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Medicines dispensers' knowledge on the implementation of an artemisinin-based combination therapy policy for the treatment of uncomplicated malaria in Tanzania

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ABSTRACT

Objective: In 2005, Tanzania changed its policy for uncomplicated malaria treatment from sulphadoxine–pyrimethamine (SP) to artemisinin-based combination therapy (ACT), specifically artemether-lumefantrine (ALU). SP remains the medicine of choice for intermittent preventive treatment in pregnancy (IPTp). There is a need to assess dispensers' knowledge regarding the treatment of uncomplicated malaria and IPTp in Tanzania given appreciable self-purchasing to improve future care. **Methods:** Descriptive cross-sectional design with structured questionnaires to capture quantitative data, with qualitative data captured using focus groups. The study was performed at 32 private pharmacies and 33 Accredited Drug Dispensing Outlets (ADDOs) in the Nyamagana and Sengerema Districts in Tanzania, with 20 dispensers included in the qualitative discussions. **Key findings:** The knowledge level of dispensers in the private medicine outlets was variable. Most dispensers knew ALU was first line treatment in uncomplicated malaria; however variable knowledge about taking ALU with fatty meals. Generally poor knowledge about dosing intervals for SP in IPTp and variable knowledge regarding treatments in the first trimester. Overall, 49% had good knowledge and 48% moderate knowledge of ACT in uncomplicated malaria. There was a significant relationship between dispenser type and knowledge of ACT but no statistical relationship between the level of knowledge on IPTp and the dispenser. **Conclusion:** Majority of dispensers in private medicines outlets have good knowledge on ACT policy in the treatment of uncomplicated malaria, however; few dispensers had good knowledge on IPTp, which may contribute to irrational dispensing of SP. This needs addressing given the extent of self-purchasing in Tanzania.

Key Words: Artemisinin Based Combination Therapy Policy, Pharmacists Knowledge, private medicine outlets, Sulphadoxine Pyrimethamine, Tanzania.

1. INTRODUCTION

Malaria occurs most often in pregnant women and young children (1, 2). The greatest burden is in tropical regions (2-4), and in Africa malaria remains one of the most common diagnoses (5). For many years, malaria has been a leading cause of death in Sub-Sahara Africa especially among children (6, 7), although the number of deaths are decreasing (6, 8-10), helped by the availability of rapid diagnostic tests, prevention programmes and antimalarial medicines (10, 11). Malaria also has a significant impact on morbidity (7, 12). As a result, malaria is one of the leading public health concerns in infected countries, causing up to 660,000 deaths per year or higher (4, 10). Malaria is also a public health concern in Tanzania where in 2000, malaria accounted for over 43% of outpatient attendance, 42% of all hospital admissions and 32% of hospital deaths (6), with a similar situation in Uganda (13). The prevalence of confirmed malaria in children under five in Tanzania using a rapid diagnostic test (mRDT) in 2011 to 2012 was 9% (14). The number of deaths have decreased in recent years in Tanzania, down 68% between 2005 and 2015 (8), with the number of reported cases down to six hundred and eight thousand in 2014 from 1.28 million in 2010 (15). Never-the-less, malaria was the seventh highest cause of death in Tanzania in 2015 (8, 15).

The impact of malaria can be far reaching. In pregnancy, malaria can lead to birth complications, an increased risk of communicable and non-communicable diseases, and a high risk of both maternal and perinatal morbidity and mortality (2, 16, 17). Malaria in pregnancy contributes to an estimated 100,000 neonatal deaths and 10,000 maternal deaths annually (17). In Nigeria, up to 11% of maternal deaths and 30% of childhood deaths are due to malaria (2). Malaria also results in considerable economic burden for households, including high co-payments for medicines in countries including Tanzania (4, 6, 9, 18-20) and reduced economic growth (4, 13, 21). In addition in children who survive, reduced educational attainment and intellectual development as a result of the time lost from schooling and the long-term sequelae (22). There is also loss of quality of life. The continued impact of malaria on morbidity and mortality in Tanzania ensures it is still a considerable public health problem necessitating appropriate care.

In 2005, the Ministry of Health and Social Welfare, United Republic of Tanzania, changed the recommended treatment for uncomplicated malaria from sulphadoxine–pyrimethamine (SP) to artemisinin-based combination therapy (ACT) – specifically artemether-lumefantrine (ALU) (23). However, SP remains the medicine of choice for intermittent preventive treatment in pregnancy (IPTp) in Tanzania and across Africa (2, 10, 23, 24). ACT is also the recommended first line treatment in the second and third trimesters of pregnancy for uncomplicated malaria (2, 7, 25-27), with quinine still recommended for severe malaria across all trimesters as dihydroartemisinin/piperaquine (DPQ) as well as for second line treatment (2, 17, 28). This is because of the suspected teratogenic effects of artemether during the first trimester. As a result, quinine is used in early pregnancy if needed unless the risks outweigh the benefits (2, 28). It is particularly important that medicines used in pregnancy are known to be safe (2, 26). IPTp has recently been shown to be highly cost effective for both prevention of maternal malaria and reduction in neonatal mortality in areas with moderate or high malaria transmission (29). Despite the spread of SP resistance, IPTp continues to provide significant benefit, resulting in protection against both neonatal mortality as well as and low birth weights (30). As a result, it continues to be recommended.

The implementation of any new policy can be divided into technical and operational components as well as monitoring and evaluation. The technical components include regulatory changes, development and dissemination of essential medicines lists and standard treatment guidelines (STGs), as well as training and supervision of health care workers (31). To date, there has been greater efforts in training health service providers in the public sector in Tanzania on the use of ACT relative to the private sector, despite the vital role they both play in malaria treatment (32, 33). This has also been seen in other countries (2, 33). In Burundi, the highest knowledge regarding ACT therapy was in the charitable sector (90%), with lower levels in the private sector (55%) (34). Education of healthcare professionals is also important to

reduce over diagnosis of malaria, with implications for the development of resistance (35, 36). This is particularly important in sub-Saharan Africa where over 70% of patients with suspected malaria treat their illness with traditional remedies or medicines bought from pharmacies and other stores (35).

The assumption that healthcare professionals will routinely follow STGs simply by just being available is optimistic, especially with their variable availability (37-40). This is a concern (40). with typically multiple approaches needed to enhance adherence to STGs(41-44). Multiple approaches resulted for instance in high adherence rates to recommended treatments in Sweden and other countries (45, 46).

Currently, data evaluating health professional knowledge before or during the implementation of the new ACT policy and IPTp in the private sector in Tanzania are scarce. Minzi *et al* (47) found a lack of involvement of pharmacy personnel working in private pharmacies in the development of guidelines, or training in their implementation, which contributed to poor knowledge and skills on how to correctly dispense medicines for malaria. Furthermore, only 30% and 7% respectively of pharmacy personnel knew the correct dosing regimen for SP and ALU(47), with no one knowing the recommendation of taking ALU with a fatty meal for improved absorption (47). There are also concerns with the level of testing for malaria across facilities (48), with the availability of rapid tests, coupled with training, significantly reducing dispensing of antimalarials to patients without malaria (5).

Consequently, we sought to address this gap by assessing the knowledge of dispensers in private medicine outlets in Tanzania regarding the treatment of uncomplicated malaria. We chose to investigate the private sector first given appreciable self-purchasing of antimicrobials in Tanzania including treatments for malaria in private facilities (6, 19, 20, 49), and there have been concerns with their knowledge of malaria treatment as well as other disease areas (6, 20, 47, 49, 50). Self-purchasing can arise from long waiting times and shortages of medicines at health facilities, long distances to access health facilities as well as inability by some to pay for both health care and treatment (6).

The findings of this study will be used to plan future interventions in Tanzania, if needed, to improve future management of these patients.

2. MATERIAL AND METHODS

2.1 Study area and population

This was a descriptive cross-sectional study including both qualitative and quantitative data. Qualitative data were captured based on focus group discussions among dispensers using guided questions. Quantitative data were captured using structured questionnaires.

The study was conducted between October 2014 and May 2015 in the Mwanza region of Tanzania. This was conveniently selected because it is highly populated and is a holoendemic area for malaria transmission (49). The study population consisted of dispensers working at private pharmacies and Accredited Drug Dispensing Outlets (ADDOs) located in the Nyamagana and Sengerema Districts of the Mwanza region. Overall, this region has 7 districts. ADDOs currently have limited training compared to community pharmacists and can only dispense a limited number of medicines including those for uncomplicated malaria.

2.2 Sample size, sampling technique

For the quantitative study, we conducted interviews using structured questionnaires in 65 medicines outlets. This consisted of 33 ADDOs and 32 private pharmacies (out of a total of 47 Pharmacies and 50 ADDOs in Nyamagana and Sengerema districts), with only one interviewee per outlet. We used the Daniel and Cross formula for calculating the sample size (51) and randomly sampled outlets (simple random sampling). The questionnaire was developed in English then translated in Swahili. It was piloted, with the final questionnaire refined to robustly assess the knowledge of dispensers on ACT policy and IPTp (Appendix 1).

Four focus group discussions were conducted among dispensers in the private medicine outlets with five participants in each, making a total of 20 dispensers. Purposive sampling was employed for their selection. For qualitative data, the information obtained was transcribed and translated. The analysis was done manually using content analysis techniques (52).

2.3 Data collection and analysis

There were 22 questions to assess the knowledge of dispensers (Appendix 1). Table 1 shows the knowledge scale based on the number of correctly answered questions using the method of Kamuhabwa *et al.* (50).

Table 1: Scale for measuring level of knowledge based on the number of correct answers

	POOR	MODERATE	GOOD	Total questions
Treatment of uncomplicated malaria using ACT	0-5	6-10	11-15	15
IPTp	0-2	3-5	6-7	7

The coded data were analyzed using Statistical Package for Social Sciences (SPSS - Version 20.0) computer analysis software. A *P*-value of less than 0.05 was considered as statistically significance. To protect dispensers' privacy, no names were recorded and names of outlets were not mentioned in connection with the study's results. Table 2 depicts the characteristics of the 55 respondents completing the questionnaire.

Table 2: Social demographics of respondents in ADDOs (n=33) and Community Pharmacies (n=32)

Demographics		Pharmacies		ADDOs	
		Frequency	Percentage	Frequency	Percentage
Sex					
	Male	15	46.9	11	33.3
	Female	17	53.1	22	66.7
Age (in years)					
	15-24	1	3.1	4	12.1
	25-34	12	37.5	9	27.3
	35-44	8	25	11	33.3
	Above 45	11	34.4	9	27.3
Profession					
	Pharmacist	5	15.6	0	0
	Pharmaceutical technician	15	46.9	0	0
	Pharmaceutical assistants	4	12.5	0	0
	5 weeks trained ADDO dispenser	6	18.8	26	78.8
	Clinical officer	0	0	1	3
	Nursing officer/nurse midwife	1	3.1	1	3
	Nurse Assistant	0	0	3	9.1
	Others	1	3.1	2	6.1
Experience in dispensing					
	Less than 1 year	6	18.8	8	24.2
	1 to 5 years	8	25	9	27.3

	6 to 10 years	9	28.1	9	27.3
	11 years and above	9	28.1	7	21.2
Attended training					
	Yes	4	12.5	1	3
	No	28	87.5	32	97

NB: *Others included Assistant clinical officer, Assistant medical officer and one year course medicine dispenser.

The majority of dispensers in community pharmacies were pharmaceutical technicians, while in ADDOs none of the dispensers were pharmacists, with the majority undergoing five weeks training.

For qualitative data, the information obtained was transcribed and translated. The analysis was done manually using content analysis techniques (52).

2.4 Ethical Considerations

Ethical clearance was obtained from the Ethical Review Committee of Muhimbili University of Health and Allied Sciences (MUHAS).

3. RESULTS

3.1 Results from Structured Questionnaire

Table 3 shows the results of the dispensers' knowledge survey. Dispensers in ADDOs had consistently lower knowledge than dispensers in private pharmacies with the exception that respondents knew the number of days for dosing of ALU. However, only 40.2% of pharmacy dispensers and 18.2% of ADDOs dispensers correctly identified quinine tablets as recommended for uncomplicated malaria in first trimester of pregnancy. Dispensers also showed poor knowledge of secondary treatment of uncomplicated malaria with only 34.4% of pharmacy and 9.1% of ADDOs dispensers mentioning DPQ tablets. Very few respondents were also able to mention the interval recommended for pregnant mother to take SP for IPTp.

Table 3: Positive responses to questions assessing the knowledge of dispensers in the treatment of malaria using ACT and on IPTp

	Private Pharmacies (n=32)	ADDOs (n=33)	Total (n=65)
Q: Mention the first line medicine for treatment of uncomplicated malaria A: ALU is the first line medicine for the treatment of uncomplicated malaria	100%	90.9%	95.4%
Q: ALU is not recommended to which group of individuals? A: ALU is not recommended in pregnancy during first trimester	65.6%	42.4%	54.1%
Q: Which medicine is recommended for treatment for uncomplicated malaria in first trimester of pregnancy? A: Quinine tablets are the medicine recommended in first trimester where benefits outweigh the risks	40.6%	18.2%	29.4%
Q: What is the reason for ALU to be taken with fat meals? A: ALU should be taken with fat meals so as to increase its absorption	56.3%	24.2%	40.2%
Q: The dosage of ALU has to be taken for how many days? A: A dosage regimen of ALU is taken for 3 days	100%	100%	100%
Q: Mention second line medicine for treatment of uncomplicated malaria	34.4%	9.1%	22%

A: Second line anti-malarial treatment is DPQ tablets			
Q: What is the interval recommended for the pregnant mother to take SP for IPTp A: Interval recommended for the pregnant mother to take SP for IPTp it is every clinic visit from second trimester, i.e. monthly	6.3%	6.1%	6.2%
Q: What will be the effect of administering SP for the use other than IPTp e.g. for treatment of uncomplicated malaria A: When SP is used for treatment of malaria rather than IPTp - it may result in SP resistance for IPTp	53.1%	24.2%	38.6%

NB: Q: question; A: answer

Encouragingly, most dispensers in ADDOs (72.7%) and 50% of dispensers in private pharmacies mentioned SP respectively, and 40.6% of dispensers mentioned quinine, as the treatment of uncomplicated malaria in the first trimester of pregnancy. However only 18.2% of ADDOs mentioned quinine. The remainder, i.e. 9.4% of community pharmacies and 9.1% ADDOs, included respondents who did not know the treatment; alternatively, suggested DPQ and sulphamethoxypyrazine / pyrimethamine (SPP).

Overall, 49.2% of dispensers had good knowledge on the treatment of malaria using ACT based on Table 1, 47.7% moderate knowledge and 3.1% poor knowledge. There was worse knowledge regarding IPTp with only 15.2 % of dispensers in community pharmacies having good knowledge (0% in ADDOs), 66.7% having moderate knowledge (65.6% in ADDOs) and 18.2% poor knowledge (34.4% for ADDOs).

Tables 4 and 5 summarizes the knowledge levels of dispensers by type and if the dispenser attended any training session on malaria treatment. Table 4 evaluates dispenser's level of knowledge on ACT by the type of dispenser and their training whilst Table 5 assess dispensers' level of knowledge on IPTp, again by the type of dispenser and their training (n=65). There was a statistical significant relationship between the type of dispenser and his/her level of knowledge on ACT (P=0.007). However, there was no statistical significant relationship between type of dispenser and his/her knowledge on IPTp (P=0.075).

Table 4: Dispenser's level of knowledge on ACT by type of dispenser and attending training (n=65)

Demographics		Level of Knowledge			Total	P value
		Poor	Moderate	Good		
Profession/ Type of dispenser						
	Pharmacist	0(0%)	2(40%)	3(60%)	5	0.007
	Pharmaceutical technician	0(0%)	2(13.3%)	13(86.7%)	15	
	Pharmaceutical assistant	0(0%)	2(40%)	3(60%)	5	
	ADDO dispenser	1(3.1%)	20(62.5%)	11(34.4%)	32	
	Clinical officer	0(0%)	0(0%)	1(100%)	1	
	Nursing officer/nurse midwife	0(0%)	2(100%)	0(0%)	2	
	Nurse assistant	1(50%)	1(50%)	0(0%)	2	
	Others	0(0%)	2(66.7%)	1(33.3%)	3	
Attending training						
	Yes	0(0%)	0(0%)	5(100%)	5	0.066
	No	2(3.3%)	31(51.7%)	27(45%)	60	

Table 5: Dispenser's level of knowledge on IPTp by profession of the dispenser and attending training (n=65)

Demographics		Level of Knowledge			Total	P value
		Poor	Moderate	Good		
Profession						
	Pharmacist	1(20%)	3(60%)	1(20%)	5	0.075
	Pharmaceutical technician	2(13.3%)	9(60%)	4(26.7%)	15	
	Pharmaceutical assistant	1(20%)	4(80%)	0(0%)	5	
	ADDO dispenser	10(31.2%)	22(68.8%)	0(0%)	32	
	Clinical officer	0(0%)	1(100%)	0(0%)	1	
	Nursing officer/nurse midwife	1(50%)	1(50%)	0(0%)	2	
	Nurse assistant	2(100%)	0(0%)	0(0%)	2	
	Others	0(0%)	3(100%)	0(0%)	3	
Attended training						
	Yes	0(0%)	5(100%)	0(0%)	5	0.416
	No	17(28.3%)	38(63.4%)	5(8.3%)	60	

3.2 Results from focus group discussion

None of the participants in the focus discussion groups had attended training or a seminar on the treatment of uncomplicated malaria. All participants mentioned ALU as the first line medicine.

When asked why SP was prohibited for use as treatment, only one respondent knew the reason. One of them said:

"The government has forgotten private sector, there are new changes in malaria treatment but we didn't receive any training, we depend on reading drug leaflets. So the Ministry of Health should conduct trainings for the private sector." (Private Pharmacy Participant)

Dispensers typically didn't know that DPQ is the recommended second line medicine for treatment of uncomplicated malaria. SP was mentioned by all for IPTp.

One of the participants said *"From what I know, Quinine tablets is the second line anti malaria and in case of treatment failure Quinine injections should be used"* (ADDO Participant)

Most participants when asked why SP should not be used for treatment of uncomplicated malaria failed to mention it is because of a change in the treatment policy from SP to ALU due to potential treatment failure of SP, although they were aware of potential allergic reactions. Consequently, they continued dispensing SP for malaria treatment, which can lead to SP resistance in IPTp.

One of them said:

"SP is reserved for pregnant mothers because it kills malaria parasite available in the placenta." (ADDO Participant) and another one said *"SP is not supposed to be used for treatment of malaria because of allergic reaction to patients, but it doesn't have allergic reaction to pregnant mothers due to their antibodies."* (Private Pharmacy Participant)

Another participant said *"Some years ago SP was used for treatment of Uncomplicated Malaria but recently I heard some news through mass media that new medicine to be used should be ALU since it is more effective than SP"* (ADDO Participant)

4. DISCUSSION

The use of artemisinin-based combinations is recommended for the treatment of uncomplicated malaria in all age groups, except during the first trimester of pregnancy (2, 7, 25, 27). Dispensers' knowledge of malaria treatment recommendations is vital to enhance appropriate prescribing and dispensing of ACT, even more so given the extent of self-treatment for malaria in Tanzania (6, 19, 20).

There were encouraging signs in the knowledge of dispensers regarding the management of patients with malaria, but also areas of concern that need to be address. This compares favourably with other countries where there were serious concerns with the level of knowledge among certain providers including issues of treatment length (2, 16, 33, 53).

Encouragingly, more than 95% of dispensers (Table 3) knew that ALU is first line treatment for uncomplicated malaria with 100% knowing the dosage regimen. This is welcomed with concerns with self-purchasing ACT in other African countries due to costs (7, 25). However, a lower number of dispensers knew why ALU should be taken with fatty meals, i.e. to increase its absorption, although an appreciable improvement on previous studies (47). This is a concern as dispensers who do not know the importance of taking ALU with fatty foods may provide inadequate instructions to their clients, which may lead to underperformance of ALU. This is because taking ALU without consuming milk or fatty food has a significant impact on its bioavailability (54). In addition, only a limited number of dispensers knew that quinine is the recommended medicine for treatment of uncomplicated malaria in first trimester pregnancy (Table 3). However, a greater number knew that ALU is not recommended in the first trimester. Rates lower than 100% though mean it is more likely that pregnant mothers in first trimester who seek self-treatment will get ALU, which could potentially endanger their fetus. This needs to be addressed.

Encouragingly, most dispensers mentioned SP as the drug of choice for malaria in pregnancy, although knowledge rates could be appreciably improved. Nearly all dispensers also had moderate or good knowledge regarding the treatment of uncomplicated malaria. This compares favourably to the greater use of non-recommended treatments for malaria in pregnant women in private versus public facilities in Nigeria (2). However, a third of ADDO personnel had poor knowledge of the management of IPTp although appreciably better knowledge in private pharmacies. This might be due to the fact that more than 75% of dispensers in ADDOs had only five weeks training and none was either pharmacist or pharmaceutical technician (Table 2), whilst the majority of pharmacists had more than six years' experience in dispensing.

Disappointingly, only 22% of dispensers knew that DPQ was the second line (Table 3); although again higher among private pharmacies than ADDOs. Overall, the use of second line treatments does not appear well known among dispensers in private medicine outlets. Other concerns include the fact that most dispensers had inadequate knowledge regarding IPTp (Table 3). This is an issue given the cost-effectiveness of treatment for IPTp (24). Very few dispensers also knew the dosing interval recommended for pregnant mothers to take SP for IPTp. In addition, only 39% of dispensers knew that the using SP for uncomplicated malaria, instead of reserving it for IPTp, may lead to SP resistant (Table 3), which in turn will compromise its future effectiveness. As seen in the focus group discussions, most participants also failed to mention the policy change from SP to ALU. This means most dispensers in private outlets may irrationally dispense SP for malaria treatment because they do not know its impact. This also needs to be addressed.

Overall, there was a statistical relationship (p value <0.05) in the level of knowledge regarding ACT for the treatment of uncomplicated malaria with the professional level of dispensers (Table 4). Disappointingly, only a third of ADDO dispensers had good knowledge (Table 4) versus higher levels among private pharmacies. This is despite the availability of a training manual for ADDO dispensers with a special section explaining in detail about malaria treatment. However, most of ADDO dispensers were trained before the change in the malaria treatment guideline and there are generally concerns with their knowledge of even basic pharmacology (49). This lack of training and their limited qualifications may have contributed to their moderate to poor knowledge (Tables 4 and 5).

Based on our findings, there does appear to be the need for more training for dispensers in the private medicine outlets in Tanzania especially ADDO dispensers. This need is further endorsed by the fact that all participants in the focus group discussion said that they have never been involved in training and most didn't know about the changes in the malaria treatment guidelines. This needs to be urgently addressed given the priority status for malaria in Tanzania coupled with the fact that malaria training has worked well in other countries (25).

The major limitation of this study is that the findings were restricted to only dispensers and private facilities in one region of Tanzania. However, we will be undertaking additional research in other regions as well as public pharmacies to further assess the level of knowledge in this priority area in Tanzania. In the meantime, we believe based on the nature of the study design that our findings are robust and give guidance to the authorities in Tanzania on ways to enhance the management of malaria in pharmacies and ADDOs.

5. CONCLUSION

Encouragingly, the majority of dispensers in private outlets in Tanzania appeared to have moderate to good knowledge regarding the ACT policy in the treatment of uncomplicated malaria. However, there are important gaps including general knowledge levels among ADDO dispensers versus private pharmacists. These include low awareness that ALU should be taken with fatty foods, that quinine is the recommended treatment in the first trimester and that DPQ is generally second line treatment. Knowledge regarding the management of IPTp can also be improved especially among ADDO personnel.

As a result, the Ministry of Health and other stakeholders should urgently conduct training courses and seminars for private outlet dispensers in Tanzania to address key knowledge gaps in this high priority disease area. Both the government and donors should also engage the private sector in the ACT policy implementation process in the future to improve the management of these patients to fully utilize this important sector. We will be following this up, including researching the impact of future educational interventions, to ensure the optimal management of patients with malaria in Tanzania given its public health priority.

Conflicts of interest and funding

There was no external funding for this study. All authors declare they have no conflict interests.

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