JFSP Vol.9, No.1, January-April 2023, Page: 34-39, pISSN: 2549-9068, eISSN: 2579-4558

Jurnal Farmasi Sains dan Praktis

(JFSP)

http://journal.unimma.ac.id/index.php/pharmacy

FACTORS ASSOCIATED WITH RATIONALITY OF ANTIMALARIA PRESCRIPTION IN PAPUA PROVINCE

Irene Sondang Lingga, Sarhana Rassya Aulyah Said, Dina Ayomi, Rusnaeni, Elsye Gunawan, Nur Fadilah Bakri, Elfride Irawati Sianturi

Department of Pharmacy, Faculty of Mathematics and Natural Sciences, Universitas Cenderawasih, Jayapura, Papua, Indonesia

ira_sianturi@yahoo.co.id

https://doi.org/10.31603/pharmacy.v9i1.8207

Article info:

Submitted : 23-11-2022

Revised : 30-01-2023

Accepted : 23-02-2023

Publisher:

Universitas Muhammadiyah Magelang

ABSTRACT

Malaria remains a leading cause of death in Papua and combination of Dihydroartemisin -Piperaquine (DHP) and Primaquine (PQ) is recommended treatment to replace chloroquine out since chloroquine resistance present. Moreover, awareness of rational prescription and adherence may be the first priority in malaria treatment in preventing death and resistance in Papua. This study aimed to assess the rationality of antimalaria prescription in the public and private sectors of Papua Province. This cross-sectional study was conducted. Overall, 571 prescriptions were included in this study and more than half of prescription was rational (65%). This study was predominantly female (65%). More than half was diagnosed by *P. falciparum* (54%), using referred using the public hospital for treatment (54%) and self-identified as Papuan (50%). According to type of malaria, incorrect of prescription DHP and PQ were 20% and 18%, respectively. The multiple logistic regression model showed that female was significantly associated to receive irrational of prescriptions than males (OR = 1.549; 95% CI =1.004-2.389). Participants who had *P. falciparum* increased the likelihood of irrational of prescriptions (OR= 1.641; 95% CI =1.144-2.355). There is a need to have a continuum strategy to improve access and utilization of malaria case management in both public and private health facilities. Inequality gender based on prescribers needs to be investigated. Competence improvement among healthcare providers needs to be a priority to prevent antimalarial resistance.

Keywords: Malaria; Primaquine; Chloroquine resistance; Rational prescription; Papua; Indonesia

1. INTRODUCTION

Malaria has been reported as one of disease burden and reduction in human productivity worldwide caused by plasmodium parasite species (Mahittikorn et al., 2022). The latest report in 2017, Indonesia has been reported with high effort to eliminate malaria cases (Sitohang et al., 2018). Therefore, malaria eradication has been prioritized to be targeted as one of the Millennium Development Goals (World Health Organization & WHO, 2020). Even though the incidence cases tend to decline in some areas (Febrinasari et al., 2021), there are five provinces with high malaria incidences are Papua, East Nusa Tenggara, West Papua, Central Sulawesi, and Maluku need to be prioritized and the resistance of chloroquine adds the complexity of problems. A prior study showed that resistance to antimalarials has been reported in both *P falciparum* and *P. vivax* and this resistance is not for chloroquine alone but also to currently used for antimalarials (Farooq & Mahajan, 2004).

Papua Province has been targeted for malaria elimination by year 2030. Even though Indonesia government has covered the indigenous Papuans to have privilege for health, education and infrastructure, it may not be Papuans convenient to access healthcare facilities. Some

hindrances such as lack of communication between indigenous and migrant health care providers remains problems (Sianturi, Perwitasari, et al., 2021).

Malaria eradication efforts in Indonesia has been conducted for decades and it includes four phases: eradication, pre-elimination, elimination and maintenance of elimination status (Departemen Kesehatan RI, 2009). The quality of health care providers in malaria treatment becomes important in having rationality prescription in malaria (Zurovac et al., 2004). Besides malaria treatment guidance changes rapidly, participation of pharmacists (Anosike et al., 2020), and quality in malaria diagnostic (Uzochukwu et al., 2011) is till unavailable.

Irrational of anti-malarial prescription has led to the spread of parasite resistance to most commonly used anti-malarial drugs. Moreover, World Organization Health (WHO) recommends to promote rational prescription in developing countries especially in malaria and encourage of healthcare providers to follow the existing guideline properly. Irrational might be overused, Inappropriate drug prescribing is still a global problem (Parthasarathi et al., 2021). Misuse of drugs occurs in all countries and irrational practices are especially common and costly in developing countries (Siswantoro et al., 2006). Furthermore, Dihydroartemisinin-Piperaquine (DHP) and Primaquine (PQ) is recommended to be used in malaria treatment. This study aimed to assess factors associated with rationality of antimalaria prescription in Papua as one of chloroquine resistance area in Indonesia.

2. METHODS

2.1. Study Design, Setting and Participants

This was a cross-sectional study, assessing the prevalence and factor associated with rationality of antimalaria prescription among out-patients in one public hospital and a private clinic in Jayapura. Data were based on out-patient drug prescriptions collected from administrative databases. Data prescriptions were extracted for out-patients who were at least 18 years old, not pregnant and not breast feeding, had positive malaria lab result, and received antimalaria prescriptions.

2.2. Descriptive statistics

Sociodemographic variables were analyzed using descriptive statistics. Categorical variables data were presented as frequencies and percentages, while continuous variables data were summarized as mean (standard deviation) or median (interquartile range) depending on the nature of the variables. The outcome variable was binary-coded as rational and irrational prescription. Subsequently, Chi-square test for categorical and independent sample t-test or Mann-Whitney U test were used to analyze independent variables and rationality prescription. We included the following independent variables in the analyses: age, gender, type of malaria, type of health facility and ethnicity**.** Data were collected between April and August 2021. We excluded the age variable from multivariate since the dose of medication to all adults is the same.

2.3. Statistical modeling

In this study, potential predictors that had a p-value of<0.20 in the univariate analysis were included in the multivariate analysis (Bursac et al., 2008). In the multivariate logistic regression analysis, a stepwise procedure was used to select the final model with all independent variables significant with a p-value of ≤0.05. Odds ratios (ORs) with 95% CIs were calculated to quantify the level of association between variables and outcomes. The calibration of the multivariate analysis model was assessed using the Hosmer and Lemeshow test, whereas discrimination was estimated using a receiver operating characteristic (ROC) curve with a 95% CI. Finally, the odds ratios of independent variables and their 95% Confidence Interval were presented. All analyses were performed using two-tailed tests at a significance level of 0.05. Statistical analyses were performed using the Statistical Program for Social Sciences (SPSS) version 24.0 for Windows.

3. RESULTS AND DISCUSSION

3.1. Results

Table 1 provides the additional socio-demographic information about the patients. The mean age of participants was 32.33 ±13.49 years old. Overall, this study was predominantly female (65%). More than half was diagnosed by *P. falciparum* (54%), using referred using public hospital for treatment (54%) and self-identified as Papuan (50%). According to type of malaria, incorrect of prescription DHP and PQ were 20% and 18%, respectively.

Table 1. Socio-demographic of participants

No	Characteristic		N (%)	Rationalities (N=372), 65 %	Irrationalities (N=199), 35 %	p-value
1	Age (mean±SD) years	32.33 ±13.49		31.56 ±13.55	33.79 ±13.28	0.015
2	Gender	Female	376(65%)	233	143	0.027
		Male	194 (35%)	139	56	
3	Type of Malaria	*P. falciparum*	310 (54%)	188	122	0.048
		P. vivax	248 (43%)	175	73	
		Mix	13 (3%)	9	4	
4	Type of provider	Public hospital	311 (54%)	211	100	0.139
		Private clinic	260 (46%)	161	99	
5	Ethnicity	Papua	287 (50%)	198	89	0.127
		Non-Papua	257 (45%)	156	101	
		Not reported	27 (5%)	18	9	

SD: Standard deviation

All the prescriptions were made and the appropriateness of antimalaria can be seen from appropriate diagnosis, treatment, route of administration and duration of treatment. However, more than one-third of prescription (35%) was irrational due to inappropriateness of antimalaria dose (Table 2). The number of incorrect PQ prescription occurred in P. *falciparum*, P. *vivax*, and mix were 70, 28, and 4 respectively.

Table 2. Rationality of Primaquine prescription

Criteria of appropriateness	Rationale of antimalaria prescription					
	Correct PQ			Incorrect PQ		
	P. *falciparum*	P. *vivax*	Mix	P. *falciparum*	P. *vivax*	Mix
Patient	310	248	13	0	0	0
Drug	310	248	13	0	0	0
Dose	240	220	9	70	28	4
Time	310	248	13	0	0	0
Rute	310	248	13	0	0	0

* Primaquine (PQ)

Table 3. Univariate and multivariate analyses on the association of variables with rational antimalaria prescription

Characteristics		Univariate OR (95% CI)	p-value	Multivariate* aOR (95% CI)	p-value
Gender	Male	ref		ref	
	Female	1.523 (1.048-2.213)	0.027	1.549 (1.004-2.389)	0.048
Type of Malaria	*P. falciparum*	1.556 (1.090-2.220)	0.015	1.641 (1.144-2.355)	0.007
	P. vivax	ref		ref	
	Mix	1.065 (0.31-3.570)	0.918	1.228 (0.356-4230)	0.722
Type of provider	Private Clinic	ref		ref	
	Public hospital	0.771 (0.546-1.089)	0.139	1.092 (0.674-1.769)	0.722
Ethnicity	Papua	ref		ref	
	Non-Papua	1.440 (1.011-2.052)	0.043	1.463 (0.951-2.250)	0.083
	Not reported	1.112 (0.481-2.572)	0.803	1.002 (0.401-2.505)	0.996

*The cases were analysed using a stepwise method in the multivariate analysis; Hosmer-Lemeshow test was p: 0.592; the area under receiving operating characteristic curve was 0.405 (0.358-0.453); Ref.: Reference; OR, odds ratio; aOR, adjusted odds ratio

The multiple logistic regression model showed that female higher to receive irrational prescribing than male (OR = **1**.549; 95% CI =1.004-2.389). Patients with malaria caused by P. *falciparum* had a higher risk of having irrational prescription (OR= 1.641; 95% CI =1.144-2.355) (**Table 3**).

3.2. Discussion

This study aimed to assess rational of malaria prescription in Papua province which is chloroquine resistance present in this area. This study showed that one-third of irrational prescription were occurred. Being female and malarian cases caused by P. *falciparum* were significantly associated with irrational prescription in antimalaria. The strengths in this study were the large number of sample size and prescription data were collected from various sources.

3.2.1. Gender

Surprisingly, the inequality gender to receive rational medication occurred in this study. Some suggestions to explain this phenomenon can be related to biological and disease (Risberg et al., 2009). We suggest that there many concerns involving in this mistake. First should be counted is a concern of women patients could not determine whether they were pregnant or not and it may lead to fear using PQ for woman patient particularly most of malaria patients aged in the range of productive age. The concern of PQ is contraindicated in pregnancy because hemolysis risk of the fetus (Fried & Duffy, 2017) may play a role in this irrational occurred.

3.2.2. Type of malaria

Contrary to previous studies (Baird et al., 2016), overuse PQ remains high, particularly in P. *falciparum* induced malaria prescriptions. Using PQ in vivax malaria aims to prevent relapsing events. This may take a longer course from 7 to 14 days. This option may vary by malaria control policies, and prevalence of hemolytic events in specific genetic and area of population. In contrary to prior study, overused of PQ occurred in P. *falciparum* prescriptions instead of P. *vivax* (Chu & White, 2021). Besides for gametocidal dan hypnoidal, prescribers seem lack of knowledge that PQ should be given in a single low-dose (0.25 mg/kg) of PQ in combination with artemisinin-based combination therapies (ACTs) to prevent resistance in P. *falciparum* (Departemen Kesehatan RI, 2009). This might be different to P *vivax* treatment, whereas PQ should be taken for 14 days with 0.25 mg/kg. The competence of prescribers would be questionable. This error might be based on the lack adequate training, inadequate continuing education, and the prescribers follow outdated prescribing practices (Ofori-Asenso & Agyeman, 2016).

3.2.3. Type of providers

One of findings was contrary to previous study (Ezenduka C.C., 2014), the quality of private clinic and public hospital prescribers may not be different to rationality of prescription. In this result may comprehend prescribers could not distinguish between an ACTs and a monotherapy across the type of malaria (Oyinaka et al., 2021). Even though the laboratory results may be first to be had before the prescription made, a high number of incorrect of PQ still occurred in practice. According to prior study among HIV patients (Sianturi, Latifah, et al., 2021), the existence of pharmacist seems low in antimalaria resistance. Error in medication can be reduced by contribution of pharmacist to do screening of prescription. Pharmacist can play vital roles in this problem by screening rationality of prescription before the drugs are delivered to patients. The pharmacist may play vital roles in this stage to poses a potential risk to happen in the future, which is similar to antimicrobial use in Papua. This result should be an alert because resistance of DHP and PQ happened in the future as well as antimicrobial in Papua.

The present study had several limitations. First, there is limited information of prescribers including age, gender, and the background of prescribers in order to identify the quality of physician/general practitioner-patient relationship. It will give much information to assess the background may affect to quality of patient-doctor relationship. Second, the location of study

should involve sectors from rural areas in which limited resources, lack of management drug and insufficient of quality laboratory remain high.

4. CONCLUSION

Continued supervision considered to be added for evaluation on appropriate treatment and prescription. Pharmacists should act and act and contribute more since they are competent in evaluating rationality of antimalaria prescriptions.

5. ACKNOWLEDGMENT

The authors would like to express their gratitude to PLWH who participated in this study.

6. CONFLICT OF INTEREST

The author states that there is no conflict of interest in this research.

7. REFERENCES

Anosike, C., Chu-Madu, C. N., Igboeli, N. U., Adibe, M. O., & Ukwe, C. V. (2020). The participation of community pharmacists in the case management of malaria in enugu metropolis, nigeria: A cross-sectional survey. *Malawi Medical Journal*, *32*(4), 218–225. https://doi.org/10.4314/mmj.v32i4.7

Baird, J. K., Valecha, N., Duparc, S., White, N. J., & Price, R. N. (2016). Diagnosis and treatment of plasmodium vivax malaria. *American Journal of Tropical Medicine and Hygiene*, *95*(Suppl 6), 35–51. https://doi.org/10.4269/ajtmh.16-0171

Bursac, Z., Gauss, C. H., Williams, D. K., & Hosmer, D. W. (2008). Purposeful selection of variables in logistic regression. *Source Code for Biology and Medicine*, *3*, 1–8. https://doi.org/10.1186/1751-0473-3-17

Chu, C. S., & White, N. J. (2021). The prevention and treatment of Plasmodium vivax malaria. *PLoS Medicine*, *18*(4 April), 1–21. https://doi.org/10.1371/journal.pmed.1003561

Departemen Kesehatan RI. (2009). *Buku Saku Penatalaksanaan Kasus Malaria*.

Ezenduka C.C., O. M. J. . E. C. O. (2014). Adherence to treatment guidelines for uncomplicated malaria at two public health. *Journal of Pharmaceutical Policy and Practice*, 1–10.

Farooq, U., & Mahajan, R. C. (2004). Drug resistance in malaria. *J Vect Borne Dis*, *41*(September & December), 45–53. https://doi.org/10.1007/978-3-319-48683-3_19

Febrinasari, N., Santoso, A., Rosyid, A., Meilani, A. D., Sultan, U. I., & Rasional, P. O. (2021). Penggunaan obat rasional (POR) berdasarkan indikator pelayanan kefarmasian pada Puskesmas di Semarang. *Jurnal Farmasi Sains Dan Praktis*, *7*(1), 44–51.

Fried, M., & Duffy, P. E. (2017). Malaria during Pregnancy. *Cold Spring Harb Perspectives Medicine*, *7*(6). https://doi.org/10.1101/cshperspect.a025551

Mahittikorn, A., Mala, W., Wilairatana, P., Siri, S., Masangkay, F. R., Kotepui, K. U., & Kotepui, M. (2022). Prevalence, anti-malarial chemoprophylaxis and causes of deaths for severe imported malaria: A systematic review and meta-analysis. *Travel Medicine and Infectious Disease*, *49*(July), 102408. https://doi.org/10.1016/j.tmaid.2022.102408

Ofori-Asenso, R., & Agyeman, A. (2016). Irrational Use of Medicines—A Summary of Key Concepts. *Pharmacy*, *4*(4), 35. https://doi.org/10.3390/pharmacy4040035

Oyinaka, B., Umar, N., Aminu, N., Akinleye, C., & Nuhu, T. (2021). Knowledge and attitude of primary healthcare workers towards rational prescription of Artemisinin-based combination therapy in the treatment of uncomplicated malaria in Ondo State, southwestern Nigeria. *Journal of Pre-Clinical and Clinical Research*, *15*(1), 5–14. https://doi.org/10.26444/jpccr/131762

Parthasarathi, A., Puvvada, R., Patel, H., Bhandari, P., & Nagpal, S. (2021). Evaluation of Medication Errors in a Tertiary Care Hospital of a Low- to Middle-Income Country. *Cureus*, *13*(7). https://doi.org/10.7759/cureus.16769

Risberg, G., Johansson, E. E., & Hamberg, K. (2009). A theoretical model for analysing gender bias in medicine. *International Journal for Equity in Health*, *8*, 1–8. https://doi.org/10.1186/1475-9276-8-28

Sianturi, E. I., Latifah, E., Pane, M., Perwitasari, D. A., Satibi, Kristina, S. A., Hastuti, E. B.,

Pavlovich, J., & Taxis, K. (2021). Knowledge, empathy, and willingness to counsel patients with HIV among Indonesian pharmacists: a national survey of stigma. *AIDS Care*, 1–8. https://doi.org/10.1080/09540121.2021.1883506

Sianturi, E. I., Perwitasari, D. A., Soltief, S. N., Atiqul Islam, M., Geboers, B., & Taxis, K. (2021). Health literacy of people living with HIV in a rural area in Indonesia: A cross-sectional study. *Health and Social Care in the Community*, *29*(1), 127–134. https://doi.org/10.1111/hsc.13075

Siswantoro, H., Ratcliff, A., Wuwung, M., Marisela, R., Rumaseuw, R., Laihad, F., Ebsworth, P., Ansley, N., Price, R., & E Tjitra. (2006). Efficacy of existing antimalarial drugs for uncomplicated malaria in Timika Papua, Indonesia. *Med J Indonesia*, *15*(4).

Sitohang, V., Sariwati, E., Fajariyani, S. B., Hwang, D., Kurnia, B., Hapsari, R. K., Laihad, F. J., Sumiwi, M. E., Pronyk, P., & Hawley, W. A. (2018). Malaria elimination in Indonesia: halfway there. *The Lancet Global Health*, *6*(6), e604–e606. https://doi.org/10.1016/S2214-109X(18)30198-0

Uzochukwu, B. S. C., Onwujekwe, E., Ezuma, N. N., Ezeoke, O. P., Ajuba, M. O., & Sibeudu, F. T. (2011). Improving rational treatment of malaria: Perceptions and influence of RDTs on prescribing behaviour of health workers in Southeast Nigeria. *PLoS ONE*, *6*(1), 1–7. https://doi.org/10.1371/journal.pone.0014627

World Health Organization, & WHO. (2020). World Malaria Report: 20 years of global progress and challenges. In *World Health Organization*.

Zurovac, D., Rowe, A. K., Ochola, S. A., Noor, A. M., Midia, B., English, M., & Snow, R. W. (2004). Predictors of the quality of health worker treatment practices for uncomplicated malaria at government health facilities in Kenya. *International Journal of Epidemiology*, *33*(5), 1080–1091. https://doi.org/10.1093/ije/dyh253