Asian Journal of Epidemiology

ISSN 1992-1462

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OPEN ACCESS Asian Journal of Epidemiology

ISSN 1992-1462
DOI: 10.3923/aje.2017.32.36

Research Article
Algorithm Malaria Diagnosis as a Result of the Comparison Between Clinical Symptoms and Microscopy Test in the Population Central Sulawesi Province

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Abstract

Background and Objective: Malaria is a contagious disease that is still a public health problem in the world, including in Indonesia. The aims of the study was make algorithm of malaria diagnosis as a result of the comparison between clinical symptoms and microscopic test. **Methodology:** The study was observational with cross sectional study. The population is the whole population in Tinombo Puskesmas. The sample is suspected malaria March-April 2016. A sample of 142 people were examined clinically and microscopically. Test used chi square and logistic regression. **Results:** The results showed that the variable clinical symptoms associated with the microscopic examination is fever ($p = 0.001$), chills ($p = 0.000$) and joint pain ($p = 0.005$). Multivariate logistic regression test with in getting the symptoms of chills, diarrhea and joint pain as an algorithm with sensitivity (74.28%) and specificity (85.98%). **Conclusion:** Algorithm of Malaria is an alternative in early diagnosis for endemic areas who have limited facilities of microscopic laboratory examination.

Key words: Algorithm, malaria diagnosis, clinical symptoms, microscopic test, diarrhea, joint pain

Received: July 31, 2016 Accepted: September 14, 2016 Published: December 15, 2016

Citation: Noer Bahry Noor, A.A. Arsunan, Ni Made Rai Marleni and Anwar Mallongi, 2017. Algorithm malaria diagnosis as a result of the comparison between clinical symptoms and microscopy test in the population central Sulawesi province. Asian J. Epidemiol., 10: 32-36.

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Malaria is a contagious disease that is still become a public health problem both in the world and in developing countries. In 2015, there are 3.2 billion people at risk and settle in the local transmission of malaria and 438,000 deaths occur when 70% of all deaths occur in children under the age of five[1].

The prevalence of malaria in Indonesia in 2013 was 6.0%. Five provinces with the highest incidence and prevalence are Papua (9.8 and 28.6%), East Nusa Tenggara (6.8 and 23.3%), West Papua (6.7 and 19.4%), Central Sulawesi (5.1 and 12.5%) and Maluku (3.8 and 10.7%). From the 33 provinces in Indonesia, 15 provinces have malaria prevalence rates above the national average (1.9%), mostly located in the eastern part of Indonesia[2].

In the District of Parigi Moutong, the malaria positive patients continues to increase in 2013 as many as 70 cases and with microscopic examination found 970, in 2014 found as many as 116 people with positive malaria and by microscopic examination found 1,168. In 2015 as many as 354 people with positive malaria and microscopic examination found 805 people[3].

Rapid and precise diagnosis of malaria is indispensable in the management of malaria cases. It is associated with infection *P. falciparum* can cause severe or complicated malaria. In endemic areas malaria patients already have immunity, especially in adults, symptoms are usually mild and nonspecific, clinical symptoms felt by people with malaria can include: Fever, headache, shivering, gastrointestinal disorders, muscle tension and other[4].

For the diagnosis of malaria one that needs to be seen is the examination of blood clots. Microscopic examination of the parasite has been used for over 100 years and has become the gold standard for diagnosing malaria cases. Though overall investigation to malaria has evolved with the Rapid Diagnostic Test (RDT) and Polymerase Chain Reaction (PCR)[5].

Various efforts to control malaria continues had been conducted but the results have not been up to reduce morbidity and mortality due to malaria, especially in highest endemic areas. However, those effort did not show any significant good results in reducing the number of malaria cases in the area District of Moutong Parigi. Thus, this study was conducted to compile algorithm as a strategy for distinguishing positive parasitaemia and negative parasitaemia from the results of microscopic examination in the invention of early malaria patient in Health Centre Tinombo, District of Moutong Parigi, Province of Central Sulawesi.

MATERIALS AND METHODS

Location and design of study: The location of this study conducted in Health Centre Tinombo, sub district of Tinombo Moutong Parigi district, Province of Central Sulawesi. This type of study is observational by using cross sectional design.

Population and sample: The population was all patients with suspected malaria in Health Centre Tinombo. A sample of 142 patients with suspected malaria were found both in health centers and at home and are willing to participate in the study by signing the informed consent issued by the Ethics Committee of the Medical Faculty, Hasanuddin University.

Method of collecting data: Collecting data is conducted by health workers. The primary data using questionnaires covering the physical examination and the identity of suspected malaria patients conducted by doctors and assisted by nurses while the data for the examination of blood clots in the laboratory conducted by local laboratory. Secondary data obtained in the location of study.

Data analysis: The collected data was processed and analyzed using SPSS. Data characteristics and clinical symptoms using the distribution frequency. To assess the association of clinical symptoms with the results of microscopic examination using chi square test. To determine the clinical symptoms associated with the microscopic examination used multivariate analysis using logistic regression.

RESULTS

A total of 142 patients, attending the Tinombo Health Centre between January-May, 2016 and given a presumptive clinical diagnosis of malaria, were interviewed. We asked about their presenting symptoms and what diseases they perceived themselves to be suffering from. Table 1 shows the clinical symptoms complained of suspected malaria patients.

There were patients have suffered from fever with (78.2%), shivering (45.1%), headache (73.2%), joint pain (43.7%), nausea (23.2%), vomiting (27.5%) and diarrhea (22.5%). Patients with suspected malaria positive by microscopic examination were 24.6%. Cases of malaria were significantly more likely to report fever, shivering, joint pains and headache.

Table 2 shows the clinical symptoms associated with the microscopic examination that show with fever (p = 0.001, χ^2 = 11,330), joint pain (p = 0.005, χ^2 = 8.032), shivering (p = 0.000, χ^2 = 48.120).

Table 3 is based on multivariate analysis showed clinical symptoms associated positively with the microscopic examination were shivering (p = 0.000, wald = 14.305, CI 95% = 10.801-1.806E3), headache (p = 0.028, wald = 4.815, CI 95% = 1.188-21.126), joint pain (p = 0.012, wald = 6.334, 95% CI = 1.415-16.331) and diarrhea (p = 0.010, wald = 6.559, 95% CI = 2.065-23.860).

The most frequently report of algorithm of positive malaria incidence are presented in the Table 4.

Table 4 shows the algorithm of positive malaria incidence in Health Centre Tinombo were shivering (p = 0.000, wald = 17.055; CI 95% = 17.619-3.140E3), joint pain (p = 0.030, wald = 4.713; 95% CI = 1.122-9.476) and diarrhea (p = 0.011, wald = 6.413; 95% CI = 1.874-138.085).

Table 5 shows the sensitivity and specificity of each combination of malaria clinical symptoms was shivering result has a value of 97.14% sensitivity and specificity value of 96%. The combination of clinical symptoms of shivering and joint pain has a value of 65.71% sensitivity and specificity value of 89.71%. While, the combination of all three clinical symptoms of shivering, joint pain and diarrhea have a sensitivity value of 74.28% and specificity value of 85.98%.

Table 1: Distribution of clinical symptoms malaria suspect suffered in Puskesmas Tinombo, 2016

Clinical symptom	No.	Percentage
Fever	111	78.2
Shivering	64	45.1
Joints pain	62	43.7
Headaches	104	73.2
Nausea	33	23.2
Vomiting	39	27.5
Diarrhea	32	22.5

Table 2: Relationship between clinical symptoms in patients with suspected malaria microscopic examination results in Puskesmas Tinombo, 2016

Clinical symptom	χ^2	p-value
Fever	11.330	0.001
Shivering	48.120	0.000
Joints pain	8.032	0.005
Headache	1.589	0.207
Nausea	0.029	0.866
Vomiting	0.150	0.699
Diarrhea	1.483	0.223

Table 3: Analysis of the relationship between clinical symptoms with microscopic examination results positive in Puskesmas Tinombo, 2016

						95% CI for Exp (B)	
Clinical symptom	B	Wald	df	Significant	Exp (B)	Lower	Upper
Fever	19.243	000	1	0.998	2.275E8	0.000	
Shivering	4.939	14.305	1	0.000	139.651	10.801	1.806E3
Head ache	1.611	4.815	1	0.028	5.009	1.188	21.126
Joint paint	1.570	6.334	1	0.012	4.808	1.415	16.331
Nausea	-642	0.870	1	0.351	0.526	0.137	2.028
Vomiting	0.28	0.002	1	0.967	1.028	0.277	3.820
Diarrhea	3.090	6.559	1	0.010	21.976	2.065	23.860
Constant	-3704	6.467	1	0.011	0.025		

Table 4: Algorithm of positive malaria incidence in Tinombo Puskesmas, 2016

						95% CI for Exp (B)	
Clinical symptom	B	Wald	df	Significant	Exp (B)	Lower	Upper
Step 1 (a) Fever	4.469	18.566	1	0.000	87.267	11.429	666.336
Constant	-125	0.250	1	0.617	0.882		
Step 2 (b) Fever	4.432	18.050	1	0.000	84.079	10.889	649.223
Joint paint	112	4.848	1	0.028	3.041	1.130	8.185
Constant	-655	3.374	1	0.066	0.520		
Step 3 (c) Fever	5.460	17.055	1	0.000	235.197	17.619	3.140E3
Joint paint	1.182	4.713	1	0.030	3.260	1.122	9.476
Diarrhea	2.778	6.413	1	0.011	16.084	1.874	138.085
Constant	-3.133	7.752	1	0.005	0.044		
Step 4 (d) Fever	5.635	17.226	1	0.000	280.108	19.571	4.009E3
Joint paint	1.473	6.261	1	0.012	4.362	1.376	13.827
Head ache	1.340	3.815	1	0.051	3.820	0.995	14.662
Diarrhea	2.910	6.555	1	0.010	18.358	1.979	170.342
Constant	-3.751	9.289	1	0.002	0.023		

Table 5: Specificity values and specificity of genesis 3 clinical symptoms against malaria in Puskesmas Tinombo, 2016

	Malaria			
Observation	Positive	Negative	Sensitivities	Spesivisity
Step 1: Malaria				
Positive	34	30	97.14	71.96
Negative	1	77		
Step 2: Malaria				
Positive	23	11	65.71	89.71
Negative	12	96		
Step 3: Malaria				
Positive	26	15	74.28	85.98
Negative	9	92		

DISCUSSION

This study found clinical symptoms of fever experienced by malaria in the region suspected at Health Centre Tinombo, based on test chi square get significant results between clinical symptoms of fever with microscopic examination ($p = 0.001$; $\chi^2 = 11,330$). Patients with suspected malaria have had the awareness to seek treatment to the health center for check-up. According to Harijanto[6], the fever caused by the triggering factors contained in the blood schizonts rupture issued various allergens antigenic causing the host immune response and stimulate lymphocyte cells, monocytes and macrophages to form sitokon. Tumor Necrosis Factor (TNF), which together with the flow of blood reaches the hypothalamus which is the central regulator of temperature resulting in fever. Fever usually start with irregular after a while formed quotient (intervals of 24 h). In the phase of the heat, the temperature does not drop to normal, the temperature becomes remitter or continua, even sometimes with two peaks. It can even happen unexplained fever or without fever. This is caused by differences in the immune status and synchronicity of skizogoni asexual parasites. Furthermore, the multivariate analysis showed that the clinical symptoms fever is not related to the results of microscopic examination ($p = 0.998$, wald = 0.000, 95% CI = 0.000). It is addressed that the data cannot be analyzed properly because of all the positive malaria patient with symptoms of fever and there are no positive malaria patients who did not have a fever. So, the clinical symptoms of fever cannot be used as a constituent algorithms malaria. This study is in line with the results of the study in Uganda that the clinical symptoms of fever had a significant relationship with parasitaemia[7] aPRR 2:23; CI 1.18-4.24.

This study found the symptoms of joint pain is a clinical manifestation of expenditure triggering substances emitted together with merozoites which rupture erythrocytes. Joint pain can be caused by the presence of histamine release and TNF-p which causes an increase in body temperature and cause joint pain sensation. The TNF and IL-1 have the physiological and metabolic properties that coincide with body pain and other clinical symptoms. From the results of research conducted in Health Centre Tinombo, based on test chi square get significant results between clinical symptoms of joint pain with microscopic examination ($p = 0.005$; $\chi^2 = 8.032$). The sensitivity of the symptoms of joint pain obtained 65.7% of patients in order to obtain a suspect who did not experience joint pain but the result was positive by microscopy as much as 34.3%. Specifity Values obtained was 63.5%, it is suspected malaria patients who experience joint pain but the results were negative by microscopy as much as 36.5%. Furthermore, by multivariate analysis obtained by the clinical symptoms of joint pain was significantly associated with microscopic examination results with the results ($p = 0.012$, wald = 6.334, 95% CI = 1.415-16.331). This study is in line with the results of Martins *et al.*[8] found clinical symptoms of joint pain associated with malaria with $p<0.001$.

Shivering is a symptom that arises due to the compensation body against fever. After the outbreak of the schizonts in and out eritrosit antigenic substances it can cause symptoms of shivering. This arises because the compensation body against fever. These sensations arise with the characteristic drop in body temperature relative to ambient temperature so that people who experience these symptoms felt very cold[9]. From the results of study conducted in Health Centre Tinombo, based on test chi square get significant results between clinical symptoms of shivering with microscopic examination ($p = 0.000$, $\chi^2 = 48.120$). These symptoms which have the highest sensitivity value of 97.14% and accuracy of 78.16%. Furthermore, by multivariate analysis obtained symptoms of shivering are the most significant symptom with values ($p = 0.000$, wald = 14.305, CI 95% = 10.801-1.806E3), so it can be used as predictor in the clinical diagnosis of malaria. The results are consistent with the results of Roestenbery *et al.*[10], which states that in the Netherlands the shivering clinical symptoms is significantly with p-value = 0.001.

Algorithm malaria is a accurate, fast, easy, safe and cheap clinical strategy to distinguish positive parasitaemia with parasitaemia negative from results of microscopic examination in an effort to improve the quality of early case detection. From the results of study conducted in Health Centre Tinombo, based on multivariate analysis showed that there are three clinical symptoms can be the symptoms of clinical malaria algorithms shivering ($p = 0.000$, wald = 17.055, 95% CI = 17.619-3.140E3), joint pain ($p = 0.030$, wald = 4.713, 95% CI = 1.122-9.476) and diarrhea ($p = 0.011$, wald = 6.413,

95% CI = 1.874-138.085). With sensitivity (74.28%) and specificity (85.98%). Previous study conducted by Hasmar[11], in the Health Centre Mapane, Regency of Poso shows the results of constituent algorithms malaria are shivering, joint pain, fever and headache.

Other study by Mutanda[12] in Kenya, the fever had a sensitivity of 88.9% and specificity have 15.4% when combined with symptoms of headache sensitivity to 94.4% but specificity value decreased to 9.9%.

CONCLUSION

Conclusion of the study is a clinical symptom of malaria is related significantly to the results of microscopic examination of fever, shivering and joint pain. Clinical symptoms of shivering is the most meaningful symptom to do with the results of microscopic examination. The clinical symptoms of malaria as a constituent algorithms are shivering, diarrhea and joint pains. The clinical diagnosis of malaria can be an alternative diagnosis of malaria in the difficult area to be reached and in areas that have limitations in conducting microscopic examination.

SIGNIFICANCE STATEMENTS

This study revealed the effectiveness of malaria control program by comparing clinical symptoms and microscopic test. As a large percentage of population lives in extreme poverty areas in District of Moutong Parigi, Province of Central Sulawesi. they are in high threat of malaria due to their poor sanitation, without access to potable water and adequate healthcare. Traditionally, Chloroquine was a common treatment for Malaria. However, with the increase in chloroquine resistant malaria, additional methods of control must be employed. A multidimensional approach should be used in the control strategy, such as good management of clinical malaria. Various efforts to control malaria continues had been conducted but the results have not been up to reduce morbidity and mortality due to malaria, especially in highest endemic areas Moutong Parigi. This study compile algorithm as a strategy for distinguishing positive parasitaemia and negative parasitaemia from the results of microscopic examination in the invention of early malaria patient in Health Centre Tinombo, District of Moutong Parigi, Province of Central Sulawesi. It is a rapid and precise diagnosis of malaria is indispensable in the management of malaria cases.

ACKNOWLEDGMENT

Authors would like to express grateful thanks to the chief of Health Centre District of Moutong Parigi, especially to the Governor of Province of Central Sulawesi who have given a permission to conduct this study in the malaria area. Then to those communities in the area of who have very cooperative in giving contribution in sampling process.

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