

Knowledge And Practices Of Malaria Case Management As Per The National Guideline: A Survey Among Physicians In Aden,

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Abstract:

Background:

Malaria is a public health problem in Yemen where 78% of people are at some risk to contract it. After the emergence of chloroquine resistance in Yemen, the national anti-malaria policy has been changed in 2009 to artemisinin-based combination therapy. To ensure that treatment is effectively utilized and to prevent drug resistance development, it is important to assess knowledge and practices of physicians regarding the recent national guideline for anti-malaria case management recommended by the National Malaria Control Program.

Methods:

A cross-sectional survey was conducted in Aden (March to April 2014). Two hundreds and ten physicians involved in managing malaria patients were enrolled from selected public and private hospitals. A self-administered semi structured questionnaire was used to obtain information on socio-demographic characteristics, and knowledge about the national anti-malaria case management guideline. Statistical analysis was done using SPSS-20. Different descriptive tests were used as appropriate. Bivariate analysis was set at a significance level of $P < 0.05$.

Result:

Sixty percent of the participants didn't know about the national guideline; 23.8% had the guideline and only 11% received training on it. The first line drug treatment for uncomplicated malaria was identified correctly by the following percentages: 3.3% for adult, 3.8% for children, and 27.1% for first trimester of pregnancy, whereas none of them mentioned the correct first line anti-malaria drug for the second and third trimesters of pregnancy. Regarding physicians' knowledge about the first line drug treatment for complicated malaria,

84.8%, 66.7%, 49.0 % and 6.2% mentioned the correct drugs to treat adult, children, first trimester and the second and third trimesters of pregnancy respectively. No significant difference in the knowledge was detected between specialists and general practitioners except for first line treatment for complicated malaria in first pregnancy trimester. The highest percentage (92.7%) rely on parasitological confirmation in malaria diagnosis.

Conclusion:

This study reveals poor knowledge among physicians regarding national anti-malaria guideline, especially regarding the treatment of uncomplicated malaria of the vulnerable groups. Involvement of all stakeholders during the adoption and implementation of new national policies, providing training sessions and refresher courses is recommended to ensure correct and effective use of current policy.

Key words :

Knowledge, Practices, Malaria case management, National guideline for anti-malaria drugs, Yemen

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معرفة وممارسات إدارة حالات الملاريا وفقا للمبادئ التوجيهية الوطنية: مسح بين الأطباء في عدن، اليمن

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الخلاصة:

الملاريا هي مشكلة صحية عامة في اليمن حيث ان 78 % من الناس معرضون لخطر الإصابة. بعد ظهور مقاومة الكلوروكين في اليمن، تم تغيير السياسة الوطنية لمكافحة الملاريا في عام 2009 إلى العلاج المركب القائم على مادة الأرتيميسينين. ولضمان استخدام العلاج على نحو فعال ولمنع تطور المقاومة للدواء، كان من المهم تقييم معارف وممارسات الأطباء فيما يتعلق بالمبادئ التوجيهية الوطنية الأخيرة لإدارة حالات مكافحة الملاريا التي أوصى بها البرنامج الوطني لمكافحة الملاريا.

الاستنتاج:

تكشف هذه الدراسة عن ضعف المعرفة بين الأطباء فيما يتعلق بالمبادئ التوجيهية الوطنية لمكافحة الملاريا، وخاصة فيما يتعلق بمعالجة الملاريا غير المعقدة. ويوصى بإشراك جميع المشاركين في علاج الملاريا من خلال اعتماد وتنفيذ سياسات وطنية جديدة وتوفير دورات تدريبية ودورات لتجديد المعلومات لضمان الاستخدام الصحيح والفعال للسياسة الحالية.

منهجية الدراسة:

أجريت دراسة مقطعية في عدن في الفترة من مارس إلى أبريل 2014، وقد شملت الدراسة مائتين وعشرة أطباء مشاركين في إدارة مرضى الملاريا من مستشفيات عامة وخاصة. وقد استخدم استبيان منظم للحصول على معلومات عن الخصائص الاجتماعية والديموغرافية، والمعرفة حول المبادئ التوجيهية الوطنية لإدارة حالات مكافحة الملاريا، وقد تم تحليل النتائج باستخدام البرنامج الإحصائي SPSS.

الكلمات المفتاحية:

المعرفة، الممارسات، إدارة حالات الملاريا، المبادئ التوجيهية الوطنية للأدوية المضادة للملاريا، اليمن .

النتائج:

لم يكن 60% من المشاركين على دراية بالمبادئ التوجيهية الوطنية، 23.8% كان لديهم المبدأ التوجيهي، و 11% فقط تلقوا التدريب على ذلك. تم تحديد العلاج الأول ضد الملاريا غير معقدة بشكل صحيح من خلال النسب التالية: 3.3% للبالغين، 3.8% للأطفال، و 27.1% للثلاثة الأشهر الأولى من الحمل، في حين لم يذكر أحد منهم العلاج الأول الصحيح لمكافحة الملاريا للمرحلة الثانية والثالثة من الحمل. وفيما يتعلق بمعرفة الأطباء حول العلاج الأول للملاريا المعقدة، أشار 84.8% و 66.7% و 49.0% و 6.2% إلى الأدوية الصحيحة لعلاج البالغين، الأطفال، المرحلة الأولى، الثانية والثالثة من الحمل على التوالي.

ولم يوجد أي فرق كبير في المعرفة بين المتخصصين والممارسين العامين باستثناء علاج الخط الأول للملاريا المعقدة في المرحلة الأولى من الحمل.

Introduction :

Malaria is acknowledged to be by far the most important parasitic disease globally. Nearly 40% of the world's population at risk of contracting it [1] and most of the victims are children under- five and pregnant women [2,3]. Despite the fact that the disease is preventable and treatable, it is estimated that 214 million new cases of malaria and around 0.5 million deaths occurred in 2015 [4].

According to the World Malaria Report 2015 [4], malaria remains a major public health problem in Yemen, where 78% of the population are at some risk of contracting malaria and 25% at high risk of transmission, and with confirmed reported 67513 and estimated 290000-710000 malaria cases. The reported number of deaths was 19 with an estimated number of 35-2500 in 2013. The dangerous species *Plasmodium falciparum* is responsible for 99% of the cases.

In Aden, malaria control activities started very early in the 1900s [5]. However, the social and political unrest, as well as the environmental factor in the country lead to the resurgence of malaria with a high level of endemicity reach to a similar level to that of highly endemic African countries at the end of the 20th century [6]. This lead to the reestablishment of National Malaria Control Program (NMCP) in the Unified Republic of Yemen under the presidential appointment of a Supreme National Malaria Control Committee, which has developed a multi-strategic plan to control malaria [2,6,7]. The latest national strategy (2011-2015) states that by the end of 2015, the burden of malaria disease in Yemen will be reduced by 75% and near zero mortality [2]. One of these strategies is the early diagnosis and treatment to reduce morbidity and to prevent mortality [2,7]. However, several factors can affect the efficacy of treatment, including drug resistance.

The irrational prescription of anti-malaria drugs for treating fever in malaria endemic areas (even in the absence of malaria) increases the risk of drug resistance [8]. As a result, WHO recommends parasitological confirmation of malaria infection before treatment of suspected malaria cases [9]. This recommendation had also adopted by Yemen national malaria case management policy [2,10]. Additionally, the WHO issued a new guidance in 2001, calling on all countries with high levels of treatment failures to change to Artemisinin Combination Therapy (ACT) as first-line treatment in order to reduce the spread of resistance that may arise when artemisinin derivative

used as monotherapy [9,11].

In Yemen, the generalization of the treatment with ACT rolled out since 2009 after several anti-malaria drug efficacy studies that targeted the public and private sectors[2]. The national malaria treatment policy recommended that the first-line treatment for uncomplicated (simple) malaria is Artesunate + Sulphadoxine-Pyrimethamine (AS+SP) and the second-line is Artemether-Lumefantrine (AL). Recommended treatment for severe malaria is Quinine (QN). For pregnant women, QN is used for the treatment of both uncomplicated and complicated (severe) malaria in the first trimester of pregnancy. In the second and third trimesters, AS+SP is used for uncomplicated malaria while Artemether (AM) is used for the treatment of complicated malaria [10].

Therefore, there is a need to assess the knowledge and practices of physicians with regard the use of national malaria treatment policy. Therefore, the objective of this study is to assess the knowledge and practice of physicians in Aden, Yemen regarding the recommendations of NMCP guidelines of anti-malaria drugs policy.

Methods:

Study design, area and study population

This is a cross-sectional study carried out in March to April 2014 in Aden city, which is the economic capital of Yemen. Aden has eight districts with major five public and ten private hospitals in which services for malaria diagnosis and treatment are offered to those people who are in need.

The study population was general medical practitioners or specialists, from medical, gynecology and pediatrics wards as well as from the outpatients and emergency departments, who involved in managing patients attending these hospitals seeking for malaria diagnosis and treatment.

Sampling

The enrolled sample of studied physicians was calculated assuming that the expected proportion of anti-malaria policy knowledge among the physicians is 21% (as found by a recent study in nearby Yemeni governorates) [12] with absolute precision of 5%. The needed sample size was estimated using Lwanga and Lemeshow practical manual [13] to be 204. In addition, we added 10% of the estimated sample size in order to compensate for the non-response rate. Thus, the targeted sample size was 225.

To obtain this sample, the first step was the random selection of 50% of all public and private hospitals in the city. Three public hospitals and five private hospitals were selected. All physicians in the selected hospitals who were present at the time of the study and who were eligible and agreed to take part in the study were recruited until the required number of 225 respondents was completed. After providing consent, the participants were given the questionnaire from one of the study members by hand. Physicians who were not involved in managing malaria patients or who did not provide consent to participate were excluded from the study.

Measures

A self-administered, structured, pre-tested questionnaire was used as a data collection instrument for this study. Data collected included socio-demographic characteristics of the study participants, Malaria diagnosis practices, knowledge about the national policy, first line treatment for malaria, and physicians' knowledge on the ACTs. The Yemen national guideline for anti-malaria drugs, 2009 were used in this study as the benchmark for recommended malaria treatment practices [10]. The participants either returned back the questionnaire at the same day or it was collected during the following two days from their hospitals.

Data analysis

Data were entered and analyzed by using SPSS (version 20.0) software. Categorical variables were described by using frequency distribution and percentage while continuous variables were described using means, standard deviations, medians and interquartile ranges. Comparison of categorical data was performed using the Chi-square test or Fisher's Exact test if necessary. P value <0.05 was considered statistically significant.

Ethics approval and consent to participate

Permission was obtained from the Research Ethics Committee of the Faculty of Medicine and Health Sciences, University of Aden before initiating the research. Before any data were obtained, physicians were informed about the aim of the study and the consent for participation was obtained from each of them after including information about the purpose of the study and its scope in the questionnaire itself. To ensure confidentiality, each questionnaire was assigned a study number and the participants were asked not to provide their names.

Results:

The responses were obtained from 210 participants giving a response rate of 93.3%.

Characteristics of the study population

The mean age of the participants was 34.1 years and median duration of their experience was 5 years. Most of the studied physicians were females (67.0%), general practitioners (61.4%), and were from public hospitals (58.7%). Further information on the characteristics of the participants is shown in Table 1.

Table 1: The characteristics of the participants (n=210).

Characteristic		
Age in years, Mean (SD)	34.1 (7.51)	
Duration of experience in years, Median (interquartile range)	5 years (2-10)	
	No.	%
Sex		
Male	69	33.0
Female	141	67.0
Professional degree		
General practitioner	129	61.4
Specialist	81	38.6
Work sector		
Public	123	58.7
Private	55	26.4
Both	32	14.9

Knowledge on anti-malaria national policy:

Table (2) revealed that less than half (n=85/210) of the participant had heard about the national anti-malaria drug policy and only around one quarter (n=50/210) and about one tenth (n=23/210) of the studied physicians were having the national guidelines of anti-malaria drug policy and had received training on this guideline respectively.

Table 2: Knowledge on anti-malaria management national policy guideline (n=210).

Variable	No.	%
Heard about the guideline:		
Yes	85	40.5
No	125	59.5
Having the guideline:		
Yes	50	23.8
No	160	76.2
Received training on the guideline		
Yes	23	11.0
No	187	89.0

Physicians' knowledge regarding the first line treatment of malaria:

When the participants were asked to mention the first line treatment, the answers were as follow for different targeted groups:

- Uncomplicated malaria in adults and children (Figure 1):

The AS+ SP was reported by 10% for adults and 5.7% for children. Of them only 3.3% and 3.8% reported the correct combination respectively. The most frequent drugs reported to treat uncomplicated malaria in adult and children were artemisinin mono therapy (AS or AM) followed by chloroquin (CQ).

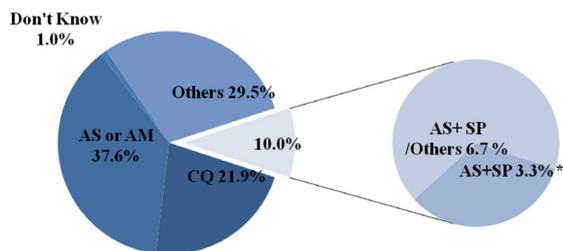


Fig. 1: The percentage of the reported drugs by physicians as a first line treatment for uncomplicated malaria in adult.

- Uncomplicated malaria in pregnant women (Figure 2):

Drugs which were frequently reported to treat malaria in pregnant women were QN, artemisinin mono-therapy and CQ. Only 27.1% mentioned QN as a correct answered. In addition, 38.1%, 19.0% of the physicians claimed that they don't know the first line anti-malaria for the pregnant women in the first trimester, and second and third trimesters respectively.

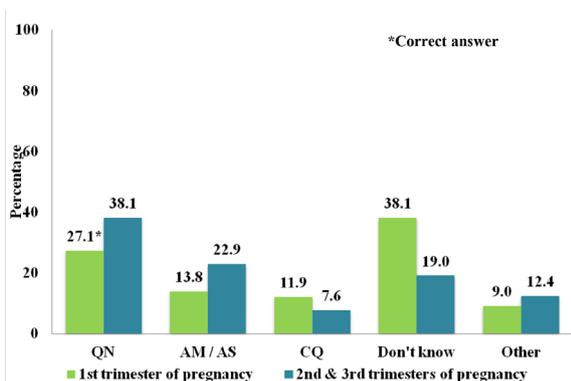


Fig. 2: The percentage of the reported drugs by physicians as a first line treatment for uncomplicated malaria in pregnant women.

- Complicated malaria in adults and children (Figure 3):

QN was correctly mentioned by high percentage of participants (84.8% for adults and 66.7% for children). Other drugs were mentioned less frequently. However, 25.2% stated that they don't know the drug recommended for children as first line treatment of complicated malaria. Regarding treatment of severe malaria ; authors wish to clarify that this study was conducted before the recent recommendation of the national malaria control program regarding change the drug of first choice for treatment of severe malaria from QN to artesunate injections, so the obtained answer of respondents about QN is the drug of choice is considered correct answer.

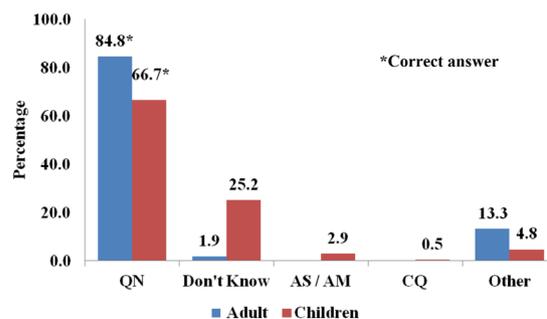


Fig. 3: The percentage of the reported drugs by physicians as a first line treatment for complicated malaria in adult and children

- Complicated malaria in pregnant women (Figure 4):

Forty nine percent and 6.2% had mentioned the correct answer for the first and second and third trimesters of pregnancy respectively. The highest "don't know" answer was reported here with 39.4% for the first the trimester and 37.1% for the second and third trimesters of pregnancy.

In Table 3, neither the general practitioners nor the specialists could identify the correct answer for the first line treatment of uncomplicated malaria in the second and third trimester of pregnancy. There is no statistically significant differences between general practitioners and specialists in their knowledge about the first line treatment of all groups, except for complicated malaria treatment during the first trimester of pregnancy (p=0.0056) where specialists has higher percentages of correct answers (61.7%) compared to general practitioners (41.1%).

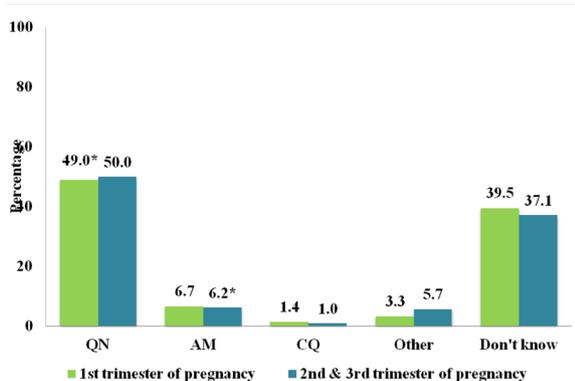


Fig. 4: The percentage of the reported drugs by physicians as a first line treatment for complicated malaria in pregnant women.

Table 3: Correct responses regarding the first line treatment of malaria by physicians' professional degree.

Treatment Policy	Correct Responses						p-value
	Total (n=210)		General Practitioners (n=129)		Specialists (n=81)		
	No.	%	No.	%	No.	%	
First line treatment of uncomplicated malaria							
Adult	7	3.3	4	3.1	3	3.7	1.000
Children	8	3.8	3	2.3	5	6.2	0.2656
1 st trimester of pregnancy	57	27.1	30	23.3	27	33.3	0.1501
2 nd & 3 rd trimesters of pregnancy	0	0.0	0	0.0	0	0.0	1.000
First line treatment of complicated malaria							
Adult	178	84.8	113	87.6	65	80.2	0.1697
Children	140	66.7	89	69.0	51	63.0	0.7964
1 st trimester of pregnancy	103	49.0	53	41.1	50	61.7	0.0056*
2 nd & 3 rd trimesters of pregnancy	13	6.2	9	7	4	4.9	0.7700

* Statistically significant by Chi square test

Knowledge on ACTs

Knowledge drugs comprising ACTs are shown in Table 4. Out of 205 respondents, 145 (71.7%) claimed that they know ACTs. When asked to mention ACTs they know, 77.9% (n=113/145) of the participants mentioned AS+SP and / or AL. However, anti-malaria drugs other than ACTs were mentioned 34.5% of the time as being ACTs.

Table 4: Drugs mentioned as ACTs by the respondents (n=145).

Drugs	No.	%*†
Correct ACTs (n=113)		
AS+SP	53	36.5
AL	60	41.4
Drugs other than ACTs	50	34.5

* Percentages were taken from the total 145.

† Percentages cannot be summed to 100% due to multiple responses.

Malaria diagnosis practices

Table 5 shows that the majority of the respondents reported that they diagnosed malaria using microscopy and / or Rapid Diagnostic Test (RDTs) (92.7%, n=191/206). The use of blood film among the respondents was particularly high (86.9%, n=179/206).

Table 5: Methods used for malaria diagnosis (n=206).

Methods	No.	%*†
Microscopy and / or RDTs (parasitological confirmation)	191	92.7
Microscopy (blood film)	179	86.9
Clinical manifestation & (blood film &/ or RDT)	173	84.0
Clinical manifestation & blood film	162	78.6
RDT	40	19.4
Clinical manifestation & RDT	38	18.4
Don't rely on clinical manifestation	18	8.7
Microscopy only	16	7.8
Clinical manifestation only	15	7.3
RDT only	1	0.5
Microscopy & RDT only	1	0.5

* Percentages were taken from the total 206

† Percentages cannot be summed to 100% due to multiple responses.

Discussion:

This study has been conducted to assess the knowledge of physicians of anti-malaria case management and their practices regarding the current NMCP guidelines. The study reveals a poor knowledge of the current national anti-malaria management policy. Despite the fact that the guideline has implemented since 2009, 59.5% did not know about the national anti-malaria policy. This is a serious and critical issue concerning the communication of the information between the policy makers and the frontline implementer of the policy. Earlier studies conducted in India [14] and some African countries [8,15–17] on health professional practices following anti-malaria policy change, have shown their inappropriate level of adherence to the new policy, even after several years from the introduction of the new guidelines. Moreover, a study conducted in Yemen showed that, only 23% of the participants describe AS+ SP as first-line treatment [12]. However, in our study, AS+SP was described as the first line drug by only 10% of the participants for the adult group.

Our findings have revealed that the participants' knowledge was low regarding the treatment of uncomplicated malaria in the most vulnerable population; children and pregnant women. In areas where the malaria is endemic, such as Yemen [18,19], the burden of uncomplicated malaria in these groups is

substantial; and effective treatment is necessary to prevent severe complications [3,20]. This finding is concordant with other studies conducted in Yemen [12] and Africa [16,17] that has shown a lower level of knowledge regarding the anti-malaria treatment policy in these groups in comparison to the knowledge in the adult group. The participants' poor knowledge regarding ACTs in general was obvious, as 34.5% from the participants who claimed knowledge on ACTs confused it with other anti-malaria drug class.

Since educating and training the health professionals among others, are essential prerequisites for effective implementation of new policy [11], we claim that the low training level among the participants (11%) and the percentage of the participants who possess the guideline (23.8%) were contributing factors to their poor knowledge [17].

Yet, a similar study in Malawi [16], research participant level of knowledge was higher than the percentage of those received training in the new policy implementation. Nevertheless, the knowledge regarding the first line treatment in our study was even lower than their level of training (10%, 5.7% and 0% in the adult, children and second and third trimesters of pregnancy, respectively). Thus, further studies to identify and correct these poor knowledge's contributing factors must be carried out. On the other hand, despite that knowledge regarding the treatment of complicated malaria was generally good among both groups of physicians except for second and third trimester of pregnancy; still, it is not sufficient.

In contrast to a study conducted in Pakistan [21], there were no statistical differences between the general practitioners' knowledge and that of the specialists except for first line treatment for complicated malaria in the first pregnancy trimester. This could indicate the need for planned training and knowledge upgrading activities for both groups.

Although this study has revealed the poor knowledge regarding the current malaria policy among the physicians, the drugs mentioned by them as being the first line could represent two trends:

1. The use of the earlier guideline drugs such as CQ [22] which may improve the patients' clinical symptoms without clearing the parasitemia [23] and

2. The use of artemisinin monotherapy and /or QN. Many physicians seem aware of anti-malaria drug resistance to CQ through their practice, but not in the current national policy, and thus they use the artemisinin monotherapy or QN to treat uncomplicated malaria. These drugs may have a satisfactory clinical

result. However, the public health impact of this drug misuse would be significant, as resistances to these two drugs have already reported in Southeast Asian countries [24–27].

The diagnosis practice, through microscopy and / or RDT besides the clinical symptoms of the majority of the respondent (92.7%) complies with WHO recommendation and NMCP recommendation [2,9,10]. Nevertheless, more sensitization to the recommended malaria diagnosis and the complicated malaria treatment is essential, since malaria has a substantial burden on the Yemen public health and the health system.

The study has the following limitations: the study population was physicians in hospitals and they approached through convenient sampling. Thus, they may differ from other health care provider, such as physicians in primary health centers, pharmacist and other health allies and non-sampled population. Therefore, the generalizability of the study findings may be dealt with caution. In addition, the survey tool was a self-administrated questionnaire and some participants did not fill in all the required information. Moreover, the participants' knowledge and claimed practices may also differ from their actual prescription practices as previously reported [12].

Conclusion:

This study reveals serious knowledge gap regarding the current national policy among physicians especially for the first line treatment of uncomplicated malaria in vulnerable groups. Inadequate endorsement for the national policies, unaffordable guidelines for the physicians and inadequate training was a contributing factor for the physicians' poor knowledge. The guidelines must be available to all health care providers. Universal training and refresher courses for physicians on using the current anti-malaria policy must be scaled up. We recommend engaging all the stakeholders (including academia) in the adoption and implementation of the national guidelines in order to emphasize the adherence to national policies for common endemic diseases in both undergraduate and postgraduate medical curricula. We also are recommending further studies to evaluate the factors affecting the utilization of the national guidelines.

List of abbreviations: ACT: Artemisinin Combination Therapy; AM: Artemether; AL: Artemether-Lumefantrine; AS: Artesunate; CQ: Chloroquine; QN: Quinine; NMCP: National Malaria Control Program; SP: Sulphadoxine-Pyrimethamine; RDTs: Rapid Diagnostic Tests; WHO: World Health Organization.

Competing interests: The authors declare that they have no competing interests

Funding: The study is self-funded

Authors' contributions

All authors contributed to the work presented in this manuscript, read and approved the final manuscript. KA designed the study, developed the study tools, analyzed the data, and participated in writing the manuscript. HB designed the study, developed the study tools, and participated in writing the manuscript. AB designed the study, developed the study tools, performed the field work, analyzed the data and participated in writing the manuscript.

Acknowledgements

Our thank goes to the physicians participated in the study. Deep gratitude extends to the colleagues helped in collecting back the filled questionnaires.

References:

1. World Health Organization. Global technical strategy for malaria 2016–2030. Geneva: World Health Organization; 2016.
2. Ministry of Public Health and Population (Yemen). Yemen ' s National Malaria Control and Elimination Strategic Plan 2011-2015. 2011.
3. Sevene E, González R, Menéndez C. Current knowledge and challenges of antimalarial drugs for treatment and prevention in pregnancy. *Expert Opin Pharmacother*. 2010;11(8):1277–93.
4. World Health Organization. World malaria report 2015. Geneva; 2016.
5. Colbourne M, Smith S. Problem of malaria in Aden protectorate: (report on a visit). England; 1964.
6. Snow RW, Amratia P, Zamani G, Mundia CW, Noor AM, Atta H. The malaria transition on the Arabian Peninsula : progress toward a malaria-free region between 1960 – 2010. In: Rollinson D, editor. *Advances in Parasitology*. Elsevier Ltd; 2013. p. 205–51.
7. Ministry of Public Health and Population (Yemen). Report on the final results of the national malaria indicators survey. 2009.
8. Kamuhabwa AA, Silumbe R. Knowledge among drug dispensers and antimalarial drug prescribing practices in public health facilities in Dar es Salaam. *Drug Healthc Patient Saf*. 2013;5:181–9.
9. World Health Organization. WHO briefing on Malaria Treatment Guidelines and artemisinin monotherapies. Geneva: World Health Organization

- tion 2006; 2006.
10. Ministry of public health and population (Yemen). The national guideline for anti-malaria drugs. 2009.
11. World Health Organization. Malaria case management: operations manual. Geneva: World Health Organization; 2009.
12. Bin Ghouth AS. Availability and prescription practice of anti-malaria drugs in the private health sector in Yemen. *J Infect Dev Ctries*. 2013;7(5):404–12.
13. Lwanga SK, Lemeshow S. Sample size determination in health studies: a practical manual. Geneva: World Health Organization; 1991.
14. Ahir G, Bala D V. Perceptions and attitudes of resident doctors about malaria treatment as per national drug policy in malaria. *Natl J Community Med*. 2012;3(1):71–3.
15. Manirakiza A, Njuimo SP, Le Faou A, Malvy D, Millet P. Availability of antimalarial drugs and evaluation of the attitude and practices for the treatment of uncomplicated malaria in bangui, Central African Republic. *J Trop Med*. 2010;2010:10–5.
16. Kalilani-phiri L V, Lungu D, Coghlan R. Knowledge and malaria treatment practices using artemisinin combination therapy (ACT) in Malawi : survey of health professionals. *Malar J*. 2011;10(279).
17. Harrison NE, Olufunlayo TF, Agomo CO. Utilization of the current national antimalarial treatment guidelines among doctors in army hospitals in Lagos , Nigeria. *Open J Prev Med*. 2012;2(3):390–3.
18. Al-mekhlafi AMQ, Mahdy MAK, Azazy AA. Clinical situation of endemic malaria in Yemen. *Trop Biomed*. 2010;27(3):551–8.
19. Bamaga O a, Mahdy M a, Mahmud R, Lim Y a. Malaria in Hadhramout, a southeast province of Yemen: prevalence, risk factors, knowledge, attitude and practices (KAPs). *Parasit Vectors*. 2014;7(1):351.
20. Brabin B, Romagosa C, Abdelgalil S, Menéndez C, Verhoeff F, McGready R, et al. The Sick Placenta—The Role of Malaria. *Placenta* [Internet]. 2004;25(5):359–78. Available from: <http://www.sciencedirect.com/science/article/pii/S0143400403003072>
21. Malik M, Shafie AA, Hussain A. Knowledge and perceptions of prescribers regarding adherence to standard treatment guidelines for malaria : a

- comparative cross-sectional study from Pakistan. *EMHJ*. 2014;20(4):221–8.
22. Bashrahil KA, Bingouth AS, Baruzaig AS. Antimalarial drugs : availability and mode of prescribing in Mukalla , Yemen. *EMHJ*. 2010;16(2):146–50.
 23. Vestergaard LS, Ringwald P. Responding to the challenge of antimalarial drug resistance by routine monitoring to update national malaria treatment policies. *Am J Trop Med Hyg* [Internet]. 2007 Dec;77(6 Suppl):153–9. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/18165488>
 24. World Health Organization. Status report on artemisinin resistance. Geneva; 2014.
 25. Cui L, Mharakurwa S, Ndiaye D, Rathod PK, Rosenthal PJ. Antimalarial drug resistance : literature review and activities and findings of the ICEMR network. *Am Soc Trop Med Hyg*. 2015;93(Suppl 3):57–68.
 26. Tun KM, Imwong M, Lwin KM, Win AA, Hlaing TM, Hlaing T, et al. Spread of artemisinin-resistant *Plasmodium falciparum* in Myanmar: A cross-sectional survey of the K13 molecular marker. *Lancet Infect Dis*. 2015;15(4):415–21.
 27. Achan J, Talisuna AO, Yeka A, James K Tibenderana FNB, Rosenthal PJ, D'Alessandro U. Quinine , an old anti - malarial drug in a modern world : role in the treatment of malaria. *Malar J*. 2011;10(144).