Uncomplicated Malaria Management Practices and Cost of Illness Implications on Patients in Nigeria: A Systematic Review of Evidence

Nanloh S Jimam^{1,2}, Nahlah E Ismail^{1*}

¹Department of Clinical Pharmacy, Faculty of Pharmacy, MAHSA University, Selangor, MALAYSIA.

²Department of Clinical Pharmacy and Pharmacy Practice, Faculty of Pharmaceutical Sciences, University of Jos, Jos, NIGERIA.

ABSTRACT

Background: High prevalence of malaria has been reported in Nigeria. However, there are scanty information on the management practices and cost burdens of the disease on patients. The purpose of this review was to document related previous studies on healthcare workers and patients' uncomplicated malaria management practices, financial cost and intangible burdens on patients in Nigeria.

Methods: A systematic review of literature was carried out using the preferred reporting items for systematic reviews and meta-analyses' (PRISMA) approach on previous related studies published between 2005 and 2018 in Medical Subject Headings (MeSH), Medline[®], PubMED[®], Web of ScienceTM-Clarivate Analytics, Embase, Global Health Database, Google Scholar, websites of government department and major multilateral organizations involved in malaria control in Nigeria, and manual references of relevant studies. Only articles that met the inclusion criteria were finally evaluated.

Results: Out of identified and retrieved 336 relevant articles, 175 were identified as duplicate and removed. Further screening of titles and abstracts of the remaining 161 articles led to identification of 100 articles and their full texts were further reviewed which resulted in identification of 15 patients-, 13 healthcare workers-, and 9 cost burdens-related studies, with adequate data related to patients' and healthcare workers'

INTRODUCTION

Malaria is a major contributor to public health problem especially in the sub-Saharan Africa and it remains as one of the leading causes of morbidity and mortality worldwide, with pregnant women and children being more vulnerable¹. It has been shown that about 88% of the global malaria cases and 90% of the deaths occurred in Africa, with about 82% of the deaths occurred among children of under-five years in 2015. About 25% of the African malaria burdens are in Nigeria² with approximately 100 million cases and more than 300,000 deaths annually, in addition to the fact that the disease is responsible for about 60% outpatient visits to health facilities, 30% childhood death with 25% of it predominantly in children under one year, and 11% maternal death.

According to malaria treatment guideline for Nigeria, the control of the disease involved different approaches including vector control to reduce the malaria parasites transmission from humans to mosquitoes and then back to humans using insecticide-treated nets (ITNs) or indoor residual spraying (IRS), and the use of intermittent preventive treatment (IPT) for malaria prevention during pregnancy (sulfadoxine-pyrimethamine (S-P))³⁻⁵. The third approach is malaria case management which involve early diagnosis and prompt treatment of the disease with effective and recommended anti-malarial drugs^{1,3}. Effective uncomplicated malaria management implied the provision of comprehensive and effective care services by trained healthcare workers using the needed infrastructures and resources in healthcare facilities based on the treatment guideline for the purpose of achieving effective outcomes^{3,6,7}. The processes can be summarised in a pathway known as 'treatment effectiveness pathway', as described in Figure 1. In addition to ensuring the availability of quality anti-malarial drugs, it should be ensured that the right patients have access to healthcare facilities at minimal cost, and the healthcare workers and patients as well as caregivers mostly practice in accordance management practices, and cost burdens of managing uncomplicated malaria in Nigeria. Many studies (36.11%) were conducted in the southeastern region of the country, while the least percentage (5.56%) was from north-eastern part of the country.

Conclusion: Inappropriate healthcare workers' and patients' management practices based on malaria treatment guideline were observed, which was reflected in the significant cost implications on patients. There were scanty information on studies from some regions of the country, with observed limitations in study methodologies and sparse information on validity and stability of study scales used.

Key words: Artemisinin-based combination therapy, cost burdens, healthcare workers, uncomplicated malaria management practices, patients.

Correspondence:

Nahlah E Ismail

Department of Clinical Pharmacy and Pharmacy Practice, Faculty of Pharmaceutical Sciences, University of Jos, Jos, NIGERIA. Phone no: Tel: +60162731677.

E-mail: nahlah@mahsa.edu.my DOI: 10.5530/srp.2019.1.18



to the treatment guidelines during the management processes to be able to achieve the desired patients' therapeutic outcomes⁸.

Practicing otherwise might result in wrong diagnosis and prescriptions, or inadequate patients' instructions on how to take the medications, which have been reported as the major limiting factors that encourage patients' intentional or unintentional inappropriate intake of the medicines. These remained a major problem across the world; with worsen situations seen in developing countries, including Nigeria^{9,10}.

Due to the high prevalence and great consequences of the disease on the healthcare system and the patients in Nigeria, the need for conducting studies on how to eliminate the disease has been a great task in the healthcare system, especially as it relates to factors that influence the management of the disease and its cost burdens^{9,11-14}.

SIGNIFICANCE OF THE REVIEW

The consequences of inappropriate malaria medications on the health population of Nigeria include increased risk of adverse drug reactions and emergence of antimicrobial resistance leading to treatment failure, poor patient outcome of management, and high cost of treatment. 4,15,16. One of the ways to overcome inappropriate management practices of malaria in Nigeria is to encourage researches to elicit relevant information on the management practices of the disease and possible factors that influenced such practices and economic burdens of the disease. These would be helpful in raising awareness, making the needed resources available, encouraging rational treatment practices among healthcare workers and patients, improving healthcare providers-patients' communication, which result in achieving desired quality outcome of patients treatment at minimal cost. This review presented summary of related previous studies that elicit information regarding healthcare workers and patients' uncomplicated malaria management practices and/or try to identify factors influencing their practices, financial cost and intangible burdens in managing the respective disease on patients in Nigeria.

METHODS

Inclusion criteria

For a journal article to be included in this review, it was ascertained that:

- i. The study was a quantitative or qualitative estimate of patients' uncomplicated malaria management, and/or factors influencing management practices, and/or cost and/or intangible burdens on patients
- ii. The study reported a design and detail of how to estimate healthcare workers and/or patients' uncomplicated malaria management practices
- iii. The article was published in an English language peer-reviewed journal
- iv. The study was conducted in Nigeria from 2005 after the country adopted artemisinin-based combination therapy (ACT) as the first line drug for uncomplicated malaria, to 2018¹⁷.

Exclusion criteria

The study excluded:

- i. Related studies conducted before 2005
- ii. Reported abstracts
- iii. Other interventions in malaria management such as the use of insecticides and bush clearing, which did not include the use of antimalarial drugs

Search methods

A systematic review of the published literature was carried out using both the electronic search of different databases including Medical Subject Headings (MeSH), Medline^{*}, PubMED^{*}, Web of Science^{**}-Clarivate Analytics, Embase, Global Health Database and Google Scholar, websites of government department and major multilateral organizations involved in malaria control in Nigeria, and manual search of references of relevant studies. Terms like "healthcare workers or patients' knowledge, attitudes and practices (KAP) on uncomplicated malaria", "healthcare workers or patients' uncomplicated malaria management practices", "adherence to Nigeria malaria treatment guidelines", "non-adherence to Nigeria malaria treatment guidelines", "pharmacoeconomics of malaria", "cost burdens of malaria management on patients", "health-related quality of life (HRQoL) of malaria-infected patients", combined with "Nigeria" were used during searching in different databases.

Data extraction and presentation

The identified and sorted articles considered to be relevant in the study were ascertained by two reviewers who read them before the detailed extraction of the relevant information began. This was necessary for improving the quality of the extracted data in addition to meeting the above inclusion and exclusion criteria. The characteristics of each of the identified articles were then reviewed according to the year of publication, study design, study sample, main outcome measures, and the results appropriately documented.

RESULTS

Out of the identified and retrieved 347 relevant articles, 181 were found to be duplicate studies and were removed. Further screening of the titles and abstracts of the remaining 166 articles led to the identification of 102 articles for further review of their full text, which resulted in identification of 15, 13, and 9 publications, respectively, with adequate data related to patients' and healthcare workers' management practices, and cost burdens of managing uncomplicated malaria in Nigeria (Figure 2). The outcome of the review showed that some studies on healthcare workers and patients aimed at assessing uncomplicated malaria management, factors influencing management practices, and cost and intangible burdens on patients had been conducted across the six geo-political regions of Nigeria (Tables 1-3).

DISCUSSION

Malaria case management involve early diagnosis and prompt treatment of malaria cases with effective and recommended antimalarial drugs^{1,3}. Malaria treatment guideline for Nigeria stated the use of artemether-lumefantrine as the recommended anti-malarial drug for case management of uncomplicated malaria after diagnosis using either microscopy or RDTs approach to identify the parasite, or artesunateamodiaquine, in the case of artemether-lumefantrine unavailability³. This review documented related previous studies on healthcare workers' and patients' uncomplicated malaria management practices, and cost implications on patients in Nigeria, and it was the first of its kind to be reported in the country based on literature review. Tables 1-3 showed sub-optimal quality of healthcare workers' and patients' management practices based on malaria treatment guideline which were linked to knowledge and attitudes-related attributes and availability of ACTs in the healthcare facilities, and this was evident in the reported significant cost implications on patients. In addition, the review study indicated scanty information on studies from some regions of the country, with observed limitations in study methodologies and sparse information on validity and stability of study scales used.

The sub-optimal levels of healthcare workers' knowledge on uncomplicated malaria and its management based on malaria treatment guideline were evident in both their diagnostic and prescription practices (Table 1). There were observed presumptive diagnoses and irrational prescription practices, such as monotherapy and polypharmacy practices among the prescribers. In some cases, ACTs were prescribed to patients based on availability of the antimalarial drugs. Also, some of the prescriptions were made without first conducting test as recommended in the malaria treatment guideline or standing orders in the case of PHC facilities^{1,3,53}. Ensuring diagnosis either through microscopy or RDT is necessary in order to know who has the infection and needs an anti-malarial drug, and who does not have it and needs an alternative treatment⁵³. This might be more applicable in differentiating between malaria and other common acute febrile illnesses such as invasive bacterial diseases with similar symptoms before initiation of medication which may result in achieving the desired patients' therapeutic outcome of management. These approaches have been reported as among major strategies for the effective control of the infection particularly in the sub-Saharan



Figure 2: Flow chart adapted from 'preferred reporting items for systematic reviews and meta-analyses' (PRISMA)¹⁸ describing the systematic review of literature on uncomplicated malaria management and cost of illness burdens.

Table 1: Characteristics of previous studies on healthcare workers' uncomplicated malaria management in Nigeria

References	Zone	Study location	Study design	Sample size calculation	Sample size	Study population	Sampling method	Data collection method	Main outcome
[19]	SW	Public and private health facilities	Comparative cross- sectional	-	432	Private and public healthcare workers	Multistage sampling	Semi- structured questionnaires	Public and private health workers had fairly good knowledge on the national malaria treatment guidelines for uncomplicated malaria. Presumptive diagnosis and use of antimalarial monotherapy drugs were common practices in private health facilities.
[20]	NC	РНС	Cross- sectional quantitative	-	105	Public health facilities	Multistage sampling	Semi- structured questionnaires	Health workers had fairly good knowledge on malaria.
[21]	SE	Community and health facilities	Cross- sectional qualitative	-	129 & 26	Community members and health workers	-	FGD & IDI	Both health workers and community members had good perception about malaria tests before medications.
[22]	NC	РНС	Qualitative	-	16	Health managers and health care workers	Purposive sampling	In-depth interviews	Prescription of ACTs as a first line of treatment for uncomplicated malaria without a parasite-based diagnosis was the standard case management practice.
[23]	NW	РНС	Cross- sectional	-	-	Health workers involved in prescription of drugs	Multistage sampling	Self- administered questionnaires	Prescription of ACTs was based on availability rather than recommendation of treatment guideline.
[24]	SE	Rural communities	Cross- sectional	Calculated	270	Patent Medicine Vendors (PMVs)	Purposive and random sampling	Interviewer administered questionnaire	There were inadequate knowledge and low utilization of ACTs by PMVs.

Jimam, et al.: Uncomplicated Malaria Management Practices and Cost of Illness Implications on Patients in Nigeria: A Systematic Review of Evidence

References	Zone	Study location	Study design	Sample size calculation	Sample size	Study population	Sampling method	Data collection method	Main outcome
[25]	SE	Three levels of health facilities in Enugu	Cross- sectional	Calculated	600	Prescribers	Purposive and systematic sampling	Retrospective	Predictors of adherence to treatment guideline included years of practice, practice volume, awareness and training.
[26]	SS	Three levels of health facilities in Edo	Cross- sectional survey		2,500	Doctors	Random and systematic sampling techniques	Retrospective	Irrational prescribing practices in the three categories of hospitals, especially in the general and private hospitals.
[27]	SE	Two public and two private hospitals	-	Calculated	52	Healthcare workers in antennal clinics	Purposive sampling	Self- administered questionnaires	Ihere is sub-optimal level of knowledge about current best practices for treatment and chemoprophylaxis for malaria in pregnancy especially in the private sector. Also, intermittent preventive treatment of malaria in pregnancy (IPTp) was hardly used in the public sector.
[28]	NW	Aminu Kano Teaching Hospital, Kano (AKTH)	Descriptive	-	500	Prescribers at the general outpatient unit	Systematic random sampling	Retrospective	There were observed polypharmacy, low rate of generic prescriptions and overuse of antibiotics in the facility.
[29]	SE	Public and private health facilities in Cross River State	-	-	463	Prescribers at public PHC and secondary health facilities	Simple random sampling	Retrospective	There was observed fair utilization of ACTs for treating uncomplicated malaria, but clinical assessment of patients and laboratory confirmation of diagnosis were suboptimum.
[30]	SE	Children's out- patient clinic (CHOP) of the University of Nigeria Teaching Hospital (UNTH)	Descriptive	-	2,394	Doctors at children out- patient's clinic	-	Retrospective	Presumptive diagnosis of malaria, especially among children under five years of age is high, and many had received ACTs without confirmation.
[31]	SE	Public and private healthcare facilities in urban and rural Enugu state	Descriptive cross- sectional	-	82	Heads of public and private health facilities	Stratified and simple random sampling	Self- administered questionnaires	Although many health workers were knowledgeable about RDTs, not many facilities used it, ACTS were readily available and used in public compared to private health facilities.

Note: SW = South-West; NE = North-East; NW = North-West; SE = South-East; NC = North-Central; SS = South-South; FCT = Federal Capital Territory; PHC = Primary healthcare; RDT = Rapid diagnostic test; FGD & IDI = Focus group discussion and in-depth interview; ACT = artemisinin combination therapy; PMV = Patent medicine vendor

African countries^{3,53-56} The quality of these services required availability of trained healthcare workers with good skill who are knowledgeable to make patients know the importance of his/her medication through appropriate counselling, which might influence their willingness to take the prescribed medication accordingly. In addition, the availability and utilization of required material resources in the healthcare facilities, especially sources of information like treatment guidelines and essential drug lists, diagnostic materials and the recommended medicines are essential.^{9,57-60}

The review study also showed inappropriate patients' treatment practices during uncomplicated malaria management as exemplified by the reported self-medication practices, especially the rampant use of chloroquine and sulphadoxime-pyrimethemine for suspected malaria without first conducting test. This was attributable to their poor knowledge and attitudes toward the disease and its management, although, some of the studies indicated fair knowledge of the respondents on the disease. In addition, employment status of the respondents and affordability of treatment were reported barriers to patients' appropriate medication practices as revealed in the review study. Generally, patients' poor management practices can either be due to intentional or unintentional reasons. Intentional is when the patient actively decides on his/her own not to use treatment or follow treatment recommendations, which might be after the patient have weigh the pros and cons of the treatment⁶¹. Patients' lack of trust on the healthcare workers' judgement on the ailment being treated may also be a possible reason for stopping or not taking the medication in accordance to instructions, and this might be linked to several reasons including cultural and religious belief systems of the patients⁶². Similarly, as observed in the present review, patients' level of understanding is another factor that influenced uncomplicated malaria management practices of patients. This is possible because getting conflicting information from trusted friends, internets and other sources about their ailments causing them to misunderstand the purpose of the drug or the nature of their illness, and hence questioning the effectiveness of any medication given to them by healthcare workers for the ailment^{9,63,64}. In some instances, they might even intentionally stop taking their medications because of side effects and other

References	Zone	Study location	Study design	Sample size calculation	Sample size	Study population	Sampling method	Data collection method	Main outcome
[32]	SW	Household survey	Community-based study	Calculated	422	Mothers of ≤ 5 years old children	Multistage sampling technique	Semi-structured questionnaire	Mothers in the study areas had poor perception and misconceptions about malaria in children and practiced self-medications.
[8]	SW	Household survey	Comparative Study	Calculated	280	Mothers/ caregivers	-	Household Survey questionnaire	Improvement in knowledge of respondents led to increasing adherence to malaria treatment at home.
[33]	SW	Tertiary Institutions	-	-	643	Tertiary students	-	Structured Questionnaire	Respondents had low perception regarding diagnosis and use of recommended anti-malarials. Respondents had relatively
[34]	SW	Higher institutions	Cross-sectional survey	Calculated	1195	Non-medical students	Simple random sampling	Interviewer- administered structured questionnaire	reasonable knowledge about malaria management and practices. They did not understand well certain aspects such as prophylaxis, species, and laboratory diagnostic technique.
[35]	SW	Household survey	-	-	310	Adults with recent malaria episodes	Simple random sampling	Household survey questionnaire	CQ was the most preferred anti- malarial drugs in the communities followed by sulphadoxine- pyrimethamine, while ACT was the least used, though better than what it used to be.
[36]	SW	Community survey	Cross-sectional survey	Calculated	440	Adults of 18 years old and above on malaria medication	Convenient and random sampling	Semi-structured questionnaire	The main outcome of the study showed that employment status of respondents significantly increased their non-adherence to medications.
[37]	NE	Household survey	Cross-sectional	-	186	Mothers	Multiple- stage approach	Household survey questionnaire	Respondents had strong spiritual beliefs about malaria aetiology and treatment.
[38]	NW	Household	Community-based study	-	200	Heads of households	Random sampling	Structured questionnaire	The respondents had good knowledge on the cause and symptoms of malaria, but poor attitude and practices regarding malaria control.
[39]	SE	PHC, pharmacies and PMDs	Exit survey	Calculated	1642	Febrile patients of all ages or their caregivers	Multi-stage random sampling	Interviewer- administered questionnaire	The quality of malaria treatment among the respondents was low especially the poorest socio- economic groups.
[40]	NE	UMTH	Cross-sectional	-	350	Women above 14 years of age	-	Interviewer- administered structured questionnaire (KAP)	Respondents had good knowledge on symptoms of malaria with perceptions that ACTs were effective, though scarce, expensive, unsafe, and cumbersome doses, thus, most preferred herbs.
[41]	NC	BUTH	Cross-sectional	Calculated	441	Male and female malaria patients	-	Interviewer- administered structured questionnaire (KAP)	Respondents had poor knowledge on cause and medications, though aware of vector transmitting the malaria and its symptoms.
[42]	SS	Port Harcourt Metropolis	Cross-sectional	-	900	Malaria patients of ≥ 15 years old	Random sampling	Structured questionnaire	Most respondents took ACTs for the treatment of uncomplicated malaria compared to previous reports in Nigeria.

Table 2: Characteristics of previous studies on patients' uncomplicated malaria management in Nigeria

Jimam, et al.: Uncomplicated Malaria Management Practices and Cost of Illness Implications on Patients in Nigeria: A Systematic Review of Evidence

References	Zone	Study location	Study design	Sample size calculation	Sample size	Study population	Sampling method	Data collection method	Main outcome
[43]	NW	Health centers within Sokoto town	Cross-sectional	-	200	Outpatients	-	Structured questionnaire	The main outcome of the study showed that over one-quarter of respondents could not afford anti- malarial medications, and more than one-half of diagnosis was through presumptive methods.
[44]	SS	Central Hospital Benin	-	-	231	-	-	Structured questionnaire	The findings showed that uncontrolled use of herbal medications and self-prescribed medications were common practices in rural areas.
[45]	NC	Community survey	-	-	400	People of 15 - 70 years old who had used ACTs within the past one month	-	Semi-structured questionnaire	There was poor adherence to ACT use which could be linked to poor awareness of the public on the importance of adhering strictly to their prescribed treatment regimen.

Note: SW = South-West; NE = North- East; NW = North-West; SE = South-East; NC = North-Central; SS = South-South; PHC = Primary healthcare; ACT = Artemisinin combination therapy; PMDs = Patent medicine dealers; KAP = Knowledge, attitudes and practices; CQ = Chloroquine; UMTH = University of Maiduguri Teaching Hospital; BUTH = Bingham University Teaching Hospital

Table 3: Characteristics of previous studies on financial and intangible burdens of uncomplicated malaria in Nigeria

References	Zone	Study location	Study design	Sample size calculation	Sample size	Study population	Sampling method	Data collection method	Main outcome
[46]	SE	University of Benin Teaching Hospital	Cross- sectional cost-of- illness approach	Calculated	487	Adult outpatients	-	Semi-structured questionnaires for patients	The mean values of direct cost and indirect cost of treatment of malaria illness per adult outpatient were \$ 20.34 and \$ 29.0, respectively.
[11]	SE	Nnamdi Azikiwe University Medical Center (NAUMC), Awka	Cross- sectional cost-of- illness approach	-	-	Healthcare provider perspectives	-	Audit of patients' medical records, finance/audit department records	Uncomplicated malaria consumed about 25% of the health facility's expenditure, driven mainly by personnel cost and high proportion of malaria cases.
[47]	SE	Household and hospital based surveys	Cross- sectional cost-of- illness approach	-	500 and 125	Household and workers' cost	Systematic random and purposive sampling	Patients' interviewer administered questionnaire, exit interviews, retrospective and prospective data abstraction from case records	The cost of treating malaria is high both to the household and to the health system.
[48]	SW	Private hospitals in Ibadan	Cross- sectional study	-	40	Doctors	Simple random sampling	Self-administered questionnaire	Malaria accounts for high patronage of private hospitals and drugs cost constitute the bulk of expenses on treatment.
[49]	NC	Households in Asa LGA of Kwara	Cost of illness approach	-	1200	Household members treated for malaria	Systematic sampling	Interviewer administered questionnaire	Malaria imposed significant costs on the affected households.
[50]	SW	Household in Oyo state	cost of illness approach	-	416	Malaria affected households	Multi- stage- sampling	Structure questionnaire	The study showed that 10% of gross domestic output of Oyo state is lost annually due to malaria attack.

Jimam, et al.: Uncomplicated Malaria Management Practices and Cost of Illness Implications on Patients in Nigeria: A Systematic Review of Evidence

References	Zone	Study location	Study design	Sample size calculation	Sample size	Study population	Sampling method	Data collection method	Main outcome
[51]	Nigeria	Households in Nigeria	Willingness- to-pay (WTP) approach	-	1,600	Households	Multi- stage- sampling	Structured questionnaire	The results showed a high level of willingness to pay for malaria control in Nigeria.
[31]	SE	Household and health center in Enugu	Willingness- to-pay (WTP) approach	Calculated	1020 and 600	Households and patients with fever	Simple random sampling	Interviewers administered questionnaires	The ex post WTP was higher than the ex ante WTP and both were greater than the current cost of RDTs. Urban dwellers were more willing to pay than the rural dwellers.
[52]	SS	Madonna University Teaching Hospital	Cross-section studies	-	120	Patients with confirmed malaria	-	Acceptance of Illness Scale, The Satisfaction With Life Scale, and WHO Quality of Life/BREF Scale	The study demonstrated statistically significant relationships between patients' level of acceptance of illness and quality of life and satisfaction with life.

Note: SW = South-West; NE = North- East; NW = North-West; SE = South-East; NC = North-Central; SS = South-South; RDT = Rapid diagnostic test; LGA = Local Government Area; WTP = Willingness-to-pay; WHO = World Health Organization; BREF = Biomedical Research and Education Facility

disadvantages, after reading the patient information leaflet that comes with the drug and this might contribute to their lack of motivation to use such medication, or they might also stop medication when the symptoms of the ailment is gone thinking that they are better⁶². On the contrary, unintentional reason for poor medication refers to unplanned behaviour that is less strongly associated with patients' beliefs and the level of cognition⁶⁵. This could be linked to cognitive reasons leading to patients forgetting to take their medications or knowing exactly how to use the medication^{63,64}. It has been considered as a passive process that is associated with the complexity of a medication regimen (poly-pharmacy) which was also noticed in the present study, and the patient's memory, thereby making them to either forget to take the drug at the prescribed time or poor recall of instructions of how to take the drug^{61,65}. Economic reason for unintentional poor practices as reported in some of the reviewed articles, especially in poor or low income individuals and the high cost of medications can certainly contribute to poor management practices9,66.

In all, the reported cost implications of these inappropriate management practices on patients were significant (Table 3), which was consistent with report of similar studies conducted in Ghana⁶⁷ and in southcentral Ethiopia⁶⁸. Also, the only identified QoL-related study among uncomplicated malaria-infected patients during the review study indicated significant relationships between patients' level of acceptance of illness and QoL and satisfaction with life. This was similar to a study conducted by Das and Ravindran⁶⁹ in India demonstrated patients that accepted their illness were less likely to experience negative emotional reactions associated with such illness, hence, high chance of better HRQoL.

LIMITATIONS OF THE REVIEW

Most of the reviewed articles were quantitative in nature, therefore exploring uncomplicated malaria disease and barriers to appropriate management such as cultural and contextual factors influencing adherence may need the involvement of qualitative studies.

There were also issues of variability in the study populations which could also be influencing factors in the observance of some of the differences and their relative importance as non-adherence factors. This is possible since some of the studies were conducted in tertiary healthcare facilities while others were from primary or secondary healthcare facilities. It has been shown that those in the urban areas whereas the tertiary healthcare facilities mostly located, might be more knowledgeable and financially buoyant compared to those living in the rural areas, which are the most populated portion of the country's population living in poverty⁶⁹.

CONCLUSIONS

This review presented summary of key studies on uncomplicated malaria management that have been conducted in Nigeria involving healthcare workers and patients as well as financial and intangible burdens. The review revealed that some related studies had been conducted across the six geo-political regions of Nigeria. The review also showed inappropriate healthcare workers' and patients' management practices based on malaria treatment guideline which were linked to knowledge and attitudes-related attributes and availability of ACTs in the healthcare facilities, and this was evident in the reported significant cost implications on patients.

However, there were scanty information on the studies from some regions of the country. Some research gaps in study methodologies were also observed, in addition to sparse information on validity and stability of the study scales used. There is a need for detailed studies on the barriers that are associated with inappropriate malaria medication for the purpose of improving the quality of malaria treatment in the country.

REFERENCES

- World Health Organization. Guidelines for the Treatment of Malaria. WHO (Third), Geneva; 2015. [Online], from: www.who.int [accessed on 24th June, 2017].
- Muhammed JU, Aminu C, AO. Compliance of Primary Health Care Providers to Recommendation of Artemesinin-Based Combination Therapy in the Treatment of Uncomplicated Malaria in Selected Primary Health Care Centres in Sokoto, North-Western Nigeria. Int J Trop Med. 2011; 6(3):70-72.
- Federal Ministry of Health (FMOH). National Guidelines for Diagnosis and Treatment of Malaria (3rd Edition) Abuja, Nigeria; 2015. [Online], from www. fmh.gov.ng [accessed on 17th october, 2017].
- Federal Minstry of Health (FMOH) and Roll Back Malaria (RBM). National Malaria Strategic Plan 2014 -2020. Abuja and Maryland; 2014. [Online], from: http://endmalaria.org [accessed on 17th october, 2017].
- Bhatt S, Weiss DJ, Cameron E, Bisanzio D, Mappin B, Dalrymple U. Europe PMC funders group: The effect of malaria control on plasmodium falciparum in Africa between 2000 and 2015. Nature. 526(7572): 207-211.
- O'Meara WP, Noor A, Gatakaa H, Tsofa B, McKenzie FE, Marsh K. The impact of primary health care on malaria morbidity – Defining access by disease burden. Trop Med Int Health. 2009; 14:29-35.

- Ajayi IO, Falade CO, Bamgboye EA, Oduola AM, Kale OO. Assessment of a treatment guideline to improve home management of malaria in children in rural south-west Nigeria. Malar J. 2008; 7(1): 24.
- The Malaria Eradication Research Agenda (malERA) Consultative Group on Health and Operational Research. A research agenda for malaria eradication: health systems and operational research. PLoS Med. 2011; 8(1): e1000397.
- Brown MT, Bussell JK. Medication adherence: WHO Cares? Mayo Clinic Proceed. 2011; 86(4): 304-314.
- Ezenduka CC, Ogbonna BO, Obinna EI, Mathew JO, Esimone CO. Anti-malarial drugs use pattern in retail outlets in Enugu urban south-eastern Nigeria, implication for malaria treatment policy. Malar J. 2014; 13: 243.
- Ezenduka CC, Falleiros DR, Godman BB. Evaluating the treatment costs for uncomplicated malaria at a public healthcare facility in Nigeria and the implications. PharmacoEcons Open. 2017.
- Martin MY, Kim Y, Kratt P, Litaker M, Kohler CL, Schoenberger YM, et al. Medication adherence among rural, low-income hypertensive adults: a randomized trial of a multimedia community-based intervention. Am J Health Promo. 2011; 25(6): 372-378.
- Obieche OA, Odili VU. Evaluation of cost of treatment of malaria in adults in Benin City, Nigeria: patients' perspective. Malar World J. 2016; 7:12
- Wardrop NA, Barnett AG, Atkinson JA, Clements AC. Plasmodium vivax malaria incidence over time and its association with temperature and rainfall in four counties of Yunnan Province, China. Malar J. 2013; 12(452).
- Olayemi IK, Ande AT, Odeyemi MO, Ibemesi G, Emmanuel R. Temporal ecologic adaptability of the principal vector of malaria anopheles gambiae s.l. (Diptera: Culicidae), in north-central Nigeria. Applied Sci Reports. 2014; 5(3): 110-117.
- 16. World Bank. World Development Indicators 2014. Group; 2014.
- Federal Ministry of Health (FMOH). National Anti-malarialTreatment Policy. Abuja, Nigeria; 2005.
- Moher D, Liberati A, Tetzlaff J, Altman DG. The PRISMA Group Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009; 6(7): e1000097.
- Bamiselu FO, Ajayi I, Fawole O, Dairo D, Ajumobi O, Oladimeji A, et al. Adherence to malaria diagnosis and treatment guidelines among healthcare workers in Ogun state, Nigeria. BMC Public Health. 2016; 16: 828.
- Bello DA, Tagurum YO, Afolaranmi TO, Chirdan OO, Zoakah AI. Knowledge and pattern of malaria case management among primary healthcare workers in Jos. J Med Trop. 2013; 15: 91-95.
- Ezeoke OP, Ezumah NN, Chandler CCI, Mangham-Jefferies LJ, Onwujekwe OE, Wiseman V, et al. Exploring health workers' and community perceptions and experiences with malaria tests in south-eastern Nigeria: a critical step towards appropriate treatment. Malar J. 2012; 11: 368.
- Jegede AS, Ajayi IO, Oshiname FO, Falade CO, Chandramohan D, Prudence H, et al. Qualitative assessment of rural health workers' management of malaria in sick children. Malar World J. 2015; 6:7.
- 23. Umar MT, Chika A, Jimoh AO. Compliance of primary health care workers to recommendation of artemesinin-based combination therapy in the treatment of uncomplicated malaria in selected primary health care centres in Sokoto, north-western Nigeria. Internat J Trop Med. 2011; 6(3): 70-72.
- Nduka SO, Agbata CA, Eze BH, Ezeobi I, Nwadukwe CC, Uzodinma SU. (2013). Assessment of artemisinin based combination therapy utilisation among patent medicine vendors in some rural areas in Nigeria. Internat J Collaborat Res Intern Med Pub Health. 2013; 5(10): 619-629.
- Ogochukwu AM. Predictors of adherence to national anti-malarial treatment guidelines in some Nigerian hospitals. Internat J Drug Develop. Res. 2010; 2(3): 545-554.
- Okoli RI, Isah AO, Ozolua RI, Ohaju-Obodo JO, Nwokike OC, Ovienria WA. Drug prescribing pattern in three levels of health care facilities in the north and central senatorial districts of Edo state, Nigeria. Internat J Herbs Pharmacol Res. 2015; 4(3): 46-57
- Onwujekwe OC, Soremekun RO, Uzochukwu B, Shu E, Onwujekwe O. Patterns of case management and chemoprevention for malaria-in-pregnancy by public and private sector health workers in Enugu state, Nigeria. BMC Res Notes. 2012; 5, 211.
- Tamuno I, Fadare JO. Drug prescription pattern in a Nigerian tertiary hospital. Trop J Pharm Res. 2012; 11(1): 146-152.
- Udoh E, Oyo-Ita A, Odey F, Effa E, Esu E, Oduwole O, et al. Management of uncomplicated malaria in underfives in private and public health facilities in south-eastern Nigeria: A clinical audit of current practices. Malar Res Treat. 2013; 6:575080.
- Ughasoro MD, Okafor HU, Okoli CC. Malaria diagnosis and treatment amongst health workers in University of Nigeria Teaching Hospital Enugu, Nigeria. Nig J Clin Pract. 2013; 16(3): 329-333.
- Uzochukwu BSC, Onwujekwe OE, Uguru NP, Ughasoro MD. Ezeoke OP. Willingness to pay for rapid diagnostic tests for the diagnosis and treatment of malaria in south-eastern Nigeria: ex post and ex ante. International J Equity Health. 2010; 9: 1.

- Orimadegun AE, Ilesanmi KS. Mothers' understanding of childhood malaria and practices in rural communities of Ise-Orun, Nigeria: implications for malaria control. J Fam Med Prim Care. 2015; 4(2): 226-231.
- Adetola OT, Aishat II, Olusola O. Perception and treatment practices of malaria among tertiary institution students in Oyo and Osun states, Nigeria. J Nat Sci Res. 2014; 4(5): 33-43.
- 34. Edet-Utan O, Ojediran T, Usman S, Akintayo-Usman N, Fadero T, Oluberu O, et al. Knowledge, perception and practice of malaria management among nonmedical students of higher institutions in Osun state, Nigeria. Am J Biotech Med Res. 2016; 1(1): 5-9.
- 35. Efunshile AM, Fowotade A, Makanjuola OB, Oyediran El, Olusanya OO, Koenig B. Anti-malarial use and the associated factors in rural Nigeria following implementation of affordable medicines facility-malaria (Amfm) price subsidy. Afr J Clin Exptal Microbio. 2013; 14(2): 88-94.
- Okuboyejo S. Non-Adherence to Medication in Outpatient Setting in Nigeria: The Effect of Employment Status. Glob J Health Sci. 6(3): 37-44.
- Akogun OB, John KK. Illness-related practices for the management of childhood malaria among the Bwatiye people of north-eastern Nigeria. Malar J. 2005; 4(1):13.
- Singh R, Musa J, Singh S, Ebere UV. Knowledge, attitude and practices on malaria among the rural communities in Aliero, northern Nigeria. J Fam Med Prim Care. 2014; 3(1):39-44.
- 39. Ibe OP, Mangham-Jefferies L, Cundill B, Wiseman V, Uzochukwu BS, Onwujekwe, OE. Quality of care for the treatment for uncomplicated malaria in south-eastern Nigeria: how important is socio-economic status? Internat J Equity Health. 2015; 14(1):19.
- 40. Balogun ST, Jibrin J, Tahir R, Bassi PU, Balogun FA, Fehintola FA. Perceptions of artemisinin-based combination therapies among Nigerian women seven years after adoption as first line drugs. Am J Res Communicat. 2015; 3(4):107-116.
- Builders MI, Ogbole E, Peter JY. Assessment of anti-malarial drug use among the patients in tertiary hospital in northern part of Nigeria. Internat J Trop Dis Health. 2013; 3(4): 283-289.
- Shorinwa OA, Ebong O. Use of Artemisinin-combination therapies in PortHarcourt. J Applied Sci Environtl Mgt. 2012; 16(1): 35-40.
- Hudu SA, Jimoh AO, Abubakar K, Bello A. Common anti-malarial drug prescription and patient affordablility in Sokoto, Nigeria. International Journal of Pharmacy and Pharmaceutical Sciences. 2013; 5(2): 428-431.
- 44. Tatfeng YM. The attitude of patients towards the treatment of malaria in Edo state, Nigeria. East & Central Afr J Pharm Sci. 2011; 14: 95-97.
- Aboh M, Emeje M, Oladosu P, Akah I, Gamaniel K. Artemisinin combination therapy use in Federal Capital Territory, Nigeria. Afr J Pharm Pharmacol. 2016; 10(38): 805-809.
- Obieche OA, Odili VU. Evaluation of cost of treatment of malaria in adults in Benin City, Nigeria: patients' perspective. Malar World J. 2016; 7(12): 1-7.
- Onwujekwe O, Uguru N, Etiaba E, Chikezie I, Uzochukwu B, Adjagba A. The economic burden of malaria on households and the health system in Enugu state southeast Nigeria. PLoS ONE. 2013; 8(11).
- Salawu AT, Fawole OI, Dairo MD. Patronage and cost of malaria treatment in private hospitals in Ibadan north LGA south-western Nigeria. Annals Ibd Postgrad Med. 2016; 14(2): 81-84
- Salihu OM, Sanni NA. Malaria burden and the effectiveness of malaria control measures in Nigeria: a case study of Asa local government area of Kwara state. J Econs Sustain Develop. 2013; 4(3): 295-308.
- Alaba OA, Alaba OB. Malaria in rural Nigeria: Implications for the Millennium Development Goals; 2015. [Online], from www.saga.cornell.edu/saga/aercconf/ alaba.pdf accessed on 15 June, 2018].
- Jimoh A, Sofola O, Petu A, Okorosobo T. Quantifying the economic burden of malaria in Nigeria using the willingness to pay approach. Cost Effect Res Allocat. 2007; 5: 6.
- 52. Damme-Ostapowicz KV, Krajewska-Kułak E, Rozwadowska E, Nahorski WL, Olszański R. Quality of life and satisfaction with life of malaria patients in context of acceptance of the disease: quantitative studies, Malar J. 2012; 29(11): 171.
- World Health Organisation (WHO). World malaria report, Geneva, 2017. Licence: CC BY-NC-SA 3.0 IGO; 2017. [[Online], from: https://apps.who.int/iris/bitstream/ handle/10665/259492/9789241565523-eng.pdf [accessed on 20th July, 2018].
- Bartoloni A, Zammarchi L. Clinical aspects of uncomplicated and severe malaria. Mediterr J Hemat Infect Dis. 2012; 4(1): e2012026.
- Boschi-Pinto C, Young M, Black RE. The child health epidemiology reference group reviews of the effectiveness of interventions to reduce maternal, neonatal and child mortality. Internat J Epidemio. 2010; 39(Suppl. 1), 3-6.
- Galactionova K, Tediosi F, de Savigny D, Smith T, Tanner M. Effective coverage and systems effectiveness for malaria case management in sub-Saharan African countries. PLoS ONE. 2015; 10(5): e0127818.

- Inkster ME, Donnan PT, MacDonald TM, Sullivan FM, Fahey T. Adherence to antihypertensive medication and association with patient and practice factors. J Human Hyperten. 2006; 20(4): 295-297.
- Longtin Y, Sax H, Leape LL, Sheridan SE, Donaldson L, Pittet D. Patient participation: current knowledge and applicability to patient safety. Mayo Clinic Proceeds. 2010; 85(1): 53-62.
- Mooney G, Ryan M. Agency in healthcare: getting beyond first principles. J Health Econs. 1993; 12(2): 125-135.
- Zyoud SH, Al-Jabi SW, Waleed M, Sweileh WM, Morisky DE. Relationship of treatment satisfaction to medication adherence: findings from a cross-sectional survey among hypertensive patients in Palestine. Health Qual Life Outcomes 2013; 11(191): 3-7.
- National Council on Patient Information and Education (NCPIE). Enhancing prescription medicine adherence : a National Action Plan, NCPIE, USA; 2007. [Online], from: www.talkaboutrx.org [accessed on 23 May, 2017].
- Haynes RB, Ackloo E, Sahota N, Mcdonald H, Yao X. Interventions for enhancing medication adherence (Review). The Cochrane Library. 2008.
- Greenley RN, Kunz JH, Walter JBA, Hommel KA. Practical strategies for enhancing adherence to treatment regimen in inflammatory bowel disease. Inflamm. Bowel Dis. 2013; 19(7): 1534-1545.

- 64. Yadav SP, Yadav S, Kuma P, Yadav S. Knowledge, treatment-seeking behaviour and socio-economic impact of malaria in the desert of Rajasthan, India. Southern Afr J Epidemio Infect. 2013; 28(1): 41-47.
- Jimmy B, Jose J. Patient medication adherence: measures in daily practice. Oman Med J. 2011; 26(3): 155-159.
- 66. Mwenesi HA. Sociocultural and behavioural issues in the treatment and prevention of malaria. Working Group on Malaria, Geneva; 2003. [Online], from: http://www.tropika.net/review/030324-Malaria_4/article.pdf [accessed on 23 May, 2017].
- Akazili JMA, Aikins M, Binka FN. Malaria treatment in Northern Ghana: What is the treatment cost per case to households? Afr J Health Sci. 2007; 14:70-79.
- Hailu A, Lindtjørn B, Deressa W, Gari T, Loha E, Robberstad B. Economic burden of malaria and predictors of cost variability to rural households in south-central Ethiopia. PLoS ONE. 2017; 12(10), e0185315.
- Das A, Ravindran TS. Factors affecting treatment-seeking for febrile illness in a malaria endemic block in Boudh district, Orissa, India: policy implications for malaria control. Malar J. 2010; 9:377.
- Omorogiuwa O, Zivkovic J, Ademoh F. The role of agriculture in the economic development of Nigeria. Europ Sci J. 2014; 10(4): 1857-7881.