Artemisinin-based antimalarial combination therapy amongst healthcare professionals in a tertiary facility in south-south Nigeria: preferences, tolerability, and cost considerations

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Abstract

Background: Nigeria adopted the Artemisinin-Based Combination Therapy (ACT) as the mainstay of treating uncomplicated malaria in February 2005. However, the individual preferences for the use of these medicines by health care professionals (HCP) as distinct from their observed prescribing practices is largely unknown. This study determined the preferences, tolerability and cost of the ACTs among HCP in Benin-City.

Methods: This descriptive cross-sectional study was conducted in the University of Benin Teaching Hospital, Benin-City, Nigeria. Consenting HCPs were recruited consecutively for the study. Semi-structured questionnaires were administered to doctors, nurses and pharmacists in the hospital. Information obtained included demographics, treatment of malaria in the previous year, antimalarial medication preferences and tolerability as well as cost of ACT.

Results: A total of 556 HCPs, 295 doctors (54.1%), nurses 200 (36.0%), pharmacists 61(11.0%) completed the questionnaire. In the previous year, 224 (75.9%) doctors, 153 (79.1%) nurses, and 48 (70.5%) pharmacists had treatment for malaria and self-medication was highest among doctors (228, 77.3%). Artemether-Lumenfantrine was the most preferred antimalarial used, 294 (52.8%); however, 1.6% used chloroquine sulphate and ACTs were perceived to be ineffective by 25.4%. Adverse effects were experienced by 167 (29.1%) resulting in 50 (9.0%) discontinuing their medication. Between 500 and 1500 Naira (~US$1-4) was expended on ACT by 66.3% of the staff, while 21.4% were concerned about the high cost of medications.

Conclusion: This study highlights the use and preferences, self-medication practices, perceived lack of effectiveness and high cost of ACTs from a HCP perspective. There is an urgent need to address these concerns in view of adverse consequences as well as the likely possibility of its the impact on prescribing practices.

Keywords: Artemisinins; Health Behavior; Health Personnel; Antimalarials; Malaria; Nigeria

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Thérapie combinée antipaludique à base d'artémisinine parmi les professionnels de la santé dans un établissement tertiaire du sud-sud du Nigéria: préférences, tolérabilité et considérations de coût

Résumé

Contexte général de l'étude: Le Nigéria a adopté la thérapie combinée à base d'artémisinine (TCA) comme pilier du traitement du paludisme non compliqué en février 2005. Cependant, les préférences individuelles pour l'utilisation de ces médicaments par les professionnels de la santé (MPS) par opposition à leurs pratiques de prescription largement inconnue. Cette étude a déterminé les préférences, la tolérabilité et le coût des TCA parmi les MPS à Benin-Ville.

Méthode de l'étude : Cette étude transversale descriptive a été menée à l'hôpital universitaire de l'Université du Bénin, Benin-City, Nigéria. Les professionnels de la santé consentants ont été recrutés consécutivement pour l'étude. Des questionnaires semi-structurés ont été administrés aux médecins, infirmières et pharmaciens de l'hôpital. Les informations obtenues comprenaient les données démographiques, le traitement du paludisme au cours de l'année précédente, les préférences et la tolérabilité des médicaments antipaludiques ainsi que le coût de Le TCA.

Résultat de l'étude : Un total de 556 professionnels de la santé, 295 médecins (54,1 %), infirmières 200 (36,0 %), pharmaciens 61 (11,0 %) ont rempli le questionnaire. Au cours de l'année précédente, 224 (75,9 %) médecins, 153 (79,1 %) infirmières et 48 (70,5 %) pharmaciens avaient reçu un traitement contre le paludisme et l'automédication était la plus élevée chez les médecins (228, 77,3 %). L'artéméther-lumenfantrine était l'antipaludéen le plus utilisé, 294 (52,8 %) ; cependant, 1,6 % utilisaient du sulfate de chloroquine et les TCA étaient perçus comme inefficaces par 25,4 %. Des effets indésirables ont été ressentis par 167 (29,1 %) entraînant chez 50 (9,0 %) l'arrêt de leur médication. Entre 500 et 1500 ~~Naira~~ (~US$1-4) ont été dépensés en TCA par 66,3% du personnel, tandis que 21,4% étaient préoccupés par le coût élevé des médicaments.

Conclusion : Cette étude met en évidence l'utilisation et les préférences, les pratiques d'automédication, le manque d'efficacité perçu et le coût élevé des TCA du point de vue des professionnels de la santé. Il est urgent de répondre à ces préoccupations compte tenu des conséquences néfastes ainsi que de la possibilité probable de son impact sur les pratiques de prescription.

Mots-clés: Artémisinines, comportement de santé, personnel de santé, antipaludéens, paludisme, Nigéria

INTRODUCTION

Malaria remains a public health challenge globally and a leading cause of morbidity and mortality, especially in Sub-Saharan Africa (1). To confront the challenges posed by multi-drug resistant *Plasmodium falciparum*, which has contributed to the burden of Malaria, the World Health Organization (WHO) recommended combination therapies notably those containing artemisinin derivatives as treatment for countries experiencing such resistance (2), This concept of combination therapy was already being employed in treating other infectious diseases such as Tuberculosis, Leprosy and HIV and is based on the synergistic or additive potential of two or more drugs to improve efficacy, and also delay the development of resistance to individual components in the combination (3). WHO advocated that countries use artemisinin-based combination therapy (ACT) which were at least 90% effective and that the day 28 efficacy of the respective partner drug alone should exceed 80%. The adoption and massive scale-up of the (ACT) among other measures has been largely responsible for the reduction in incidence and mortality rates observed in recent times (3).

Nigeria switched over to the ACTs as the mainstay of treating uncomplicated malaria in February 2005, based on the WHO recommendation (4). Artemether-Lumefantrine (AL) is the first-line ACT adopted by Nigeria; other recommended ACTs include Artesunate-Amodiaquine (AA), Artesunate-Mefloquine (AM), Dihydroartemisinin-Piperaquine (DHP) and Artesunate-Pyronaridine (AP) (5). The 2018 National Therapeutic Efficacy Study (TES) demonstrated the continued high efficacy of the ACTs against *Plasmodium falciparum*. These medicines are regarded as the most efficient antimalarials both in adults and children; they are currently the cornerstone of malaria elimination programmes in most endemic countries, especially in Africa due to the development of resistance to other available antimalarial agents. In addition, they have the ability to reduce the infectivity of mosquitoes especially in low and moderate malaria transmission areas (6). The initial safety concerns observed by health care practitioners within the country with the introduction of the ACTs prompted the Federal Ministry of Health (FMOH) to carry out a pilot programme on Cohort Event Monitoring (CEM) across the six geopolitical zones of the country in 2009 (7). This was subsequently scaled up to a cohort of 10,000 patients in 2012 (8).

In Nigeria, all health care professionals irrespective of cadre or specialty are involved in the treatment of malaria (9). In addition, there is a significant self-management practice among HCPs which may be determined by both medicine factors such as the tolerability profile of the drug, the cost of the medicine as well as personal preference and preconceived ideas about a medicine. The choice of ACT for a patient may therefore be influenced by the HCPs personal preference.

Furthermore, drug surveys undertaken among health care professionals within the country usually help to identify challenges associated with drug use or adherence to treatment protocols or guidelines. Most of the hospital-based antimalarial audits focus on prescriptions usually generated during patient encounters, both in out-patient clinics and hospital admissions. These surveys may not reflect the personal preferences of health care professionals especially in managing themselves or their relatives. Lastly, it is important to find out if the HCPs who offer advice to patients are actually adhering to the country's recommendation when receiving treatment for malaria. This may determine whether interventions are needed to increase the gains made by malaria control programs. This study therefore set out to determine the preferences, tolerability and cost considerations of the Artemisinin-based Combination Therapy (ACTs) among the Health care professionals in our facility.

MATERIALS AND METHODS

This was a descriptive, cross-sectional study conducted between May and July 2019 among Health care professionals at the University of Benin Teaching Hospital (UBTH), Benin City, Edo State, South-South Nigeria. It is a Federal government owned tertiary healthcare facility with approximately 850 bed space capacity and with professional staff comprising medical doctors of various cadres and specialties, pharmacists, and nurses. It serves as a referral centre in Edo State and adjoining states of Delta, Kogi and Ondo.

Participants/Sampling Technique: All HCPs including Doctors, Nurses and Pharmacists working in the hospital were eligible to participate in the study and those who consented to the study were recruited consecutively until the calculated sample size was reached. They were also recruited proportionally according to

approximate numbers of the different professions (doctors > nurses >pharmacists) of HCP working in the hospital at the time of the study.

Study instrument: A semi-structure self-administered questionnaire was distributed all the Health Care Professionals. Information obtained included demographics of the participants, previous episodes of malaria symptoms, mode of diagnosis of malaria, previous treatment of malaria, antimalarial medication preferences, ACT of choice, reasons for preferred ACT, tolerability and cost of ACTs. The questionnaire was pre-tested by participants within the hospital who did not partake in the study. Face and content validity was done by Clinical Pharmacologists.

Sample Size determination: The sample size was determined using the OpenEpi software (10). A prevalence of 50% was used as the preferred antimalarial agent of choice by HCPs. A minimum sample size of 384 was estimated using a prevalence of 50%, at 95% confidence level. Allowing for estimated non-response of 70%, the final sample size was 549.

Ethical considerations: Ethical approval was obtained from the institutions' research and ethics committee. Written informed consent was also obtained from all the participants. HCPs information were kept securely and not shared with third parties.

Statistical Analysis

Data was initially entered into Microsoft Excel (2016) spread sheet and then exported for analysis into Statistical Product and Service Solutions (SPSS, version 21, Chicago, USA). Data were presented descriptively using means and frequencies. Chi-square was used to test for associations, and choice of antimalarial was the dependent variable. A p value of less than 0.05 (p < 0.05) was considered to be statistically significant.

RESULTS

A total of 640 HCPs were approached to participate in the study, while 557 (87.0%) of the health professionals appropriately filled and returned their forms, giving a response rate of 87.0%. There were more doctors in this study 295 (53.0%), when compared with nurses 201 (36.1%) and pharmacists 61 (11.0%). The mean age ± SD of the respondents was 33.8 ± 8.3 with a range of 20-63 years.

Among the participants, 224 (75.9%) doctors, 153 (76.1%) nurses, and 43(70.5%) pharmacists had treated between an episode to 5 episodes of malaria in the year prior to the study, and 7 (2.4%) doctors and 9 (4.5%) nurses claimed to have treated malaria more than ten times in the same year. Self-medication was highest among the doctors 229 (77.6%), followed by pharmacists 36 (59.0%) and then nurses 94 (46.8%). There was a high level of presumptive diagnosis among all the health care professionals; doctors 227 (76.9%), nurses 130 (64.7%), pharmacists 39(63.9%). Table1. However, of the 150(26.9%) health professionals who had blood film for malaria parasite conducted, 82 (54.7%) carried out other investigations such as packed cell volume 16 (10.7%), full blood count 24 (16.0%) and widal agglutination test for Typhoid fever 41 (27.3%).

The respondents' awarness of the ACTs, their antimalarial preferences and co-administered medications were as shown in Table 2. Overall, 38 (6.8%) of the health care professionals claimed not to have heard of the ACTs, while 1.6% gave no response. Awareness of the ACTs was highest among the pharmacists 57 (93.4%), a finding not statistically significant. Eighty-three percent of the respondents preferred using the ACTs when they had malaria, with artemether/lumefantrine been the most desirable 294 (52.8%).

Amongst the ACTs, the frequency of use were artemether/lumenfantrine 431 (77.4), followed by dihydroartemisinin/piperaquine 51 (9.2%), and artesunate/mefloquine 20 (3.6 %) respectively, with the least preferred been artesunate/sulphadoxine-pyrimethamine 12(2.2 %). More nurses preferred using antimalarial injections 29 (14.4 %), chloroquine monotherapy, 8, (4.0%), while Sulphadoxime/ pyrimethamine monotherapy was most preferred among doctors 6 (2.0 %). Paracetamol 507 (91.0%) was the most preferred co-administered medication among the respondents, followed by antibiotics 149 (26.8 %) and haematinics/vitamins 131 (23.5 %).

One hundred and fifty five (27%) respondents indicated that the cost of medication contributed to their choice of antimalarial. One hundred and sixty two (29.1%) of the respondents experienced at least one adverse event, with those of the Central Nervous System (CNS) most prevalent, 112 (69.1.7%) followed by the Gastrointestinal Tract (GIT), 97 (59.9%). Also 50(9.0%) respondents discontinued medications

due to adverse reactions and 11(2.0%) were admitted in the hospital for intervention following the adverse reaction. However, close to 70% of the respondents reported not having experienced any adverse reaction to the ACTs. Majority of the health care professionals 469 (84.2%) expressed satisfaction with the ACTs, and 441 (79.2%) were willing to use them to treat their next episode of malaria although ACTs were perceived to be ineffective by 141 respondents (25.4%). Table 3

Most of the respondents 193 (33.8%) purchased ACT at a rate of ? 1501-2000(? =Naira) (4.2-5.6USD), while 185 (32.4%) bought ACTs at a rate of ? 1001-1500(2.8-4.2 USD), Only 2(0.4) respondents claimed to have expended more than ? 3,000 (8.3USD). (Figure 1). A proportion of the respondents 119 (21.4%) were concerned about the high cost of the ACTs

DISCUSSION

The study showed a high level of acceptability and personal preference for the ACTs among the health care professionals in the facility. ACTs were the most preferred antimalarial in this study, with Artemether-Lumefantrine being the drug of first choice, in keeping with the National antimalarial policy. This is highly commendable since acceptability and adherence to the ACTs in the management of uncomplicated malaria by health care professionals is crucial to sustaining the progress already achieved in reducing the malaria burden. Nevertheless, the finding of 6.8% of the respondents that claimed ignorance of the Artemisinin-based Combination Therapy cannot be overlooked. It is expected that almost twenty years into adoption of these medicines in treating uncomplicated malaria, health care professionals especially in tertiary facilities should be aware of current treatment guidelines for malaria.

A meta-analysis conducted by Yakasai et al (11) in 2014 reported 76% prevalence in the utilization of ACTs in the Nigerian public sector as against a lower prevalence reported earlier by Meremiku et al (12) few years into the change of the National Antimalarial Policy. Factors that may have contributed to the slow adoption of the ACTs in the early years following the change in policy especially among public health care professionals included poor understanding of its concept, and cost, amongst others. Just recently, Welle et al (9) reported a low preference for the ACTs (39.6%) among health care providers in Lokoja, North-Central Nigeria. A closer look at

the findings by Welle et al showed that while health care professionals (doctors and nurses) had above average preference for the ACTs, the very low figures recorded among the patent and proprietary medicine vendors (PPMVs) may have affected the overall preference in the study. The high level of awareness of the ACTs by participants in this study (91.6%), was however lower than that reported amongst health professionals in Malawi by Kalilani-phari et al (13). Restricting their study participants to doctors and pharmacist, who either managed patients with malaria or dispensed antimalarials may have accounted for their higher figures (97.8%) (13) as against that found by our study.

This study also recorded a high level of self-medication especially among the doctors. This practice although not restricted to medical professionals, has been documented both locally and internationally (14-16). Fadare et al (17) in 2014, found that antimalarials were the most self-prescribed medicines among medical doctors in Nigerian public health facilities. This may not be unrelated to their knowledge of malaria transmission within the country, ease of accessing the ACTs and the high level of presumptive diagnosis. The latter may have accounted for the number of times the respondents reported to have treated malaria in the previous year. The reliance on clinical diagnosis based on the syndromic presentation of malaria is highly unreliable even with experienced doctors, which may result in malaria over-diagnosis, misdiagnosis of other febrile illnesses, high consumption of antimalarials, risk of adverse effects and risk of drug selection of resistant strains. The WHO's previous recommendation on presumptive diagnosis was on the basis of prompt treatment of suspected uncomplicated malaria in high transmission-poor resource settings where parasitological confirmation may not be feasible. However, the present guideline stipulates that all suspected cases of malaria must have a laboratory confirmation either with microscopy or rapid diagnostic test prior to commencement of treatment (1).

The near absence of artemisinin monotherapies among the preferred antimalarials is highly commendable and it may reflect the respondents' knowledge of the likely risk of developing resistance when they are utilized in the treatment of uncomplicated malaria. However, there was a significant preference for chloroquine and injectable antimalarials among the nurses. This practice runs contrary to standard

treatment guideline for management of uncomplicated malaria. There is need to discourage such drug use behaviour to ensure prompt and appropriate malaria therapy and decrease unnecessary drug use. Preference for chloroquine may encourage continued presence of chloroquine in the market against the recommendation of the WHO (18), which was adopted by Nigeria in 2005 (4). The choice of these older medicines may be related to issues of affordability and perception of efficacy.

Most of the respondents in this study purchased their ACTs for at least ? 1000 (2.8 USD), which far exceeds the cost of chloroquine or sulfadoxine/pyrimethamine. The high cost of ACTs may encourage preferences for these older medications, which although less expensive are presently highly ineffective in parasite clearance and thus constitute greater danger to patients' health and well being. This consideration thus makes the ACTs still cost-effective especially in the setting of prompt diagnosis and early treatment. Although more than half of the respondents in this study reported not having experienced any adverse reaction to the ACTs and expressed willingness to use these medicines in their next malaria episode, 29.3% said they developed adverse reactions, with 9.1% discontinuing their medication, which may again impact on their decision on whether or not to prescribe the same medication for their patients.

Limitation: There is a possibility that respondents may have recall bias in filling the questionnaires used for this study. However, it is important to note that in the setting of the endemic nature of malaria, this may not change the findings. The study did not also assess the socio-economic status of the respondents.

CONCLUSION

This study highlights the preference and acceptability for the ACTs in the treatment of malaria amongst the study respondents. However, self-medication practices, the high cost, and tolerability of the ACTs need to be urgently addressed by the policy markers, in order to discourage a switch to cheaper and less effective alternatives by the health care professionals so as not to undermine the global milestones in treatment of malaria.

REFERENCES
1. World Health Organization. *World Malaria Report 2020: 20 years of global progress and challenges.* Geneva, 30 November 2020. https://www.who.int/publications/i/item/9789240015791 (Accessed 6th March 2021)
2. World Health Organization. *The use of Artemisinin and its derivatives as anti-malarial drugs.* Geneva, 10 June 1998. https://apps.who.int/iris/handle/10665/65382 (Accessed 10th Septmember 2020)
3. World Health Organization. *Guidelines for the treatment of Malaria .* 3rd ed. Geneva: World Health Organization, 2015: https://apps.who.int/iris/bitstream/handle/10665/162441/9789241549127_eng.pdf (Accessed 6th March 2021)
4. Federal Ministry of Health (FMoH). *National antimalarial treatment policy.* Abuja, Nigeria,,2005.
5. Federal Ministry of Health (FMoH). *National Guidelines for the diagnosis and treatment of Malaria.* Abuja, Nigeria; 2020.:
6. Adjuik M, Babiker A, Garner P,Olliaro P, Taylor W, White N. Artesunate combinations for treatment of malaria: Meta-analysis. *Lancet* 2004; 363: 9–17.
7. Bassi PU, Osakwe AI, Isah A, Suku C, Kalat M, Jalol I et al. Safety of Artemisinin-Based Combination Therapies in Nigeria: A Cohort Event Monitoring Study. *Drug Saf* 2013; 36: 747–756.
8. Bassi P, Osakwe A, Suku C, Kalat M, Elagbaje C, Isah A et al. Cohort event monitoring of patients treated for uncomplicated malaria with artemisinin-based combination therapies in selected hospitals and community pharmacies in Nigeria. *Nigerian Postgraduate Medical Journal* 2016; 23: 172-.
9. Welle SC, Ajumobi O, Dairo M, Balogun M, Adewuyi P, Adedokun B et al. Preference for Artemisinin–based combination therapy among healthcare providers, Lokoja, North-Central Nigeria. *Glob Heal Res Policy*; 4. Epub ahead of print 2019. DOI: 10.1186/s41256-018-0092-9.
10. Sullivan KM, Dean A. OpenEpi: A Web-based Epidemiologic and Statistical Calculator for Public Health. *Public Health Rep* 2009; 124: 471–474.
11. Yakasai AM, Hamza M, Dalhat MM,Bello M, Gadanya MA, Yaqub ZM et al. Adherence to Artemisinin-Based Combination Therapy for the Treatment of Uncomplicated Malaria: A Systematic Review and Meta-Analysis. *J Trop Med* 2015; 2015: 1–11.
12. Meremikwu M, Okomo U, Nwachukwu C, Oyo-Ita A,Eke-Njoku J, Okebe J et al. Antimalarial

drug prescribing practice in private and public health facilities in South-east Nigeria: A descriptive study. *Malar J* 2007; 6: 1–4.

13. 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: 1–7.

14. Leape LL. When good doctors go bad: a systems problem. *Annals of surgery* 2006; 244: 649–652.

15. Bamgboye EA, Amoran OE, Yusuf OB. Self medication practices among workers in a tertiary hospital in Nigeria. *Afr J Med Med Sci* 2006; 35: 411–415.

16. Chen JY, Tse EYY, Lam TP, Li DK, Chao DV, Kwan CW et al. Doctors' personal health care choices: A cross-sectional survey in a mixed public/private setting. *BMC Public Health* 2008; 8: 183.

17. Fadare J, Desalu O. Self-prescription practices by Nigerian medical doctors. *South African Fam Pract* 2014; 56: 253–257.

18. World Health Organization. *Antimalarial drug combination therapy. Report of a WHO technical consultation*. Geneva, April 2001. https://apps.who.int/iris/handle/10665/66952 (Accessed 8th June 2020)

Table 1: Characteristics of malaria treatment among healthcare professionals in UBTH (n = 557)

Variable	HCP frequency (%)		
	Doctors n=295 (53.0%)	**Nurses** n=201(36.0%)	**Pharmacist** n=61 (11.0%)
Sex			
Male	160 (54.2)	27(13.5)	27(44.3)
Female	135(45.8)	173(86.5)	34(55.7)
Age			
Mean age(±SD)	32.07(6.0)	37.8(9.8)	28.62(7.7)
Frequency of treatment in the last year			**P=0.288**
None	50(16.9)	28(13.9)	15(24.6)
1-5 times	224(75.9)	152(76.0)	43(70.5)
6-10 times	14(4.7)	11(5.5)	3(4.9)
>10 times	7(2.4)	9(4.5)	0
Self - medication for malaria			
Yes	229 (77.6)	94 (46.8)	36 (59.0)	P=<0.000
No	59 (20.0)	86 (42.8)	24 (39.3)	LR=56.887
No response	7 (2.4)	21 (10.4)	1 (1.6)
MP checked			
Yes	62 (21.0)	66 (32.8)	22(36.1)	P=0.007
No	227(76.9)	130(64.7)	39(63.9)	LR- 13.987
No response	6 (2.0)	5 (2.5)	0

MP- Malaria Parasite

Table 2: Knowledge of ACT, Antimalarial preferences and co-administered medications of Health-Care Professionals in UBTH (n = 557)

Characteristic	Proportion (%)	Doctors n=295(%)	Nurses n=201(%)	Pharmacists n=61(%)	Chi square (p value)
Awareness of ACT					
Yes	510 (91.6)	273 (92.5)	180 (89.6)	57 (93.4)	4.542 (0.338)
No	38 (6.8)	20 (6.8)	15 (7.5)	3 (4.9)	
No response	9 (1.6)	2 (0.7)	6 (3.0)	1 (1.6)	
Type of antimalarial					
ACT	449 (83.6)	260 (90.3)	136 (72.3)	53 (86.9)	27.248 (<0.001)*
Non-ACT	88 (16.4)	28 (9.7)	52 (27.7)	8 (13.1)	
Antimalarial preferences					
Artemether-lumenfatrine	294 (52.8)	159 (53.9)	107(53.2)	28(45.9)	1.323 (0.516)
Unspecified ACT	116 (20.8)	79 (26.8)	21(10.4)	16(26.2)	20.552 (<0.001)*
Injectable antimalarial	44 (7.9)	12 (4.1)	29(14.4)	3(4.9)	17.640 (<0.001)*
Dihydroartemisinin-piperaquine	33 (5.9)	17 (5.8)	10(5.0)	6(9.8)	1.769 (0.413)
Artesunate-amodiaquine	9 (1.6)	2 (0.7)	5(2.5)	2(3.3)	3.654 (0.161)
Sulphadoxine pyrimethamine	9 (1.6)	6 (2.0)	2(1.0)	1(1.6)	0.864 (0.649)
Chloroquine	9 (1.6)	1 (0.3)	8(4.0)	0	11.480 (0.003)*
Quinine	9 (1.6)	3 (1.0)	4(2.0)	2(3.3)	1.750 (0.417)
Artesunate-mefloquine	7 (1.3)	4 (1.4)	2(1.0)	1(1.6)	0.208 (0.902)
Arterolane/Piperaquine	5 (0.9)	5 (1.7)	0	0	6.396 (0.041)
Any prescribed antimalarial	5 (0.9)	2 (0.7)	3(1.5)	0	1.941 (0.379)
Herbal medicines	3 (0.5)	1 (0.3)	1(0.5)	1(1.6)	1.150 (0.563)
First choice ACT					
Arthemether/lumenfatrine	431(77.4)	237 (80.3)	147(73.1)	47(77.0)	14.358 (0.278)
Dihydroartemisin/piperaquine	51(9.2)	20 (6.8)	22(10.9)	9(14.8)	
Artesunate/mefloquine	20 (3.6)	9 (3.1)	9(4.5)	2(3.3)	
Artesunate/amodiaquine	18 (3.2)	8 (2.7)	9(4.5)	1(1.6)	
Artesunate/sulphadoxine-pyrimethamine	12 (2.2)	5 (1.7)	5(2.5)	2(3.3)	
No first choice	8 (1.4)	5 (1.7)	3(1.5)	0	
No answers	17 (3.1)	11 (3.7)	6(3.0)	0	
Does Cost influence your choice of ACT?					
Yes	155 (27.8)	87 (29.5)	53 (26.4)	15 (24.6)	13.014 (0.011)
No	365 (65.5)	191 (64.7)	128 (63.7)	46 (75.4)	
No answer	37(6.6)	17 (5.8)	20 (10.0)	0	

ACT-Artemisinin-based Combination Therapy, UBTH-University of Benin Teaching Hospital

*= p < 0.05

Table 3: Tolerability of ACTs among Health Care Professionals in UBTH (n = 557)

Characteristic	Proportion	Frequency (%) Doctors n=295	Nurses n= 201	Pharmacists n=61	Chi square (p value)
Adverse drug reactions with ACTs					
Yes	162 (29.1)	72 (24.4)	69 (34.3)	21 (34.4)	8.003(0.091)
No	385 (69.1)	216 (73.2)	129 (64.2)	40 (65.6)	
No response	10 (1.8)	7 (2.4)	3 (1.5)	0	
Any discontinuations of ACTs					
Yes	50 (9.0)	25 (8.5)	22 (10.9)	3 (4.9)	8.104(0.088)
No	442 (79.4)	238 (80.7)	149 (74.1)	55 (90.2)	
No response	65 (11.7)	32 (10.8)	30 (14.9)	3 (4.9)	
Hospitalizations following Adverse Drug Reactions					
Yes	11 (2.0)	4 (1.4)	6 (3.0)	1(1.6)	6.566(0.161)
No	492 (88.3)	264 (89.5)	170 (84.6)	58(95.1)	
No response	54 (9.7)	27 (9.2)	25(12.4)	2(3.3)	
Satisfaction with medicines					
Yes	469 (84.2)	251(85.1)	162 (80.6)	56 (91.8)	9.278(0.055)
No	70 (12.6)	31(10.5)	34 (16.9)	5 (8.2)	
No response	18 (3.2)	13(4.4)	5(2.5)	0	
Willingness to repeat ACT for next treatment					
Yes	441(79.2)	241(81.7)	147(73.1)	53(86.9)	9.730(0.045)
No	88 (15.8)	39 (13.2)	41(20.4)	8 (13.1)	
No response	28 (5.0)	15 (5.1)	13(6.5)	0	

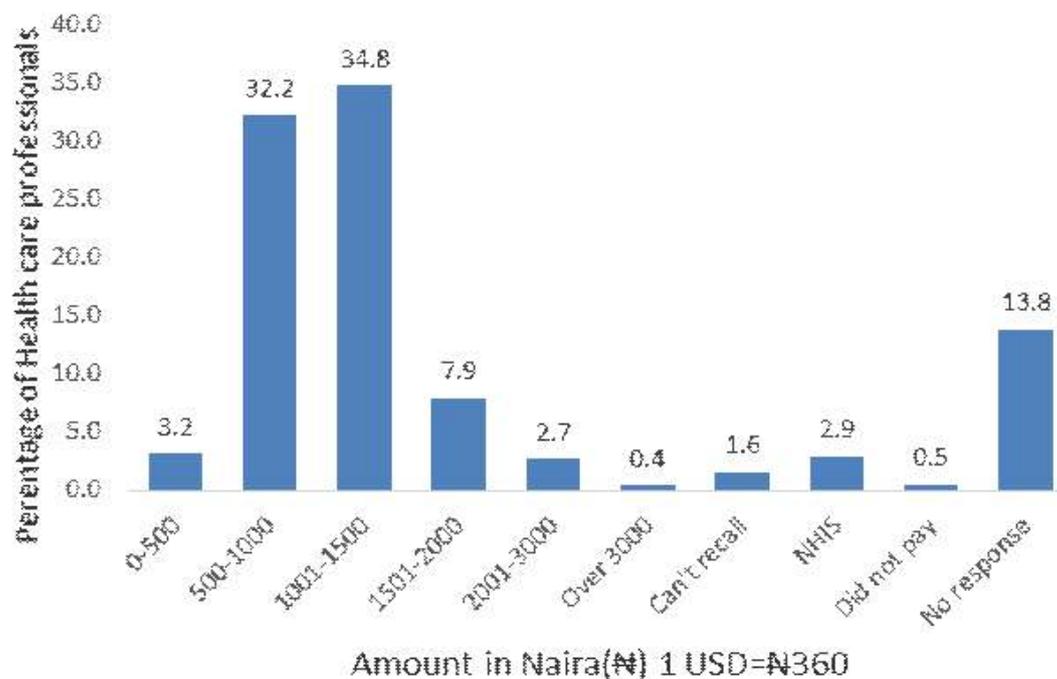ACT-Artemisinin-based Combination Therapy, UBTH-University of Benin Teaching Hospital,

Figure 1: Cost of Artemisinin-based combination therapy (ACT) purchased by the Health Care Professionals.