Journal of Community Medicine and Primary Health Care. 31 (1) 40-47

JOURNAL OF COMMUNITY MEDICINE AND PRIMARY HEALTH CARE

ORIGINAL ARTICLE

Physicians' Compliance with Malaria Treatment Guidelines of Under-five Children in a Secondary Maternal and Child Care Centre in Lagos State

Otokpa E, Ogunyemi AO, Ladi- Akinyemi TW, Onajole AT

Department of Community Health and Primary Care, College of Medicine, University of Lagos

Keywords:

Malaria, Under-fives, Compliance, mRDT, ACTs, Guidelines.

ABSTRACT

Background: The global malaria agenda has the ultimate goal of eliminating malaria in all countries of the world by 2030 through universal access to malaria prevention, diagnosis and treatment. Presumptive treatment of malaria with Artemisinin Combination Therapy (ACT) has been associated with the development of resistance, therefore parasitological confirmation of all fevers is crucial in the context of eliminating malaria. This study assessed physicians' compliance with the national guidelines in the treatment of malaria among under-five (U-5) children and their prescription pattern in a Maternal and Child Care (MCC) centre in Lagos State.

Methods: This was a descriptive cross-sectional study conducted as an exit interview among 427 mothers/caregivers of febrile U-5 children who were consecutively sampled.The data was collected using a pre-tested interviewer-administered questionnaire and a proforma. Epi-info version 7.2.1 was used to analyze the data and the level of significance was set as $p<0.05$.

Results: Malaria Rapid Diagnostic Test (mRDT) was done for 75 17.6%) of the children and 37 (49.3%) was positive. Anti-malarial drugs were prescribed at consultation to 400 (93.7%) of the febrile children. Artemisinin Combination Therapy (ACT) was prescribed for 364 (91.0%) of the children. The most prescribed ACT was Artemether-Lumefantrine (AL) in 222 (60.9%).

Conclusion: The physician's compliance with malaria treatment guidelines for febrile illnesses in U-5 children was poor with regards to parasitological confirmation before treatment. However, the use of ACTs was adhered to in almost all cases. Regular training workshops are recommended for health workers to improve adherence to parasitological confirmation before treatment.

Correspondence to:
Dr Adedoyin Ogunyemi
Department of Community Health and Primary Care, College of Medicine, University of Lagos
E-mail: doyinogunyemi@gmail.com
Telephone: +2348063068858

INTRODUCTION

The burden of malaria in Nigeria is very high, with approximately 51-100 million cases.[1] Malaria accounts for 60% of out-patient visits and 30% of hospitalizations among under-five children and during this period, children experience 2-4 attacks of malaria annually.[1] It accounts for almost 25% of infants mortality and 30% of under-fives (U-5) mortality annually.[2] The global strategy for malaria and the Sustainable Development Goals (SDGs) target a 90% reduction in the incidence and mortality rates of malaria, as well as its elimination in 35 of its endemic countries by 2030 including Nigeria.[3] The World Health

Organisation (WHO) has identified Nigeria as one of the countries without the potential to achieve pre-elimination by then if appropriate measures are not taken.[3]

Current practices in the management of malaria in Nigeria may be inimical to achieving pre-elimination despite much effort.[4] Malaria control in Nigeria involves a number of activities ranging from routine and mass distribution of Insecticide Treated Nets (ITNs), indoor residual spraying, environmental management to effective case management.[5] The national guidelines for malaria diagnosis and treatment in line with WHO, recommends that parasitological confirmation of febrile illness in the diagnosis of malaria should be carried out using microscopy or RDT before treatment and all cases with positive test results should be treated with an ACT.[6]

Presumptive diagnosis and treatment of febrile illness as malaria in endemic areas has been a subject of debate.[7] The limitations of microscopy such as technicality, waiting time, cost and access to quality reagents as well as false negative or false positive test results in the use of Malaria Rapid Diagnostic Test (mRDT) are some reasons given by physicians for presumptive treatment of fever.[8] In addition, is the fear of high mortality from untreated malaria, especially in children.[9] Studies have shown that presumptive treatment of febrile patients has become associated with high levels of antimalarial overuse and the development of resistance.[9-11] There is need to carry out appropriate diagnostic tests in patients presenting with acute febrile illnesses so that anti-malarial drugs are targeted at those who need them. Prescription pattern of anti-malarial drugs is critical to rational drug use and optimal outcome of febrile illness. The pattern of prescription has been shown to influence the emergence of resistance to anti-malarial drugs, thus the success of malaria elimination in the near future will depend on adherence of physicians and patients to treatment recommendations.[12, 13]

This study was carried out to assess physicians' compliance with the national malaria treatment guidelines using the proportion of U-5 children with febrile illness who had parasitological confirmation of malaria and were treated with ACT.

METHODOLOGY

This was a descriptive cross-sectional study conducted as an exit interview at the out-patient department of one of the eight Maternal and Child Care (MCC) centres in Lagos State from July to August 2017. The centre is located in the mainland of Lagos and provides in-patient and out-patient services to pregnant women and children. The MCC centres were established and strategically located within Lagos State to decrease maternal and child morbidity and mortality rates in the State. The respondents were mothers or caregivers of children between the age of 1 and 59 months who had a history of fever or were febrile at the time of presentation in the facility. The sample size of 427 mothers/caregivers was calculated using the Cochran formula ($n = z^2pq/d^2$), [14] where n = the sample size, z = standard normal deviate at 95% confidence interval (CI) which is 1.96, p = prevalence of the study population estimated as 50%, q =1-p, d = precision level set at 5%. This was increased by 10% to account for non-response.

Respondents who met the eligibility criteria were consecutively recruited according to the out-patient register on each clinic day until the sample size was reached. The out-patient paediatric clinic runs daily from Monday to Friday from 9 am to 4 pm. An average of

fifteen respondents was interviewed per day over a period of 6 weeks. On each day, mothers/caregivers of U-5 children were interviewed and their prescription forms checked following their exit from the doctor's consulting room. The patient's identity number, laboratory test form(s) issued and drugs prescribed for the index child was noted.

Data was collected using an interviewer-administered structured questionnaire which had two sections: Section A consisted of questions on the socio-demographic characteristics of the mother/caregiver and the index child. Section B included questions on the characteristics of fever and the home management of fever prior to visiting the hospital. A proforma was used to extract laboratory tests requested from the form issued and the drugs prescribed including the anti-malarial drugs. For malaria test ordered, the results and other prescribed drugs recorded were extracted from the case notes using the patient's unique identifier on the following day. Pre-testing of the data collection tools was conducted among mothers/caregivers of under-fives in Mushin General Hospital, Mushin, Lagos State.

All the collected data were checked for errors and cleaned. The data was entered in an excel sheet and analysed using Epi Info 7.2.1. The socio-demographic data, treatment compliance and prescription pattern were presented as frequency tables. Means and standard deviation was calculated for the ages of respondents and the children. Fisher's exact test was used to determine the association between mRDT results and malaria treatment. The level of significance was set at $p<0.05$.

Ethical approval (ADM/DCST/HREC/APP /1688) was obtained from Health Research Ethics Committee (HREC), Lagos University Teaching Hospital (LUTH), Idi Araba, Lagos State and permission from the Health Service Commission (HSC), Lagos State. Written informed consent was obtained from the mothers/caregivers and they were assured of the confidentiality of the information they had provided. To overcome possible Hawthorne effect, the consulting physicians in this centre were not aware of the study being carried out but the chief medical director was duly informed.

RESULTS

Majority 295 (69.1%) of the under-five children in this study who had a history of febrile illness were less than or equal to 24 months. The mean age of the children and standard deviation was 20.9±15.2 months. There were more males 227 (53.2%) than female children 200 (46.8%). Two hundred and ten (49.2%) of the mothers/caregivers were between the age of 21-30 years old and only 4 (0.9%) of them were ≤ 20 years. The mean age of the respondents was 31.5±5.8 years and 403 (94.4%) caregivers were females of which 393 (97.5%) were mothers. Almost all the respondents had at least one form of formal education; tertiary 225 (52.7%), secondary 195 (45.7%) and primary education 3 (0.7%). Only 4 (0.9%) respondents had no formal education. Eighty-five (19.9%) of the respondents were professionals, 144 (33.7%) were skilled and 143 (33.5%) were unskilled workers. Only 55 (12.9%) of the caregivers were unemployed as shown in Table 1.

Table 2 shows that 83 (19.4%) of the 427 children had a laboratory test requested by the physician and 75 (90.4%) of the tests requested were specifically for malaria. Other laboratory tests included white blood cell (WBC) count and microscopy, culture and sensitivity (MCS) 8 (9.6%). Malaria was positive using the mRDT in 37 (49.3%) of the children. Four hundred (93.7%) of the children were treated presumptively with anti-malarial drugs alone

Table 1: Socio-demographics characteristics of the respondents

Variable	Frequency (n=427)	Percent
CHILDREN		
Age (Months)		
1-12	158	37.0
13-24	137	32.1
25-36	51	11.9
37-48	43	10.1
49-59	38	8.9
Mean age ± SD =20.9+15.2		
Sex		
Male	227	53.2
Female	200	46.8
MOTHERS/ CAREGIVERS		
Age (Years)		
<20	4	0.9
21-30	210	49.2
31-40	186	43.6
41-50	21	4.9
51-60	6	1.4
Mean age ± SD = 31.5±5.8		
Sex		
Male	24	5.6
Female	403	94.4
Relationship of caregiver to child		
Mother	393	92.0
Father	21	4.9
Others	13	3.1
Education		
Primary	3	0.7
Secondary	195	45.7
Tertiary	225	52.7
None	4	0.9
Occupation		
Professional	85	19.9
Skilled	144	33.7
Unskilled	143	33.5
Unemployed	55	12.9

Table 2: Physicians' compliance with malaria treatment guidelines in under-fives

Variables	Frequency	Percent
Laboratory test ordered (n=427)		
Yes	83	19.4
No	344	80.6
Type of test done (n=83)		
Malaria	75	90.4
Others	8	9.6
Malaria test results (n=75)		
Negative	38	50.7
Positive	37	49.3
Received malaria treatment presumptively (n=427)		
Yes	400	93.7
No	27	6.3
Received ACT (n=400)		
Yes	364	91.0
No	36	9.0

or in combination with antibiotics and analgesics. Twenty-seven (6.3%) of the children were treated with an antibiotic and/or analgesic. Artemisinin Combination Therapy was prescribed in 364 (91.0%) of the under-fives while 36 (9.0%) received monotherapy. The route of administration was oral only in 208 (52.1%), both oral and injectable in 156 (39.3%) and injectable only in 29 (7.3%) of the children. Among the ACTs, oral Artemether-Lumefantrine (AL) was the most prescribed 153 (38.3%) followed by a combination of Artesunate injection and oral AL 63 (15.8%). The majority 341 (63.3%) of the prescriptions were in brand names as shown in Table 3. Table 4 shows the association between positive malaria test results and presumptive treatment with ACT. Twenty-nine (46.8%) of the children who were presumptively treated with ACT tested negative while 33 (53.2%) tested positive for malaria using mRDT. However, this association was not statistically significant (p=0.22).

DISCUSSION

The global strategy for malaria control requires early diagnosis, prompt and effective treatment to prevent antimalarial overuse and reduce associated morbidity and mortality.[15] In this study, majority of all the children with a history of fever or who were febrile were

Table 3: Prescription pattern of anti-malarial drugs for under-fives

Antimalarials	Frequency	Percent
Combination therapy		
Oral ACTs (n=208)		
Oral Artemether-Lumefantrine	153	38.3
Oral Dihydroartemisinin-piperaquine	53	13.3
Oral (others)	2	0.5
Injectable (Inj) and Oral ACTs (n=156)		
Inj. Artesunate + Oral Artemether-Lumefantrine	63	15.8
Inj. Artesunate + Oral Amodiaquine	47	11.8
Inj. Artesunate + Oral Dihydroartemisinin-piperaquine	14	3.5
Inj. Arte-ether + Oral Amodiaquine	9	2.3
Inj. Artesunate + Oral Artesunate-Amodiaquine	7	1.8
Inj. Arte-ether + Oral Artemether-Lumefantrine	6	1.5
Inj. Arte-ether + Oral Artesunate-Amodiaquine	5	1.3
Inj. Artesunate + Oral Artesunate-SP	2	0.5
Inj + Oral (others)	3	0.8
Monotherapy (n=36)		
Inj. Artesunate	22	5.5
Inj. Artemether	5	1.3
Inj. Arte-ether	2	0.5
Oral Amodiaquine	5	1.3
Oral Proguanil	2	0.5
Mode of Prescription (n=400)		
Brand name	253	63.3
Generic	147	36.7

Table 4: Association between presumptive treatment with ACT and mRDT results

	ACT Prescribed		
	Yes	No	Total
RDT result	n (%)	n (%)	n (%)
Positive	33 (53.2)	4 (30.8)	37 (49.3)
Negative	29 (46.8)	9 (69.2)	38 (50.7)
Total	**62 (100.0)**	**13 (100.0)**	**75 (100)**

*Fisher exact; p=0.22

treated presumptively for malaria while less than one-fifth were tested. Of those tested, about half were negative for malaria using the rapid diagnostic test. This suggests the possibility of misdiagnosis of fever presentation as malaria among those presumptively treated with attendant consequences.[9] These include unnecessary use or wastage of anti-malarial drugs, exposure to adverse effects of the medicines, and early development of resistance to anti-malarial drugs especially the ACTs.[16] On the other hand, the underlying causes of non-malarial fevers remain untreated and the patients continue to be susceptible to these pathogens.[17] Presumptive diagnosis and treatment of childhood fevers by health providers may be attributed to the high endemicity of malaria, perceived delay in laboratory test results, non-availability of diagnostic test kits (RDTs) in consulting rooms as well as doubts about their reliability.[7, 18]

Artemether-Lumefantrine (AL) combination therapy was the first drug of choice among the ACTs in the treatment of childhood malaria in this study and it accounted for more than half of all antimalarial prescriptions. Other studies that had similar findings were in Delta State (63.7%),[19] Abuja (56.8%),[20] Tanzania (87.0%),[21] and Kenya (63.6%).[22] About two-thirds of the oral AL were co-prescribed with artemisinin-based injections. The malaria control guidelines recommend that parenteral artemisinin be initiated in patients with complicated malaria and changed to oral ACTs once the patient's condition improves to

a state that enables oral therapy.[6] The use of anti-malarial injections is recommended in less than 10% of cases but unnecessary use of injections has been reported in several studies ranging from 23-38.1%.[23-25] This is largely due to the misconceptions that injections are either more effective, or have faster onset of action, compared to other formulations.[26-27] There are safety concerns with unnecessary injection use giving rise to infections and unwanted side effects as well as increased cost to the patient, healthcare provider and the health system.[28-29]

Monotherapy was mostly artemisinin-based medicines in this study. Monotherapies like Proguanil are beneficial in children for prophylaxis or prevention depending on the country but not advisable in the treatment of malaria.[30] World Health Organization has called for a withdrawal of oral artemisinin-based monotherapies as it is considered to be a major contributing factor to the development of resistance to artemisinin derivatives.[31] The use of brand names as observed in about two-thirds of anti-malarial prescriptions in this study is contrary to recommendations by the WHO treatment guidelines that advocate generics.[6] This trend has been reported in other studies.[23, 32-33] and has implications for the potency of formulations and affordability of branded drugs.[6, 34] The main purpose of the generic versus the brand preference is to make drugs affordable to those who need them.[34]

Almost half of the children who were presumptively treated with ACT did not test positive for malaria using mRDT in this study. Although presumptive diagnosis of febrile illness can help in the treatment of all patients with malaria, it is also likely to misclassify many. This practice has low specificity and contributes to misuse of anti-malarial medicines, increased costs to health services and patient dissatisfaction.[7, 35-36] It lends credence to the debates around overuse and potentials for resistance to antimalarials.[9, 10]

Limitations of the study

This study has contributed to the body of knowledge on this subject matter but it has its limitation. Firstly, the study only relied on the mRDT results of the few cases that were requested rather than the researcher testing all children who were presumptively treated. Secondly, an inclusion of data from the physicians such as years of experience, previous training in malaria management and the reasons for treatment preference would have added to this study.

Conclusion

In conclusion, the physicians' compliance with national malaria treatment guidelines using the proportion of U-5 children with febrile illness who had parasitological confirmation of malaria was poor. However, compliance with the use of ACT was good. Regular training workshops are recommended for health workers to improve adherence to parasitological confirmation before treatment.

REFERENCES

1. Dawaki S, Al-Mekhlafi H, Ithoi I, Ibrahim J, Atroosh M, Abdulsalam M et al. Is Nigeria winning the battle against malaria? Prevalence, risk factors and KAP assessment among Hausa communities in Kano State. Malaria Journal. 2016; 15: 351-354.
2. National Population Commission (NPC). Nigeria and ICF - International. Nigeria Demographic and Health Survey 2013. Abuja, Nigeria, and Rockville, Maryland, USA 2013.
3. World Health Organisation. World Malaria Report 2017. Geneva: World Health Organisation, 2017. [Cited 10th September 2017] Available at http://www.who.int/malaria/publications/world-malaria-report-2017/report/en/.

4. Chukwuocha UM. Malaria control in Nigeria. Primary Health Care. 2012; 2: 118. doi:10.4172/2167-1079.1000118
5. Health Partners International. Support to National Malaria Elimination Programme. 2008-2016. Final report. The Support to the National Malaria Programme. [Cited 8th September 2017]. Available at http://resources.healthpartners-int.co.uk/resource/support-to-the-national-malaria-programme-2008-2016-final-report-sunmap/.
6. World Health Organisation: Guidelines for treatment of malaria, April 2015. Third edition. [Cited 17th September 2017]. Available at: http://apps.who.int/iris/bitstream/handle/10665/162441/978 9241549127_eng.pdf?sequence=1
7. Chukwuocha UM, Brown A. Malaria treatment in children based on presumptive diagnosis: A make or mar? Peadiatric Infectious Disease 2016; 1: 6. doi: 10.21767/2573-0282.100006.
8. Murray K, Bell D, Gasser A, Magil A, Miller S. Update on rapid diagnostic testing for malaria. Clinical Microbiology Review. 2008; 21: 97-110.
9. Okoro I, Chukwuocha M, Nwakwuo C, Ukaga N. Presumptive diagnosis and treatment of malaria in febrile children in parts of south eastern Nigeria. Journal of Infectious Disease and Therapy. 2015 Oct 20; 3: 240-242.
10. Oladipo O, Oladosu O and Wellington O. Over-diagnosis and over-treatment of malaria in children that presented with fever in Lagos, Nigeria. Infectious Diseases. 2013; 7: 5-11.
11. Reyburn H, Mbakilwa R, Mwangi R. Rapid diagnostic tests compared with malaria microscopy for guiding outpatient treatment of febrile illness in Tanzania: Randomised trial. BMJ 2007; 334: 403-406.
12. Gbotosho O. Potential contribution of prescription practices to the emergence and spread of chloroquine resistance in south-west Nigeria: caution in the use of artemisinin combination therapy. Malaria Journal. 2009; 8: 313-315.
13. Adibe M. Predictors of adherence to national anti-malarial treatment guidelines in some Nigerian hospitals. International Journal of Drug Development and Research. 2010; 2: 4-10.
14. Cochran WG. Sampling Techniques, 3rd Ed. New York: John Wiley and Sons; 1977.
15. World Health Organization. The role of Laboratory diagnosis to support malaria disease management: Focus on the use of rapid diagnostic tests in areas of high transmission. 2006. [Cited 20th September 2017]. Available at http://www.who.int/malaria/publications/atoz/who_htm_mal_2006_1111/en/.
16. Mosha JF, Conteh L, Tediosi F, Gesase S, Bruce J, Chandramohan D et al. Cost implications of improving malaria diagnosis: Findings from north-eastern Tanzania. PLoS One 2010; 5: e8707.
17. Reyburn H, Mbatia R, Drakeley C, Carneiro I, Mwakasungula E. Over-diagnosis of malaria in patients with severe febrile illness in Tanzania: A prospective study. British Medical Journal. 2004; 329: 1212-1213.
18. Ughasoro D, Okoli C and Uzochukwu C. Qualitative study of presumptive treatment of childhood malaria in third tier tertiary hospitals in south-east Nigeria: a focus group and in-depth study. Malaria Journal. 2013; 12: 436-441.
19. Arute JE., Ojieabu WA. Patani-Okelosi E., Iwor P. Prescribing trends of anti-malarial drugs in a Primary Health Care facility in Delta State. World Journal of Pharmaceutical Research. 2016; 5: 1-10.
20. Igboeli U, Ukwe V, Ekwunife I. Increasing use of Artemisinin-based combination therapy for treatment of

malaria infection in Nigerian hospitals. Pharmacy Practice. 2010; 8: 243-249.
21. Kamuhabwa R, Silumbe R. Knowledge among drug dispensers and anti-malarial drug prescribing practices in public health facilities in Dar es Salaam. Drug Healthcare Patient Safety. 2013; 5: 181-189.
22. Juma E, Zurovac D. Changes in health workers' malaria diagnosis and treatment practices in Kenya. Malaria Journal. 2011; 10: 1-8.
23. Koley M, Saha S, Arya S, Choubey G, Ghosh S, Purkait R et al. A study on drug utilization and prescription habits of physicians in a government homeopathic hospital in west Bengal. India Journal of Integrative Medicine. 2013; 11: 305-313.
24. Alyamani A, Hopf Y, Williams J. Prescription quality in an acute medical ward. Pharmaco-epidemiology Drug Safety 2009; 18: 1158-1165.
25. Maiga D, Diaware A. Study on the availability and cost of medicines in the private sector in Mali. Medical Tropics 2006; 66: 565-568.
26. Afriyie K, Amponsah K, Antwi R, Nyoagbe Y, Bugyei A. Prescribing trend of anti-malarial drugs at the Ghana Police Hospital. Journal of Infectious Diseases in Developing Countries. 2015; 9: 409-415.
27. Lenjisa J, Fereja T. A retrospective analysis of prescribing practices through WHO prescribing indicators at four selected hospitals of West Ethiopia. Journal of Biomedicine. 2014; 6: 29-33.
28. Centre for Disease Control and Prevention (CDC). Public health grand rounds. The impact of unsafe medical injections in the U.S. [Cited 12th September 2017]. Available at https:// www.cdc.gov/grand-rounds/pp/2012 /20121113-unsafe-injection.html.
29. Chowdhury H, Tapash R, Faroque M, Bachar S, Asaduzzaman M, Nasrin N et al. A comprehensive situation assessment of injection practices in a primary health care hospitals in Bangladesh. BMC Public Health. 2011; 11: 779.
30. Centre for Disease Control and Prevention. Choosing a Drug to prevent malaria. 2018. [Cited 20th September 2018]. Available at: https://www.cdc. gov /malaria/ travelers/drugs.html.
31. World Health Organization. Withdrawal of oral artemisinin - based monotherapies. [Cited 20th September 2018]. Available at: http://www.who.int /malaria/areas/treatment/withdrawal _of_oral_artemisinin_based_monothera pies/en/.
32. Igbiks T, Joseph O. Drug prescription pattern in a Nigerian tertiary hospital. Tropical Journal of Pharmaceutical Research 2012; 11: 146-152.
33. Bhavesh L, Hiray S, Ghongane B. Drug prescription pattern in outpatients in a tertiary care teaching hospital in Maharashtra. International Journal of Pharmacy and Biological Sciences 2012; 3: 225-229.
34. Chittaranjan A and Sathyanarayana R. Prescription writing: Generic or brand? Indian Journal of Psychiatry. 2017; 59: 133-137.
35. Graz B, Willcox M, Szeless T, Rougemont T. "Test and Treat" or Presumptive treatment for malaria in high transmission situations? A reflection on the latest WHO guidelines. Malaria Journal 2011; 10: 136-140.
36. Shillcutt S, Morel C, Goodman C, Coleman P, Bell D, Whitty C et al. Cost-effectiveness of malaria diagnostic methods in sub-Saharan Africa in an era of combination therapy. Bulletin of WHO. 2008; 86: 101-110.