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Association of Nutritional Status with Anemia on Malaria Patient with Dihydroartemisinin Pippperaquine Treatment in Southwest Sumba 2015

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ABSTRACT

This study was conducted to understand relationship between nutritional status with anemia in malaria patients with Dihydroartemisinin Pipperaquine (DHA-P) in Southest Sumba. The study was designed as longitudinal study by examined 44 patients suffered from *P. falciparum* and *P.vivax*. The univariate analysis was based on age, gender, infection types, nutritional status and anemia. Meanwhile, bivariate analysis was used to observe the relationship between dependent variable and independent variable. The DHA-P efficacy was 100% successful in 42 days for malaria patients. There was a significant chance in nutritional status with weight/height and body mass index/age indicators, where body weight had increased after treatment. In additions, there was significant recovery in anemia status between pre and post treatment. Besides, DHA-P efficacy has improved nutritional status and anemia status after treatment. There was significant relationship between nutritional status and anemia status after treatment.

CCS Concepts

- **Social and professional topics → User characteristics**

Keywords

Malaria; efficacy; dihydroartemisinin; pipperaquine; nutritional status; anemia

1. INTRODUCTION

Malaria is life-threatening disease found more in tropical or subtropical area. An estimated 214 million new Malaria cases worldwide in 2015 [1]. Africa had contributed highest Malaria cases (88%), followed by South-East Asia region (10%) and Eastern Mediterranean Region (2%). There were declined 18% in Malaria cases from year 2000 to year 2015 (range: 149-303 million). Each year, one million people were died from Malaria disease and death number had increased since past two decades.

In 2000, estimated 86% of malaria death occurred in children below than 5 years [2]. In worldwide, 12% malaria death occurred in children age 1-59 months and 22% was from sub-Saharan Africa. The young children, pregnant women and non-immune travelers from malaria frees area were easily infected to this disease. The malaria was caused by microscopic parasite called *Plasmodium* through bites of infected of Anopheles mosquito vectors [3]. There were 5 parasite species such as *Plasmodium falciparum, P. vivax, P.ovale, P.knowlesi, and P. malariae* and *Plasmodium falciparum* was most deadly. The syndrome in severe malaria such as severe anemia, acute respiratory distress and cerebral malaria [4-8].

Anemia was characterized as decreased in hemoglobin concentration. Plasmodium parasites caused anemia through hyperhaemolysis of hemoglobin and reduced in erythropoiesis operation through several ways [9]. Besides, nutritional status was related with malaria. Some studies had mentioned normal nutrition status was good in protected malaria symptomatic [10,11], and other studies shown nutritional status resulted in severe malaria and complication with immune response modification [12-14]. In additions, some studies suggested that no any relationship between malaria and nutritional status [15-19].The studies also had found children and adult had chronic malnutrition contributed in death from malaria [20].

Artemisinin-based combination therapy (ACT) had recommended by World Health Organization as first-line for uncomplicated *P.falciparum* [21-23]. This therapy was more effectively in reduced parasite biomass. Most ACT recommended was artesunate with mefloquine and used widely in Asia and Africa [24,25]. Besides, dihydroartemisinin-piperaquine (DHA-P) was new ACT that proved highly effective in cure uncomplicated *P. falciparium* [26-29]. Dihydroartemisinin was active metabolite from artemisinin derivatives that rapidly relief clinical symptom and parasites clearance from blood compared to other antimalarial drug [30]. Meanwhile, piperaquine was bisquinoline antimalarial that function same as chliroquine. Piperaquine had long elimanation half-life compared to other antimalarial. The DHA-P advantages such as one daily dose and longer half-life compared to another antimalarial drug [31].

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Indonesia is among highest malaria cases in Southeast Asia. *Plasmodium falciparum* is most common cause malaria in Indonesia, estimated 12 million clinical cases each year [32,33]. The DHA-P had introduced in Papua since 2008. Based on study, DHA-P had more effective toward *P. falciparum* and *P.vivax* compared artesunate amodiaquin. This study was conducted to understand relationship between nutritional status with anemia in malaria patients with Dihydroartemisinin Pipperaquine in Southeast Sumba.

2. METHODOLOGY

2.1 Study Type

The study design was longitudinal study toward combination of DHA-P in malaria patients.

2.2 Location and Time

This study was conducted in malaria endemic area in Sumba Barat Daya regency, East Nusa Tenggara. This study was conducted between May and September 2015.

2.3 Population and Sample

The population in this study was entire population that infected with malaria in Southwest Sumba district, East Nusa Tenggara. The samples size for this study was 44 peoples. The inclusion criteria for this study as below:

i) age between 1 and 65 years old.

ii) mono-infection with *P.falciparum /P. vivax* that confirmed positive through blood test (no mixed infection).

iii) Fever within 24 hours.

iv) able to perform oral medication.

v) able and willing follow with study protocol during intervention period and visit schedule.

vi) suffering anemia.

2.4 Data Collection

The primary data was collected using questionnaire included respondent characteristic, semi quantitative food frequency questionnaire (FFQ) and infection data. The secondary data included general description of Southwest Sumba working area population and geographical conditions that obtained by direct observation and interview with local authorities.

2.5 Data Analysis

The univariate analysis was based on age, gender, infection types, nutritional status and anemia. Meanwhile, bivariate analysis was used to observed the relationship between dependent variable and independent variable.

3. RESULT AND DISCUSSION

3.1 Univariate Analysis

Based on Table 1, distribution of malaria patients based on gender showed that female was dominated in malaria infection, 24 patients and male only 20 patients. There were 28 patients aged less than 10 years old, while 16 patients aged more than 10 years old. Most of patients had infected *P. falciparum* compared to *P. vivax* only 10 patients. Meanwhile, 19 patients had suffered anemia less than 10 years old and only 7 patients aged more than 10 years old suffered anemia. Besides, all patients had sufficient clinics and parasitological.

Table 1. Distribution of gender, age, infection types and treatment result in malaria patients in Southeast Sumba 2015.

Indicators	n	%
Gender		
Female	24	54.5
Male	20	45.5
Total	44	100.0
Age		
<10 years old	28	63.6
≥ 10 years old	16	36.4
Total	44	100.0
Infection Types		
P. falciparum	30	68.2
P. vivax	10	22.7
Mix	4	9.1
Total	44	100.0
Anemia		
Age<10 years old	19	67.9
Age ≥10 years old	7	43.8
Total	28	100.0
Treatment result		
Sufficient clinics and parasitological responses	44	100.0
Total	44	100.0

Source: Primary Data, 2015

3.2 Bivariate Analysis

Based on Table 2,There were 8 patients aged 1-9 years old had *P.falciparum* density > 360 µl, while 9 patients aged > 9 years old had density >360 µl. Besides, 4 patients aged 1-9 years old had density <360 µl and also 4 patients aged > 9 years old had parasites density > 360 µl for *P. vivax. Even though*, only 1 patients that had parasite density < 360 µl in mix infection.

Based on Table 3, BMI/age indicator showed 25 patients were in normal nutritional status on day-0 and increased to 26 patients on day-42 for patients aged ≤ 9 years old. Meanwhile, 1 patient was overweight at day-42 for aged ≤ 9 years old. In patients aged > 9 years old, there were only 1 patients was thin at day-0 and still maintained as 1 patients at day-42. Besides, 10 patients at day-0 and remained 10 patients at day-42 that were in normal nutritional status.

Table 4 showed dynamic change in hemoglobin on malaria patients, there was changed in hemoglobin status from day-0 before treatment until day-42 treatment. There was significant change in hemoglobin status after treatment intervention for 4 follow up times from day-7,14,28,42.

Table 2. Distribution age based malaria parasites density in Southeast Sumba 2015.

Age (years old)	<360 µl	%	>360µl	%	Total	p-value
P.falciparum						
1-9	8	47.1	9	52.9	17	0.23
>9	9	69.2	4	30.8	13	
P. vivax						
1-9	4	50	4	50	8	1.0
>9	1	50	1	50	2	
Mix						
1-9	1	33.3	2	66.7	3	1.0
>9	1	100	0	0	1	

Source: Primary Data,2015

Table 3. Nutritional status from day-0 and day-42 on malaria ptient in Southeast Sumba 2015.

Age ≤ 9 years old					
Nutritional status (Body Mass Index/Age)	Day-0		Day-42		p-value
	n	%	n	%	
Thin	3	10.7	1	3.6	0.184
Normal	25	89.3	26	92.9	
Overweight	0	0	1	3.6	
Total	28	100	28	100	
Age >9 years old					
Thin	1	9.1	1	9.1	-
Normal	10	90.9	10	90.9	
Total	11	100	11	100	

Source: Primary Data, 2015

Table 4. Dynamic change in hemoglobin status on malaria patients in Southeast Sumba 2015.

Observation Time	N	Mean	Mean rank	Std. deviation	Min	Max	p value
Hb day-0	43	10.76	2.59	2.49	3.50	15.40	<0.05
Hb day-7	43	10.92	2.22	1.53	7.00	14.90	
Hb day-14	43	11.33	2.56	1.20	9.20	14.90	
Hb day-28	45	12.2	3.91	1.53	9.10	15.50	
Hb day-42	45	12.1	3.72	1.25	9.10	14.30	

Source: Primary data, 2015

Table 5 had explained no failure treatment (LCF and LPF) after treatment either on *P. falciparum*, *P. vivax* or mix. The DPA-P efficacy treatment was 100% for all infection types. The parasite was reduced started in day-2 and day-3 for all infection types.

Table 5. Efficacy of DHA-P treaatment in malaria patient in Southeast Sumba 2015.

Parameter	*P. falciparum*		*P. vivax*		*P. mix*	
	n	%	n	%	n	%
LTF	0	0.0	0	0.0	0	0.0
LCF	0	0.0	0	0.0	0	0.0
LPF	0	0.0	0	0.0	0	0.0
ACPR	30	100.0	10	100.0	4	100.0
Total patients peer protocol	30		10		0	
WTH	0		0		0	
LFU	1		1		0	
Total patients LFU/WTH	1	3.2	1	16.7	0	20.0
Total patients at baseline	31		11		4	

Source: Primary data, 2015

Based on Table 6, there was no significant relationship between nutritional status with anemia since patients had thin or normal nutritional status suffered anemia. For patients aged ≤9 years old, there were 2 thin patients and 17 normal patients had suffered anemia.

Table 6. Relationship between nutritional status and anemia status on day-0 in malaria in Southeast Sumba 2015.

Nutritional status (BMI/Age)	Hb classification					
	Anemia	%	Normal	%	Total	p-value
	Age ≤ 9 years old					
Thin	2	66.7	1	33.3	3	1.0
Normal	17	68	8	32	25	
Age > 9 years old						
Thin	0	100	1	100	1	1.0
Normal	5	50	5	50	10	

Source: Primary data,2015

Based on Table 7, 9 patients that aged ≤ 9 years old had suffered anemia and 3 patients aged > 9 years old suffered anemia on day-42. Meanwhile, there was no significant relationship between nutritional status and anemia on day-42.

Table 7. Relationship between nutritional status and anemia status on day-42 on malaria patients in Southeast Sumba 2015.

Nutritional status (BMI/Age)	Hb classification					
	Anemia	%	Normal	%	Total	p-value
	Age ≤ 9 years old					
Thin	1	100	0	0	1	0.15
Normal	9	34.6	17	65.4	26	
Overweight	1	100	0	0	1	
Age > 9 years old						
Thin	1	100	0	0	1	0.36
Normal	3	30	7	70	10	

Source: Primary data,2015

Based on Table 8, for age 1-9 years, there were 100% thin patients had parasitic density >360 µl and 8 patients that normal nutritional status had parasite density ≤ 360 µl for *P.falciparum*. Similarly, based on Table 9, 3 thin patients had parasite density > 360 µl and 1 patient had parasite density ≤ 360 µl for aged >9 years old. Meanwhile, 3 thin patients had parasite density >160 µl and 4 patients had normal nutritional status that parasite density > 160 µl for *P.vivax*.

Table 8. Relationship between nutritional status and malaria parasite density (*P.falciparum*) on malaria patients in Sumba 2015.

Nutritional Status (BMI/Age)	*P. falciparum*					
	≤ 360µl	%	> 360 µl	%	Total	p value
	Age 1-9 years old					
Thin	0	0	2	100	2	0.47
Normal	8	53.3	7	46.7	15	
	Age > 9 years old					
Thin	1	25	3	75	4	0.052
Normal	8	88.9	1	11.1	9	
Obesity	-	-	-	-	-	

Source:Primary Data,2015

Table 9. Relationship between nutritional status and malaria parasite density (*P.vivax*) on malaria patients in Sumba 2015.

Nutritional Status (BMI/Age)	*P. vivax*					
	≤ 160µl	%	>160µl	%	Total	p-value
	Age 1-9 years old					
Thin	1	25	3	75	4	1.0
Normal	0	0	4	100	4	
	Age > 9 years old					
Thin	-	-	-	-	-	1.0
Normal	1	100	0	0	1	
Obesity	0	0	1	100	1	

Source: Primary data,2015

Based on Table 10, There were 8 patients that aged <9 years that suffered anemia that parasite density >360 µl and 2 patients that normal had parasite density ≤360 µl for *P.falciparum*. Meanwhile, 2 patients suffered anemia that parasite density >360 µl and 2 patients that normal had parasite density ≤360 µl for *P.vivax*. In additions, Based on Table 11, 4 anemia patients had parasite density ≤360 µl and 1 normal patients that had parasite density >360 µl for *P.falciparum*. For *P.vivax*, 2 normal patients had parasite density ≤360 µl aged > 9 years old.

3.3 Overall Discussion

The age group suffered malaria is ranged from 6 years old until 18 years since most of patients were involved in this study. Based on this study, 63.6% of malaria patients were aged lower than 10 years old. The young children and pregnant women were population group that high risk for malaria infection [4]. The children had poor immunity and pregnant women immunity reduced when malaria infection. Most of malaria patients were infected by *P.falciparum* and followed *P.vivax* and mix. There were 2 species common spread in Indonesia, *P.falciparum* and *P.vivax* particularly in Southeast Sumba. *P. Falciparum* was caused more death compared other malaria types [34]. *P. vivax* also reported caused severe multi organ dysfunction similar to *P.falciparum* [35]. In French Guiana, 10.5% of malaria cases had mixed of *P. Falciparum / P.vivax* malaria [36]. There were 67.9% malaria patients aged < 10 years old had suffered anemia.

Table 10. Relationship between anemia status and parasite density based on malaria patient's age in Southeast Sumba.

Hb classification	1-9 years old *P.falciparum*					p-value
	≤360 µl	%	>360 µl	%	Total	
Anemia	6	42.9	8	57.1	14	0.57
Normal	2	66.7	1	33.3	3	

P.vivax						
Anemia	1	33.3	2	66.7	3	1.0
Normal	2	50	2	50	4	
Mix						
Anemia	1	50	1	50	2	1.0
Normal	1	100	0	0	1	

Source: Primary Data,2015

Table 11. Relationship between anemia status and parasite density based on malaria patient's age in Southeast Sumba.

Hb classification	**1-9 years old** ***P.falciparum***					**p-value**
	≤360 µl	**%**	**>360 µl**	**%**	**Total**	
Anemia	4	80	1	20	5	1.0
Normal	5	62	3	37.5	8	
P.vivax						
Anemia	0	0	1	100	1	0.3
Normal	2	100	0	0	2	
Mix						
Anemia	-	-	1	100	1	-
Normal	-	-	1	100	1	

Source: Primary data,2015

In Africa, malaria was health problem that contributed anemia in children [37, 38]. No failure treatment was observed on this study after intervention period either on *P. falciparum*, *P. vivax* or mix. Most of treatment showed efficacy started in day-2 and day-3 for all infection types. A study indicated parasitological failure was lower in DHA-P compared in other treatment [38]. The DHA-P had half-life estimation about 2 weeks to 3 weeks. The study showed given once daily of fixed combination for 3 days was effective and well tolerated [39]. There was no significant relationship between nutritional status with anemia since thin or normal nutritional status also suffered anemia. In the study, most of patients aged below than 9 years old had suffered anemia compared to malaria patients aged > 9 years. After intervention period, patients still suffered anemia in all nutritional status types. Anemia was caused by lower hemoglobin level in body. Iron and nutritional deficiency included folate, vitamin B12 and vitamin A is common cause in anemia [40]. There were few studies on relationship between nutritional status and anemia [41- 46]. In this study showed no significant relationship between nutritional status and malaria parasite density on the patients. Meanwhile, there was relationship between nutritional status and malaria parasite density on malaria patients aged > 9 years old. In Uganda, a study showed no relationship between nutritional status and malaria mortality [47]. The patients were under nutrition or thin had high risk in infectious diseases and particularly in malaria [48].

Based on this study, there was no significant relationship between anemia and malaria parasite density on malaria patients. The malaria parasites caused anemia through hemoglobin hyperhaemolysis and erythropoiesis decreased operated through several pathways [9].The high malaria parasite density had high death risk since infection caused anemia. In addition, excessive hemolysis hemoglobin parasitized in malaria infection lead to anemia. Previous study showed correlation between malaria parasite density and blood cell parameters included hemoglobin concentration [49].The nutritional status had related with immunity responses to infection [20].The malaria was related to reduce in nutritional status and anemia. The malaria parasites had infected red blood cells that led to red blood cells were ruptured at end of infection cycle. This process lowers red blood cells amount and led to severe anemia.

4. CONCLUSION

In conclusion, DHA-P efficacy was 100% successful on 42 days for malaria patients. There was a significant change in nutritional status with weight/height and BMI/age indicators, where body weight had increased after treatment. In additions, a significant recovery in anemia status between pre and post treatment. Besides, DHA-P efficacy had improved nutritional status and anemia status after treatment. There was significant relationship between nutritional status and anemia status after treatment.

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Preface

This volume contains papers presented at the 2018 International Conference on Healthcare Service Management, which was held during June 08-10, 2018 in Tsukuba, Japan.

ICHSM provides a scientific platform for both local and international scientists, engineers and technologists who work in all aspects of medical and health informatics. In addition to the contributed papers, internationally known experts from several countries are also invited to deliver keynote and invited speeches at ICHSM 2018.

The volume includes 50 selected papers which were submitted to the conference from universities, research institutes and industries. Each contributed paper has been peer-reviewed by reviewers who were collected organizing and technical committee members as well as other experts in the field from different countries. The proceedings tend to present to the readers the newest researches results and findings in the field of Healthcare Service Management.

Much of the credit of the success of the conference is due to topic coordinators who have devoted their expertise and experience in promoting and in general co-ordination of the activities for the organization and operation of the conference. The coordinators of various session topics have devoted a considerable time and energy in soliciting papers from relevant researchers for presentation at the conference.

The chairpersons of the different sessions played important role in conducting the proceedings of the session in a timely and efficient manner and the on behalf of the conference committee, we express sincere appreciation for their involvement. The reviewers of the manuscripts, those by tradition would remain anonymous, have also been very helpful in efficiently reviewing the manuscripts, providing valuable comments well within the time allotted to them. We express our sincere and grateful thanks to all reviewers.

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