia. Hasil penelitian konsisten dengan penelitian lain di daerah endemis tinggi di provinsi Nusa Tenggara Timur.

Kata kunci: *Malaria, Plasmodium, Profil Klinis, Hemoglobin, Nusa Tenggara Timur*

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INTRODUCTION

Malaria is a disease caused by a *Plasmodium spp.* infection and transmitted through *Anopheles spp.* mosquito bites.[1,2] In 2015, there were 214 million estimated cases of malaria worldwide, with the highest prevalence in countries with a tropical climate such as Africa, South America, and Southeast Asia.[2,3] Classical symptoms of malaria include acute paroxysmal fever followed by shivering and excessive sweating. Different types of *Plasmodium spp.* may cause different fever patterns. Infection of *Plasmodium falciparum* and *Plasmodium knowlesi may* cause intermittent or continuous fever, *Plasmodium vivax* and *Plasmodium ovale* may cause 2- days interval paroxysmal fever, while *Plasmodium malaria* infection may cause 3-days intermittent fever. These classical symptoms often were found in the non-immune population from non-endemic areas.[1,2] Other non-classical symptoms such as headache, nausea, vomiting, diarrhea and muscle pain can also be found. These non-specific symptoms were often found in the population of high endemic areas regardless of high blood parasite density. Several cases also show that patients with high parasite density maybe asymptomatic.[1,4]

The endemicity of malaria is determined by the number of Annual Parasite Incidence (API), which determined by the number of morbidity per 1,000 populations at risk of infection. The endemicity of malaria can be divided into 4 categories, high endemic areas with API > 5‰, moderate endemic areas with API 1-5‰, low endemic areas with API 0-1‰ and non-endemic areas with API 0‰.[5] National health profile of East Nusa Tenggara province from the year of 2015 showed there were 4,622 malaria cases from 319,119 populations at risk in Southwest Sumba district, with API of 14.48‰.[6]

The research on the clinical profile of malaria in high endemic areas, especially in East Nusa Tenggara province was lacked. Within the last 5 years, there were only two researches conducted by Mau, et al from Central Sumba district in 2014[7] and Junardi, et al from Belu district in 2017.[8] Mau, et al[7] did not discuss physical findings in malaria patients, while Junardi, et al[8] only focused on the infection of *P. falciparum*.

This research focused on demographical data, history of clinical symptoms, finding of clinical signs and hemoglobin level to obtain comprehensive information on clinical characteristics of malaria in a high endemic area of Southwest Sumba district.

MATERIALS AND METHODS

This research was a descriptive study with cross-sectional methodology. The data were collected from medical records of patients with a microscopic diagnosis of malaria between January 1st and December 31st, 2017 in Karitas Hospital. Ethical clearance was issued by the Medical Committee of Karitas Hospital numbered 008/DIR.BPIP.E/RSK/VI/208. Inclusion criteria were patients with available Giemsa-stained thick and thin peripheral blood smears examination and positive containing asexual stages of *Plasmodium spp.*[2] Exclusion criteria were malaria patients with

coexisting diseases or who have taken medication before admitted to the hospital. A total number of 490 malaria patients involved in this study. However, 168 subjects out of them were then excluded. One hundred out of 168 subjects were due to having a coexisting disease, while 68 subjects had taken medication before admission. Therefore, the total number of 322 subjects were used in this study.

The density of the parasite was determined by a semi-quantitative or plus-system.[9,10] The data were then analyzed using cross-tabulation on the IBM SPSS Statistic 24 software.

RESULTS AND DISCUSSION

Basic Characteristics of Subjects

The basic characteristics of 322 subjects were described in Table 1.

Table 1. Basic Characteristics of Subjects

Characteristics	n (%)
Demographic characteristics	
Gender	
Male	191 (59.3)
Female	131 (40.7)
Age (years), median (range)	15 (0.79)
Age group	
0 – <6 years	73 (22.7)
6 – <15 years	86 (26.7)
≥15 years	163 (50.6)
Clinical characteristics	
Severe malaria infection	116 (36.0)
Uncomplicated malaria infection	206 (64.0)
Admission Status	
Outpatient	189 (58.7)
Inpatient	133 (41.3)

Based on the age group, malaria subjects were categorized into three age groups (0 – <6 years; 6 – < 15 years; ≥ 15 years). The majority of malaria-infected subjects were ≥ 15 years old. Most malaria research in Indonesia found that ≥ 15 years old age group was more vulnerable to malaria infection[11–15] probably due to the frequent outdoor activity of this age group. The exophagic and exophilic behavior of *Anopheles* indeed play a role in higher malaria infection in this age group.[14,16]

Microscopic-Based Diagnosis

The results of microscopic examination of Giemsa-stained thick and thin peripheral blood smears showed that 265 (82.3%) out of 322 patients were infected with *P. falciparum*, 43 (13.4%) were infected with *P. vivax* and 3 (0.9%) were infected with *P. malaria* (Table 2). Mixed infection was found in 11 (3.4%) subjects, where 10 patients were infected with *P. falciparum* and *P. vivax*. One patient was infected with *P. falciparum*, *P. vivax*, and *P. malaria*. These results were consistent with Purba, et al[16] that concluded malaria cases in East Nusa Tenggara province were mainly caused by *P. falciparum* and *P. vivax*. A low rate of *P. vivax* infection in an area indicates successful management of malaria cases because the hypnozoites that withstand inside the liver were well treated.[16] Infections of *P. ovale* and *P. knowlesi* were not found in our study. Species of *P. ovale* often found in West Africa.[2,3] While *P. knowlesi* infections occurred in the West Borneo, where *Macaca fascicularis* and *Macaca nemestrina* are the main host.[17]

Parasite Density

Parasite density was measured using a semi-quantitative method on Giemsa-stained thick

Table 2. Parasite Density based on Plasmodium Species

Parasite density	*Plasmodium spp.* [n (%)]				Total n = 322
	P. falciparum n = 265	*P. vivax* n = 43	*P. malariae* n = 3	Mixed infection n = 11	
+	35 (13.2)	8 (18.6)	1 (33.3)	1 (9.1)	45 (14.0)
++	24 (9.1)	7 (16.3)	1 (33.3)	4 (36.4)	36 (11.1)
+++	48 (18.1)	15 (34.9)	1 (33.3)	2 (18.2)	66 (20.6)
++++	158 (59.6)	13 (30.2)	0 (0.0)	4 (36.4)	175 (54.3)

and thin peripheral blood smears. This method indicated the degree of infection, (+) for 1-10 asexual parasites per 100 thick film fields, (++) for 11-100 asexual parasites per 100 thick film fields, (+++) for 1- 10 asexual parasites per single thick film field, and (++++) for > 10 asexual parasites per single thick film field.[9,10] Distribution of parasite density based on *Plasmodium* species is available in Table 2.

Clinical Symptoms

The clinical symptoms were summarized in Table 3. Fever was observed in almost all (98.4%) of malaria subjects. This finding is consistent with previous studies by Mau, et al[7] and Junardi, et al,[8] where 96.8% and 100% of malaria patients respectively underwent fever.[7,8] Fever is the most common symptom of malaria infection especially in high endemic areas of malaria, therefore, patient with fever leads to clinical suspicion of malaria infection.[1,2] Malaria toxin called *glycosylphosphatidylinositol* (GPI) and hemozoin are released when schizonts burst. The toxins trigger the immune system to release pyrogenic pro-inflammatory cytokines such as tumor necrosis factor (TNF)-α, interleukin (IL)-1 and IL-6.[18]

Headache was the most common presenting symptom in malaria subjects after fever, this finding is consistent with other studies by Mau, et al[7] and Purwanto, et al[14] in Indonesia, Herrera, et al[19] in Colombia, and Deshwal, et al[20] in

Table 3. Clinical Symptoms based on *Plasmodium* Species

System	Symptoms	*Plasmodium* species [n (%)]				Total n = 322
		P. falciparum n = 265	*P. vivax* n = 43	*P. malaria* n = 3	Mixed infection n = 11	
General Respiratory	Fever	261 (98.5)	42 (97.7)	3 (100)	11 (100)	317 (98.4)
	Cough	64 (24.2)	12 (27.9)	1 (33.3)	2 (18.2)	79 (24.5)
	Runny nose	33 (12.5)	5 (11.6)	1 (33.3)	2 (18.2)	41 (12.7)
	Breathlessness[a]	3 (1.1)	2 (4.7)	0 (0)	0 (0)	5 (1.6)
	Sore throat	7 (2.6)	1 (2.3)	0 (0)	0 (0)	8 (2.5)
Gastro-intestinal	Nausea	56 (21.1)	6 (14)	1(33.3)	3 (27.3)	66 (20.5)
	Vomiting	99 (37.4)	6 (14)	2 (66.7)	3 (27.3)	110 (34.2)
	Epigastric pain	47 (17.7)	4 (9.3)	0 (0)	0 (0)	51 (15.8)
	Anorexia	50 (18.9)	7 (16.3)	2 (66.7)	3 (27.3)	62 (19.3)
	Diarrhea	16 (6)	1 (2.3)	0 (0)	0 (0)	17 (5.3)
	Constipation	2 (0.8)	0 (0)	0 (0)	0 (0)	2 (0.6)
	Abdominal pain[b]	20 (7.5)	2 (4.7)	0 (0)	0 (0)	22 (6.8)
Neurology	Headache	111 (41.9)	19 (44.2)	1 (33.3)	2 (18.2)	133 (41.3)
	Unconscious	18 (6.8)	0 (0)	0 (0)	0 (0)	18 (5.6)
	Seizure 1x	4 (1.5)	2 (4.7)	0 (0)	0 (0)	6 (1.9)
	Recurrent seizure	12 (4.5)	1 (2.3)	0 (0)	1 (9.1)	14 (4.3)
	Behavioral change	7 (2.6)	0 (0)	0 (0)	0 (0)	7 (2.2)
Hematology	Lethargy	34 (12.8)	7 (16.3)	1 (33.3)	1 (9.1)	43 (13.4)
	Pale	24 (9.1)	1 (2.3)	0 (0)	0 (0)	25 (7.8)
	Icteric[c]	1 (0.4)	0 (0)	0 (0)	0 (0)	1 (0.3)
	Bleeding[d]	1 (0.4)	0 (0)	0 (0)	0 (0)	1 (0.3)
Musculo-skeletal	Muscle pain	11 (4.2)	7 (16.3)	0 (0)	0 (0)	18 (5.6)
	Joint pain	7 (2.6)	1 (2.3)	0 (0)	0 (0)	8 (2.5)
	Back pain	9 (3.4)	3 (7)	0 (0)	0 (0)	12 (3.7)

a: all patients had SpO_2 of > 95%
b: all other regions of abdomen beside the epigastric region
c: icteric on conjunctiva or skin
d: the only bleeding manifestation found in this study was anterior epistaxis

India. Headache in malaria infection has an acute onset with non-specific pain distribution.[21] Pro-inflammatory cytokines such as TNF-α and IL-6 are believed to play an important role in the pathogenesis of headaches.[2,17,22] Pain intensity and frequency of headache between cerebral malaria and non-severe malaria infection is clinically indistinguishable.[21]

Two studies by Muddaiah, et al[23] and Sonawane, et al[24] from India showed a higher incidence of nausea and vomiting than a headache in malaria subjects. The study by Junardi, et al[8] also found the most common symptoms in malaria subjects were nausea and vomiting, followed by headache, with an incidence of 67.7% and 50.7% respectively. These findings indicated that geographically different endemic areas of malaria are resulting in different profiles of malaria symptoms. Body responses to malaria toxins are believed to cause nausea. Vomiting has been associated with high parasite density in malaria subjects.[25] Anstey, et al[26] in Australia reported cough from malaria patients with an incidence of 36% in *P. falciparum*-infected subjects and 53% in *P. vivax*-infected subjects. The cough was not observed by subjects before malaria infection. The cough was described as non-productive and mostly found on subjects who smoked cigarettes. Auscultation and chest X-ray performed on malaria subjects with cough revealed no abnormalities. The cough is thought to be caused by increased activity of intravascular monocytes in the lungs which lead to subclinical endothelial dysfunction.[26] The suspicion of malaria infection should not be dismissed in patients presenting with fever and cough in a high endemic area. It is difficult to distinguish whether the cough is caused by malaria or other respiratory viruses. Testing for malaria is important in patients presenting with flu-like symptoms at health centers in high endemic area.[25]

Physical Findings

Meaningful physical findings found in subjects are listed in Table 4. In all cases of the Glasgow Coma Scale (GCS) <11, *P. falciparum* was found on Giemsa-stained thick and thin peripheral blood smear. Hepatomegaly (26.8%) was more prevalent in malaria subjects in Karitas hospital than splenomegaly (15.1%). This finding was in contrast with the study by Purwanto, et al[14] that found hepatomegaly (15.4%) was less prevalent than splenomegaly (27.4%). This discrepancy between the two studies was likely due to the difference in demographic characteristics of the subjects. Most subjects in Purwanto, et al[14] study was in 31-40 years old age group and just 0.6% of the subjects aged < 10 years old.[14] Children with malaria infection are more likely to develop hepatomegaly.[2] Hepatomegaly is caused by an inflammatory reaction and usually non-tender on palpation.[27,28] Histopathology observation of hepatic portal system in a patient with severe malaria showed increased activity of nuclear factor-kappa B p65 (NF-κBp65), followed by kupffer cells and lymphocytes apoptosis.[29] Malarial hepatopathy is a term used to described hepatic dysfunction in patients with severe malaria as shown by increased serum bilirubin and transaminase enzymes. Co-infection of hepatitis viruses and exposure to hepatotoxic substances must be excluded to confirm the

Table 4. Physical Findings based on *Plasmodium* Species

Physical Findings	*Plasmodium* species [n (%)]				Total n = 322
	P. falciparum n = 265	*P. vivax* n = 43	*P. malaria* n = 3	Mixed infection n = 11	
Axillary temperature > 37.5°C	233 (87.9)	35 (81.4)	3 (100)	11 (100)	282 (87.6)
Hepatomegaly	71 (26.8)	5 (11.6)	0 (0)	0 (0)	76 (23.6)
Splenomegaly	40 (15.1)	6 (14)	1 (33.3)	0 (0)	47 (14.5)
Glasgow coma scale <11	15 (5.7)	0 (0)	0 (0)	1 (9.1)	16 (5)
Icteric sclera	15 (5.7)	1 (2.3)	0 (0)	1 (9.1)	17 (5.3)
Anemic conjunctiva	82 (30.9)	2 (4.7)	2 (66.7)	2 (18.2)	88 (27.3)

diagnosis of malarial hepatopathy in malaria subjects. Splenomegaly is caused by increased erythrocytes destruction, there is also increased activity of mature lymphocytes attacking the erythrocytes, leading to hypertrophy.[27]

Decreased consciousness may indicate central nervous system involvements in malaria infection. However, not all unconscious patients should be treated as having severe malaria.

WHO 2015 criteria of severe malaria use GCS < 11 as the cut-off for clinical diagnosis of severe malaria. Comatose patients who were tested positive for *P. falciparum* infection are diagnosed with cerebral malaria which has a worse prognosis.[2,9,22,30] Erythrocytes infected by *P. falciparum* express *Plasmodium falciparum erythrocyte membrane adhesive protein* 1 (PfEMP1) which will bond with *intracellular adhesion molecule* 1 (ICAM-1) on neurovascular endothelium, causing sequestration that leads to diffuse symmetrical encephalopathy.[2,30]

The icteric sclera was found in 5.3% of subjects in this study, similar to the study by Purwanto, et al[14] which found icteric sclera in 3.4% of subjects. The icteric sclera is caused by abnormal deposition of bilirubin in the sclera. According to WHO 2015 criteria, malaria patient with total serum bilirubin > 3 mg/dL is considered to have severe malaria infection.[1,2] Icteric sclera was noticeable only in 68% of patients with total serum bilirubin >3.1 mg/dl in one study.[27] A routine check of the total of serum bilirubin in malaria subject is suggested, even when sclera appears anicteric on initial examination.

Anemic conjunctiva indicates oxyhemoglobin deficiency in conjunctiva capillaries, a common finding in patients with anemia.[27]

Hemoglobin Profile

Hemoglobin profile was observed in 270 (83.9%) out of 322 subjects as shown in Table 5. Anemia, which defined as hemoglobin level Ý 10 g/dL was found in 129 subjects, only

Anemia, which defined as hemoglobin level ≤ 10 g/dL was found in 129 subjects, only 55.8% of them appeared to have anemic conjunctiva on initial examination. From 85 subjects whose conjunctiva appear anemic on physical examination, 84.7% was confirmed to have anemia from blood count. Literature showed that anemic conjunctiva has sensitivity and specificity of 25-62% and 82-97% respectively for the diagnosis of anemia.[27] According to the Indonesian Ministry of Health[1], severe malaria in malaria cases in a high endemic area was determined by hemoglobin level < 5 g/dL in children and < 7 g/dL in adults.

Acute malaria infection usually causes normochromic normocytic anemia by causing hemolysis of *Plasmodium*-infected erythrocytes, accelerated removal by the spleen, and dyserythropoietic.[2,31,32] In this study, mean corpuscular volume (MCV) < 80 fL were found in 102 (79%) subjects with anemia. The high number of microcytic anemia in this study reflected the chronicity of malaria infection in the area. The underlying medical conditions such as iron deficiency, hemoglobinopathy, or chronic diseases may also cause microcytic anemia.[32,33] Further tests should be done to confirm the etiology of anemia in these subjects and cannot be done due to limited laboratory equipment.

Severe Malaria

Based on the clinical symptoms, physical findings and laboratory findings, 116 (36%)

Table 5. Hemoglobin Profile based on *Plasmodium* Species

Hemoglobin (g/dL)	*Plasmodium* species [n(%)]				Total n = 270
	P. falciparum n = 225	*P. vivax* n = 31	*P. malaria* n = 3	Mixed infection n = 11	
>10	111 (49.3)	22 (71.0)	0 (0)	8 (72.7)	141 (52.2)
5 – 10	96 (42.7)	8 (25.8)	3 (100)	3 (27.3)	110 (40.7)
<5	18 (8.0)	1 (3.2)	0 (0)	0 (0)	19 (7.0)

subjects in this study had met the criteria of severe malaria infection as stated by Indonesian Ministry of Health.[1] Majority (68.1%) of subjects with severe malaria were from <15 years old age group. *P. falciparum* was found in 87.9% of subjects with severe malaria. Six out of 116 subjects with severe malaria infection were deceased. All of the deceased subjects had *P. falciparum* infection with a parasite density of ++++.

Study Limitations

This descriptive study has some limitations. Medical records used in this study did not reflect all clinical symptoms underwent by malaria patients, probably did not ask by the physician during history taking or some information was not documented. Physical findings may vary between examiners as it was determined by examiner's experiences. Another limitation is ancillary tests that are not routinely done in all malaria patients, so the true incidence of severe malaria based on the Indonesian Ministry of Health criteria may be higher than reported in this study.

CONCLUSION

Research for clinical and hemoglobin profiles of malaria especially in high endemic areas has been lacking. This is important as malaria infection in high endemic areas is often not pathognomonic. This study in Karitas Hospital, Southwest Sumba District which was a high endemic area of malaria showed similar results with previous studies in other areas of East Nusa Tenggara province within the last 5 years. Our study revealed that most of the malaria subjects in Southwest Sumba district were infected by *P. falciparum.* Fever was the highest presenting clinical symptom and physical finding in malaria subjects. The most common clinical symptoms following fever were headache, vomiting, cough, and nausea. Anemia and hepatomegaly were the most common physical findings following fever. Hemoglobin profile of malaria patients in Karitas hospital showed that anemia was found in less than half of subjects. Most of the anemic subjects had microcytic anemia. Severe malaria was found mostly in *P. falciparum* infection, and all the death of patients was due to *P. falciparum* infection.

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CONFLICT OF INTEREST

There was no conflict of interest for this research.

REFERENCES

1. Samad I, Theodora M, Mulyani PS, editors. Buku Saku Penatalaksanaan Kasus Malaria. Jakarta: Ditjen Pencegahan dan Pengendalian Penyakit Kementerian Kesehatan RI; 2017.
2. White NJ, Breman JG. Malaria. In: Kasper DL, Fauci AS, Hauser S, et al, editors, Harrison's principles of internal medicine, 19th ed. New York: The McGraw-Hill Companies, Inc.; 2015.
3. Phillips MA, Burrows JN, Manyando C, van Huijsduijnen RH, Van Voorhis WC, Wells TNC. Malaria. Nat Rev Dis Primer. 2017 Aug 3;3:17050.
4. Liwan A. Diagnosis dan Penatalaksanaan Malaria Tanpa Komplikasi pada Anak. Cermin Dunia Kedokteran; 2015.
5. Anastasia H, Nurjana M, Jastul. Validitas Gejala Klinis Sebagai Indikator Untuk Memprediksi Kasus Malaria Di Indonesia. Media Litbangkes. 2013 Dec;23(4):149-57.
6. Mete K, Hala K. Profil Kesehatan Provinsi Nusa Tenggara Timur Tahun 2015. Dinas Kesehatan Provinsi Nusa Tenggara Timur; 2015.
7. Mau F, Sopi IB. Kesesuaian Gejala Klinis Malaria dengan Parasitemia Positif di Wilayah Puskesmas Wairasa Kabupaten Sumba Tengah Provinsi Nusa Tenggara Timur. Media Peneliti Dan Pengemb Kesehat. 2014;24(2):75–80.
8. Junardi RB, Somia KA. Karakteristik Klinis Malaria Tropika pada Pasien Rawat Inap di Rumah Sakit Umum Daerah MGR. Gabriel Manek, SVD Atambua Periode September 2013 - Februari 2014. E-J Med. 2017 Jul;6(7).
9. Pedoman Teknis Pemeriksaan Parasit Malaria. Direktorat Jenderal Pencegahan dan Pengendalian

Penyakit Kementerian Kesehatan Republik Indonesia; 2017.
10. World Health Organization. Manual of basic techniques for a health laboratory. 2nd ed. Geneva:World Health Organization.2003;p182.
11. Irawan H, Merry MS, Wuryaningsih NS, Baskoro T. Profil Hematologik Berdasarkan Jenis Plasmodium pada Pasien Malaria Rawat Inap di RSK Lindimara, Sumba Timur. Berk Ilm Kedokt Duta Wacana. 2017 Apr;2(2):394–401.
12. Dwithania M, Irawati N, Rasyid R. Insiden Malaria di Puskesmas Sungai Durian dan Puskesmas Talawi Kota Sawahlunto Bulan Oktober 2011 sampai Februari 2012. J Kesehat Andalas. 2013;2(2):76–9.
13. Gusra T, Irawati N, Sulastri D. Gambaran Penyakit Malaria di Puskesmas Tarusan dan Puskesmas Balai Selasa Kabupaten Pesisir Selatan periode Januari-Maret 2013. J Kesehat Andalas. 2014;3(2).
14. Purwanto DS, Ottay RI. Profil penyakit malaria pada penderita rawat inap di rumah sakit umum daerah kota bitung. J Biomedik. 2011;3(3).
15. Nababan R, Umniyati SR. Faktor lingkungan dan malaria yang memengaruhi kasus malaria di daerah endemis tertinggi di Jawa Tengah: analisis sistem informasi geografis. Ber Kedokt Masy. 34(1):11–8.
16. Purba IE, Hadi UK, Hakim L. Analisis Pengendalian Malaria di Provinsi Nusa Tenggara Timur dan Rencana Strategis Untuk Mencapai Eliminasi Malaria. SPIRAKEL. 2017 Feb 9;8(2).
17. Bartoloni A, Zammarchi L. Clinical Aspects Of Uncomplicated and Severe Malaria. Mediterr J Hematol Infect Dis. 2012 May ;4(1):2012-026.
18. Oakley MS, Gerald N, McCutchan TF, Aravind L, Kumar S. Clinical and molecular aspects of malaria fever. Trends Parasitol. 2011 Oct;27(10):442–9.
19. Arévalo-Herrera M, Lopez-Perez M, Medina L, Moreno A, Gutierrez JB, Herrera S. Clinical profile of Plasmodium falciparum and Plasmodium vivax infections in low and unstable malaria transmission settings of Colombia. Malar J. 2015;14(1):154.
20. Deshwal R. Clinical and laboratory profile of hospitalized malarial patients: An Agra-based study. J Assoc Physicians India. 2016;64:44.
21. Wiwanitkit V. Headache and malaria: a brief review. Acta Neurol Taiwan. 2009;18(1):56–9.
22. John CC. Malaria (Plasmodium). In: Kliegman R, Nelson WE, editors. Nelson textbook of pediatrics, 20th ed. Philadelphia, Pa: Elsevier, Saunders; 2016.
23. Muddaiah M, Prakash PS. A study of clinical profile of malaria in a tertiary referral centre in South Canara. J Vector Borne Dis. 2006 Mar;43:29–33.
24. Sonawane VB, Kotrashetti V, Malhotra R. Comparison of Clinical Profile and Severity of P. falciparum and P. vivax Malaria in a Tertiary Care Hospital of Navi Mumbai, India: A Descriptive Study. JMSCR; 2017.
25. Martins AC, Araújo FM, Braga CB, Guimaraes MG, Nogueira R, Arruda RA, et al. Clustering symptoms of non-severe malaria in semi-immune Amazonian patients. PeerJ. 2015;3:e1325.
26. Anstey NM, Jacups SP, Cain T, Pearson T, Ziesing PJ, Fisher DA, et al. Pulmonary manifestations of uncomplicated falciparum and vivax malaria: cough, small airways obstruction, impaired gas transfer, and increased pulmonary phagocytic activity. J Infect Dis. 2002;185(9):1326–34.
27. Dennis M, Bowen WT, Cho L. Mechanisms of clinical signs. Australia: Elsevier Australia; 2016.
28. Tarafder BK, Islam MT, Roshed MM, Siddique MAB, Hossain AM, Sarker KD. Vivax Malaria Presenting with Fever and Tender Hepatomegaly. Faridpur Med Coll J. 11(2):90–2.
29. Viriyavejakul P, Khachonsaksumet V, Punsawad C. Liver changes in severe Plasmodium falciparum malaria: histopathology, apoptosis and nuclear factor kappa B expression. Malar J. 2014;13(1):106.
30. Abhijeet M, Kanjaniindira PS. A Clinical Profile of Cerebral Malaria with P. Falciparum Infection. IJSR. 2017; 6(5):729-32.
31. Castelli F, Sulis G, Caligaris S. The relationship between anaemia and malaria: apparently simple, yet controversial. Trans R Soc Trop Med Hyg. 2014 Apr ;108(4):181–2.
32. Quintero JP, Siqueira AM, Tobón A, Blair S, Moreno A, Arévalo-Herrera M, et al. Malaria-related anaemia: a Latin American perspective. Mem Inst Oswaldo Cruz. 2011 Aug;106 Suppl 1:91–104.
33. Donker AE, Raymakers RA, Vlasveld LT, Barneveld T van, Terink R, Dors N, et al. Practice guidelines for the diagnosis and management of microcytic anemias due to genetic disorders of iron metabolism or heme synthesis. Blood J. 2014 Jun;123(25):3873-86.