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Original Article

A Study of Childhood Malaria trends at the University of Port Harcourt Teaching Hospital: 2006 – 2018

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Abstract

Background: Several efforts have been put in place to reduce the global burden of malaria especially in children and in sub-Saharan Africa. The study aimed to evaluate the impact of malaria control activities on the trend of childhood malarial diseases at a tertiary hospital in South-south Nigeria.
Methodology: A retrospective review of the case records of all malaria diagnoses including in-patient, out-patient, and emergency room, seen in the Department of paediatrics at the University of Port Harcourt Teaching Hospital from January 2006 to December 2018 was conducted.
Results: There were 41, 863 malaria cases diagnosed over the 12 years with a decline in yearly diagnosis and admissions, from the year 2006 through 2018. Total malaria admissions were 578, (44.5/ year), giving a severe malaria incidence of 1.26%, and there were 164 malaria death cases, with a yearly average of 12. The causes of death in the children with malarial parasitaemia were severe anaemia in 75 (45.7%), hypoglycaemia in 14 (8.5%), cerebral malaria in 17 (10.4%), and prostration with other co-morbidities, 22 (13.4%). Thirty-six children (22%) were convulsing and died soon after admission, with a compounding diagnosis of aspiration and respiratory failure.
Conclusion: There is a gradual reduction in childhood malaria disease, admission, and death, though this is slower than anticipated based on efforts and strategies put in place by the Nigerian government and various organizations.
Keywords: Malaria; Decline; Children; Port Harcourt; Nigeria.

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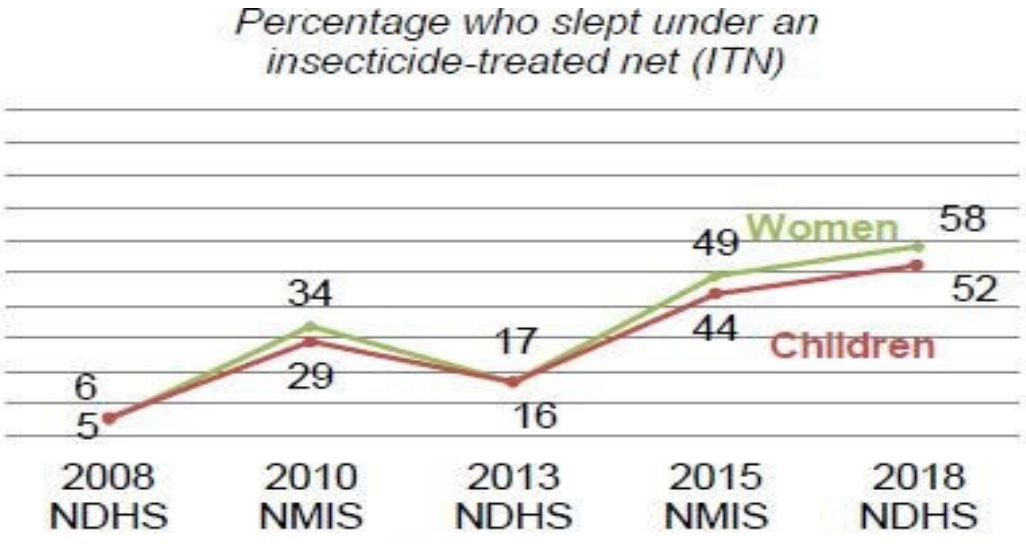
Introduction

Malaria remains a significant public health problem despite global control/elimination efforts. It contributed 5% of the estimated 5.9 million under-five deaths globally in 2015 and 14% of 750,000 under-five deaths in Nigeria. [1–3] These related deaths are preventable with specific prevention and prompt and effective management.[4 -10] For some time, malaria accounted for 60 % of outpatient visits to hospitals and led to approximately 30% child mortality, especially among children less than 5 years in Nigeria. [5, 9, 11-13] However, over the past 5 years, pneumonia has become the leading cause of childhood mortalities, and this may be possibly due to efforts in "rolling back malaria". [5, 14] Reduction of malaria morbidity/mortality was central to the attainment of Millennium Development Goal 6 (MDG-6)" Combat HIV/AIDS, malaria and other diseases". This target and several other efforts were made to achieve this goal. These efforts include the use of insecticide-treated mosquito nets by families, treatment of fever with appropriate antimalarial medicines, seasonal malaria chemoprevention for at-risk groups, having prompt and effective diagnosis, and use of artemisinin-based combination therapy to treat malaria. [4-7, 15 – 17]

Data from two Nigeria Malaria Indicator Surveys (NMIS) show ownership of at least one Insecticide Treated Net (ITN) in a household increased substantially from 8 percent nationally in 2010 to 69 percent in 2015, and a doubling of the average number of ITNs per household from 0.8 to 1.6%, fig. 1. There was also an increase in the total population that slept under ITNs from 23% to 37% within 5 years. [5, 18] Other modalities that have been implemented to reduce the malaria burden are specific case management using rapid diagnostic testing for malaria and administering artemisinin-based combination therapy medications. Several manpower training and information dissemination programmes have also spread appropriate and timely information and distribution of materials needed for the prevention and treatment of malaria, especially to the rural communities in Nigeria and other African countries. Indeed, the 2013 and 2018 Demographic and Health Surveys in Nigeria showed an increase in the ownership of at least one long-lasting insecticide-treated bed net from 48% to 61% with 65% of the de facto population in households with at least one ITN reported to have slept under an ITN the night before the survey. There was also a decrease in the prevalence of malaria among children since 2010, from 42% to 23%, and a high percentage (about 82% to 96%) of men and women surveyed in the 2018 DHS were reported to believe in the effectiveness of malaria medicine (NDHS 2013 and 2018). [2, 5, 19, 20]



Note: The definition of an ITN in surveys conducted prior to 2015 included nets that had been soaked with insecticides within the past 12 months.

Figure 1: Trends in sleeping under ITN from 2008-2018. Note the increase in ITN use by women and children from 2012 to 2018. Culled from: Nigeria Demographic and Health Survey 2018. Abuja, Nigeria, and Rockville, Maryland, USA. NPC and ICF. 2019

The improved application of malaria prevention and care-seeking practices is expected to reduce malaria mortalities in children, which are mainly due to severe anaemia, hypoglycaemia, cerebral malaria, and prostration. [5, 16, 21- 25] These complications are made worse when there are co-morbidities in the patients, like under nutrition, immune suppression, sickle cell anaemia and cancers, making it pertinent for these at-risk populations to take intermittent prophylactic therapies. Severe anaemia, defined by haemoglobin concentration < 5g/dl (in children <12 years) is common in the under-five age group with malaria if untreated, and many of these require blood transfusions. [6, 7, 15, 16] The 2018 NDHS showed that 4.8% of children aged 6-59 months in Rivers State had a haemoglobin level lower than 8g/dl compared to a national level of 8%.

During the period covered by this study, the Federal Government of Nigeria adopted the use of intravenous artesunate for severe malaria and the artemisinin-based combination therapy (ACT) for non-severe cases as against quinine and chloroquine treatment for malaria. The artesunate was initially procured but later both artesunate and ACT were provided free of charge with support from the Federal Government and the Clinton Health Assess Initiative (CHAI). [6, 7]In countries where access to free malarial testing and treatment are available to the citizens, there is an apparent reduction in morbidity and mortality from malaria. [6, 7]The aim of the study was to evaluate the impact of malaria control activities on the trend of childhood malarial diseases at a tertiary hospital in South-south Nigeria

Methodology

The study was a retrospective review of case notes, mortality reviews and other laboratory records of children aged 1 month to -16 years diagnosed with malaria and managed on outpatient or inpatient bases in the Department of Paediatrics, University of Port Harcourt Teaching Hospital. Hospital records from the children's outpatient clinic, consultant paediatric clinic, children's emergency wards, and in-patient wards were retrieved and recorded. Those with a clinical diagnosis of malaria, and /or laboratory confirmation from the paediatric side laboratory or the hospital main laboratory were included in the study. In the side laboratory and the hospital's main laboratory, thick and thin films were used, and in some cases, a quantitative buffy coat was employed. In early 2014, a rapid diagnostic test was used in the children's emergency room in conjunction with the previously mentioned test tools.

The case records of children who met the case definition for severe malaria according to the World Health Organisation, (WHO) were extracted and information was entered into the proforma. The case definitions for severe malaria necessitating admissions were; impaired consciousness (defined as Blantyre coma score (BCS) < 3) for children aged up to 4 years or Glasgow coma scale < 11 (for children aged 5 years and above); prostration (inability to breastfeed if aged < 9 months, or inability to sit unsupported if aged > 9 months), severe anaemia, packed cell volume< 15%, and hypoglycaemia as capillary blood glucose < 2.5 mmol/l using the Accu-Chek™ Active (Roche®diagnostics, Sydney, Australia; the precision of 0.1 mmol/l). Those who could be treated on an outpatient basis were given medications and reviewed within 2 days.
In the proforma, the data extracted from the records included the name, age, date of birth and date of presentation to the hospital, clinical features, diagnosis, malaria test (positive or negative), treatment received, duration of admission, additional diagnosis, and date of death. Other details were the weight and height, and the weight for age and height for age standard deviation score (SDS) using the WHO chart. Cases with incomplete data were excluded from the study.

Data analysis

From the data extracted, we calculated the incidence of uncomplicated malaria as complicated malaria subtracted from total malaria cases. The incidence of complicated malaria was calculated as complicated malaria divided by the total malaria cases/per year. The case fatality rate was calculated as mortality divided by the total malaria cases seen in the hospital. Proportions for categorical variables were compared using Chi-square or Fisher's Exact tests where appropriate. For continuous variables, Student's t-test was used to compare mean differences between groups where applicable. Significance was evaluated at $p < 0.05$ and analysis was done using Statistical Package for Social Sciences (SPSS) Version 20 (IBM, Texas, United States

Results

During the period under review, there were 41, 863 childhood malaria cases diagnosed using clinical features with blood film analyses in the department, giving a yearly average of 3, 220 (range 2, 534- 3, 893). Severe complicated malaria diagnosis was 5,427, incidence was 1.26%/ year (range 0.6 – 1.9) but total admissions were 529, with a yearly average of 40.7/ year, (range 28 – 58)., see figure 2 and table 1.

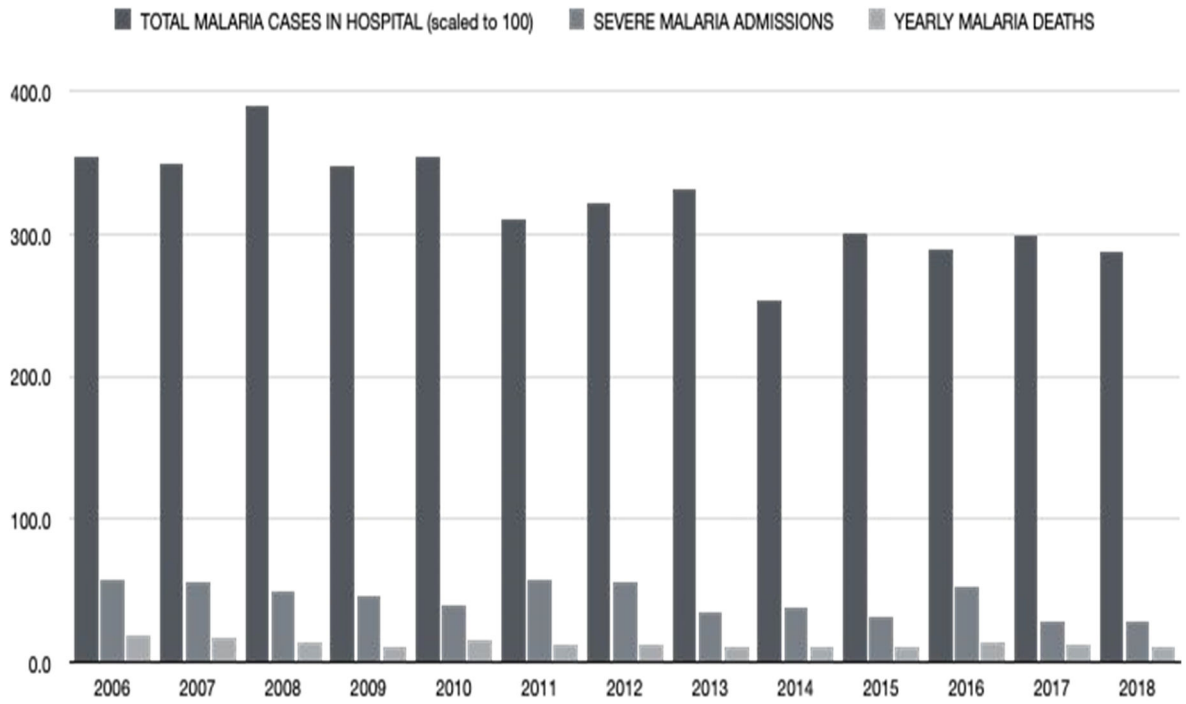


Figure 2: Malaria cases, admissions, and deaths in the University of Port Harcourt Teaching Hospital-2006-2018. Note that the total malaria cases are scaled to 100 from the absolute ʻthousand ′counts to fit into the graph.

Malaria morbidity and mortality

There were 164 malaria death cases, with yearly average of 12, and the highest number was recorded in 2006. The case-specific mortality rate for malaria was 0.39% or 3.9/ 1, 000 malaria diagnoses.

Table 1: Showing yearly distribution of malaria cases and case fatality rate

Year	Total malaria	Uncomplicated malaria	Complicated Malaria	Inpatient	mortality	Case fatality rate/1,000 cases of malaria
2006	3540	3145	395	58	18	5.1
2007	3489	2907	582	56	17	4.8
2008	3893	3521	372	19	13	3.3
2009	3472	3184	288	46	10	2.9
2010	3539	3082	457	40	15	4.2
2011	3100	2705	395	58	12	8.7
2012	3214	2632	582	56	12	3.7
2013	3321	2895	426	35	11	3.3
2014	2534	2372	169	0	10	3.9
2015	3008	2675	333	11	11	3.6
2016	2892	2427	465	13	13	4.4
2017	2982	2581	401	12	12	4.0
2018	2879	2310	569	10	10	3.5

Mortality from malaria peaked at 8.7/1,000 malaria diagnoses in the year 2011 and remained steady thereafter at an average of 3.5/ 1, 000 malaria cases.

The age and sex distributions of children with severe malaria, i.e. those admitted and those who died are shown in Table 2. The age range of children who were admitted for malaria was 6– 202 months (mean age 93.1 ± 55.0 months) and this was higher than the mean of those who died from malaria and its complications which was 6 – 133.8 months with a mean of 47.4±26.3 months. The difference in mean ages of those who died and those who were discharged from the hospital was significant, t = 19.25, p = < 0.001. The proportion of children with malaria, who died in the various age groups were 6 - 59 months 120 (73.2%), 5-10 years 40 (24.4%) and 10-18 years 4 (2.4%).

Although there were more male deaths, 89 (54.3%) than females 75 (45.7%), this difference was not significant (p = 0.310). The causes of death in the children with malaria parasitaemia were severe anaemia in 75 (45.7%), hypoglycaemia in 14 (8.5%), cerebral malaria in 17 (10.4%), and prostration 22 (13.4%). Thirty-six children (22%) came in convulsing and died soon after admission, with a compounding diagnosis of aspiration and respiratory failure, before any other laboratory tests could be performed.Of most deaths, 85% occurred within 24 hours of admission, with 4 (2.4%) children dying within 1 hour and without receiving medications and this did not change over the years.

Anthropometry of malarial morbidity and mortality

The weight of children who died from malaria ranged from 6.0 - 57.0 kg (mean 18.0 ±7.16 kg) and the mean was significantly lower than for the children who were successfully managed for malaria (t = 12.49, p <0.001). The mean height of children who died from malaria was also significantly lower than the mean height for the survivors. Nineteen children (11.6%) who died had acute severe malnutrition (WAZ < -2 SDS) and the remaining 88.4% had WAZ >- 2SDS, while 11 (6.7%) were stunted.

Table 2: Demographic and anthropometric characteristics of children with acute severe malaria and comparison between admitted cases and those that died.

	Malarial admissions 578	Malarial deaths 164	χ^2/t test	p value
Mean age (months)	93.1±55.0	47.4±26.3	10.45	<0.001*
Sex (M/F) %	31.4/37.8	16.7/14.1	3.5	0.058
Mean weight (kg)	34.44±16.64	18.01±7.16	12.49	<0.0001*
Weight for age Zscore	-0.21±6.64	0.36±1.54	1.79	0.1115
Mean height (cm)	132.47±25.26	100.11±16.44	15.13	<0.001*
Height for age Z score	-0.15±1.53	-0.10±1.36	0.514	0.732

Discussion

Efforts to reduce the malaria burden are yielding positive results as the total malaria diagnosis in this hospital decreased between 2006 and 2018 with a lower decline between 2013 and 2018. This is similar to reports from other countries in Africa, especially in West and East Africa. [2, 9, 13, 26 - 28]Though this report is later than that from the Gambia, [29, 30] other recent reports show an even more steady decline in malaria prevalence. The absolute average yearly malaria presentation was lower than that reported in Kenya[28] and the Gambia.[30] The decline in malaria prevalence in this report is also lower than that reported in the WHO World Malaria Report in 2016 which was 14%.[31] It is also noteworthy that the decrease in that report was a projection rather than actual numbers.

The decrease in malaria incidence in our hospital is possibly reflective of the increased availability and use of insecticide-treated mosquito nets, availability of antimalarial medications in informal settings or patent medicine stores and use of malarial prophylaxis by at-risk individuals in society. Sleeping under an insecticide-treated net reduces the rate of malarial transmission and thus the rate of infestation. [1–3]The increased availability of diagnostic testing for malaria in many laboratories [usually informal] outside the referral and tertiary hospitals also increased the treatment potentials and reduced hospital presentations. The fallout from this type of management style is the risk of antimalarial resistance development. This has been demonstrated in the study by Oyibo who reported that malaria parasite positivity was only present in about 18% of children who were treated for malaria according to IMCI protocol. [32] When rapid diagnostic testing was made available in late 2011 in Nigeria, the uptake was low and the objective to help in reducing malaria transmission and treatment were not immediately met. However, with time, the uptake gradually increased, and its availability improved. [16, 31, 33] This increased uptake may help reduce resistant strains of malarial parasites while improving the treatment and management process for children. The availability of antimalarial medications especially the artemisin in-based combination therapy has greatly reduced the number of patients presenting to hospitals for malaria treatment or with complicated malaria. [6 -8, 16] This availability has been made possible by efforts of various donor organisations and commitments of the Federal and State Governments, but their sustainability has been questioned.

Though the prevalence of severe forms of malaria has decreased as with overall malaria cases in our report and others, mortality from the severe forms is still occurring. [5, 9, 34, 35] The proportion of children aged less than 5 years with severe forms of malaria has remained the same and higher than the other age groups. [1–3, 5, 12] This was reported in a previous review by Yarhere et al[14]and in other studies carried out in Nigeria and Africa.[35 – 37]It is noteworthy that areas of high malarial transmissions have severe malaria predominating in the infants and younger children as seen in our study. Although deaths due to malaria have remained high despite efforts by stakeholders, there is evidence of their progressive decline in recent years. The deaths are attributed to complications which include severe anaemia with attending heart failure, multiple convulsions, hypoglycaemia, cerebral malaria, and acute renal failure. [5, 16, 22, 23, 38] A situation where almost half the mortality from malaria was due to anaemia is regrettable which means if severe anaemia is prevented or promptly treated, up to half the mortality from malaria will be prevented. The prevalence of severe anaemia in children hospitalized for malaria in this report is similar to the findings by Oladeinde, Edelu, and Mutombo. [22, 23, 25, 26] However, when compared to the number of children presenting to the hospital for malaria treatment, this prevalence is low, reflecting an improvement in the anaemia indices in Nigeria.
Co-morbidities associated with malarial deaths included acute malnutrition, sickle cell anaemia, HIV/AIDS and bacteraemia. [5, 37] Less than 15% of total malaria mortality had acute malnutritionand this was low and comparable to many reports reviewing malaria and. [5, 7, 40-43] The relative risk of dying from malaria in a severely malnourished child was estimated to be 57.3%.[40] However, the researchers used < -1SDS for WAZ to define malnutrition, and this may have been lower if the WAZ <- 2 SDS was used. While acute malnutrition significantly contributed to mortality due to malaria, stunting did not have that effect on malaria.[42-43] With acute malnutrition, there are many other co-morbidities including hypoglycaemia, bacterial and viral infections, hypothermia, and complex metabolic derangements. Controlling for these comorbidities may have reduced the mortality rates in these children with acute malnutrition that were

attributed to malaria. The same goes for HIV/AIDS and sickle cell anaemia, where these conditions independently have many comorbidities and increased susceptibility of patients to infections and metabolic derangements that can cause death without attributing this to malaria.

Conclusion

From our 13-year review, malaria morbidity and mortality are reducing possibly based on efforts and strategies put in place. The use of insecticide-treated bed nets, availability of antimalarial drugs, rapid diagnostic testing and various awareness campaign programmes may be yielding results. Children with under nutrition are more susceptible to malarial morbidity and mortality, so programmes aimed at improving the nutritional status of children can go a long way in ameliorating the effect of malaria.

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Conflict of Interest: The Authors declare no conflict of interest.

References

1. Afolabi BM, Sofola OT, Fatunmbi BS, Komakech W, Okoh F, Saliu O, et al. Household possession, use and non-use of treated or untreated mosquito nets in two ecologically diverse regions of Nigeria-Niger Delta and Sahel Savannah. *Malar J*. 2009; **8**:1-10
2. Berhe B, Mardu F, Legese H, Negash H. Seasonal distribution and seven-year trend of malaria in NorthWestTigrai: 2012-2018, Ethiopia; 2019. *Trop Dis Travel Med Vaccines.* 2019; **5**:1 -7
3. World Health Organization. World malaria report. Geneva. 2019. Assessed on January 20th, 2019. https://www.who.int/publications/i/item/9789241565721.
4. Adebayo AM, Akinyemi OO, Cadmus EO. Ownership and utilisation of insecticide-treated mosquito nets among caregivers of under-five children and pregnant women in a rural community in southwest Nigeria. *J Prev Med Hyg*. 2014; **55**:58-64.
5. Acosta A, Obi E, Ato Selby R, Ugot I, Lynch M, Marie M, et al. Design, Implementation, and Evaluation of a School Insecticide-Treated Net Distribution Program in Cross River State, Nigeria. *Glob Health Sci Pract.* 2018; **6**:272-287.
6. Morris A, Ward A, Moonen B, Sabot O, Cohen JM. Price subsidies increase the use of private sector ACTs: evidence from a systematic review. *Health Policy Plan*. 2015; **30**:397-405.
7. Dodo R, Zohoun A, Baglo T, Mehou J, Anani L. Emergency treatment of sickle cell diseases in the Blood Diseases Department at the Koutoukou Maga National Teaching Hospital, Cotonou, Benin. *Pan Afr Med J*. 2018, Jul 3; **30**:192.1-9
8. Korenromp E, Mahiané G, Hamilton M, Pretorius C, Cibulskis R, Lauer J, et al. Malaria intervention scale-up in Africa: effectiveness predictions for health programme planning tools, based on dynamic transmission modelling. *Malar J.* 2016; **15**:417.1-14
9. Adewemimo A, Kalter HD, Perin J, Koffi AK, Quinley J, Black RE. Direct estimates of cause-specific mortality fractions and rates of under-five deaths in the northern and southern regions of Nigeria by verbal autopsy interview. *PLoS One*. 2017; **12**:e0178129.
10. Korenromp E, Hamilton M, Sanders R, Mahiané G, Briët OJ, Smith T, et al. Impact of malaria interventions on child mortality in endemic African settings: comparison and alignment between LiST and Spectrum-Malaria model. *BMC Public Health*. 2017; **17**; 29-42
11. Murray CJ, Rosenfeld LC, Lim SS, Andrews KG, Foreman KJ, Haring D, et al. Global malaria mortality between 1980 and 2010: a systematic analysis. *Lancet*. 2012; **379**:413-431.
12. Bhutta ZA, Sommerfeld J, Lassi ZS, Salam RA, Das JK. Global burden, distribution, and interventions for infectious diseases of poverty. *Infect Dis Poverty*. 2014; **3**: 1-7

13. Thwing J, Eckert E, Dione DA, Tine R, Faye A, Yé Y, et al. Declines in Malaria Burden and All-Cause Child Mortality following increases in control interventions in Senegal, 2005-2010. *Am J Trop Med Hyg*. 2017; **97**:89-98.
14. Yarhere IE, Nte AR. A Ten-year review of all cause paediatric mortality in University of Port Harcourt Teaching Hospital, Nigeria (2006 - 2015). *Niger J Paediatr*. 2018; **45**:185 - 191.
15. Tobin-West CI, Kanu EN. Factors influencing the use of malaria prevention methods among women of reproductive age in peri-urban communities of Port Harcourt City, Nigeria. *Niger Postgrad Med J.* 2016; **23**:6-11.
16. Calis JC, Phiri KS, Faragher EB, Brabin BJ, Bates I, Cuevas LE, et al. Severe anemia in Malawian children. *Malawi Med J*. 2016; **28**:99-107.
17. Orji ML, Onyire NB, Chapp-Jumbo A, Anyanwu OU, Eke CB. Perception and utilization of insecticide-treated mosquito net among caregivers of children in Abakaliki, Nigeria. *Ann Afr Med.* 2018; **17**:172-177.
18. Morakinyo OM, Balogun FM, Fagbamigbe AF. Housing type and risk of malaria among under-five children in Nigeria: evidence from the malaria indicator survey. *Malar J*. 2018; **17**:311.
19. National Population Commission (NPC) Nigeria and ICF International. Nigeria Demographic and Health Survey 2013. Abuja, Nigeria, and Rockville, Maryland, USA. NPC and ICF International.
20. National Population Commission (NPC) Nigeria and ICF International. Nigeria Demographic and Health Survey 2018. Abuja, Nigeria, and Rockville, Maryland, USA. NPC and ICF International.
21. Wogu MN, Nduka FO. Evaluating Malaria prevalence using clinical diagnosis compared with microscopy and rapid diagnostic tests in a Tertiary Healthcare Facility in Rivers State, Nigeria. *J Trop Med*. 2018; 2018:3954717.
22. Oladeinde BH, Omoregie R, Osakue EO, Onaiwu TO. Asymptomatic Malaria among Blood Donors in Benin City Nigeria. *Iran J Parasitol*. 2014; **9**:415-422.
23. Oladeinde B, Omoregie R, Olley M, Anunibe J, Onifade A, Oladeinde O. Malaria and anemia among children in a low resource setting In Nigeria. *Iran J Parasitol*. 2012; **7**:31-37.
24. Manning L, Laman M, Davis WA, Davis TM. Clinical features and outcome in children with severe Plasmodium falciparum malaria: a meta-analysis. *PLoS One*. 2014; **9**:e86737.
25. Edelu BO, Ndu IK, Igbokwe OO, Iloh ON. Severe falciparum malaria in children in Enugu, South East Nigeria. *Niger J Clin Pract*. 2018; **21**:1349-1355.
26. Mutombo AM, Mukuku O, Tshibanda KN, Swana EK, Mukomema E, Ngwej DT, et al. Severe malaria and death risk factors among children under 5 years at Jason Sendwe Hospital in Democratic Republic of Congo. *Pan AfrMed J*. 2018; **29**:184. [doi: 10.11604/pamj.2018.29.184.15235]
27. Kamau A, Mtanje G, Mataza C,Mwambingu G, Mturi N, Mohammed S, et al. Malaria infection, disease and mortality among children and adults on the coast of Kenya. *Malar J*. 2020; **19**:210. https://doi.org/10.1186/s12936-020-03286-6
28. Arzika AM, Maliki R, Boubacar N, Kane S, Cook CA, Lebas E, et al. Malaria Parasitemia and Nutritional Status during the Low Transmission Season in the Presence of Azithromycin Distribution among Preschool Children in Niger. *Am J Trop Med Hyg*. 2020; **103**:1315-1318.
29. Rowe AK. Analysis of deaths with an unknown cause in epidemiologic analyses of mortality burden. *Trop Med Int Health*. 2006; **11**:540-550.
30. Binka F, Akweongo P. Prevention of malaria using ITNs: potential for achieving the millennium development goals. *Curr Mol Med*. 2006; **6**:261-267.
31. Herlihy JM, D′Acremont V, Hay Burgess DC, Hamer DH. Diagnosis and Treatment of the Febrile Child. In: Black RE, Laxminarayan R, Temmerman M, Walker N, (Editors). Reproductive, Maternal, Newborn, and Child Health: Disease Control Priorities, Third Edition (Volume 2). Washington (DC): The International Bank for Reconstruction and Development / The World Bank; 2016.
32. Oyibo WA, Ezeigwe N, Ntadom G, Oladosu OO, Rainwater-Loveth K, O'Meara W, et al. Multicenter Pivotal Clinical Trial of Urine Malaria Test for Rapid Diagnosis of Plasmodium falciparum Malaria. *J Clin Microbiol*. 2017; **55**:253-263.

33. Visser T, Bruxvoort K, Maloney K, Leslie T, Barat LM, Allan R, et al. Introducing malaria rapid diagnostic tests in private medicine retail outlets: A systematic literature review. *PLoS One*. 2017; **12**:e0173093.
34. Ndugwa RP, Ramroth H, Müller O, Jesseh M, Sié A, Kouyate B, et al. Comparison of all-cause and malaria-specific mortality from two West African countries with different malaria transmission patterns. *Malar J.* 2008; **7**. https://doi.org/10.1186/1475-2875-7-15
35. Desai M, Buff AM, Khagayi S, Byass P, Amek N, van Eijk A, et al. Age-specific malaria mortality rates in the KEMRI/CDC health and demographic surveillance system in western Kenya, 2003-2010. *PLoS One.* 2014; **9**:e106197.
36. Dhingra N, Jha P, Sharma VP, Cohen AA, Jotkar RM, Rodriguez PS, et al. Adult and child malaria mortality in India: a nationally representative mortality survey. *Lancet*. 2010; **376**:1768-1774.
37. Olofin I, McDonald CM, Ezzati M, Black RE, Fawzi WW, Caulfield LE, et al. Associations of suboptimal growth with all-cause and cause-specific mortality in children under five years: a pooled analysis of ten prospective studies. *PLoS One*. 2013; **8**:e64636.
38. Abdalla SI, Malik EM, Ali KM. The burden of malaria in Sudan: incidence, mortality and disability-adjusted life-years. *Malar J.* 2007; **6**:97. https://doi.org/10.1186/1475-2875-6-97
39. Dondorp AM, Fanello CI, Hendriksen IC, Gomes E, Seni A, Chhaganlal KD, et al. Artesunate versus quinine in the treatment of severe falciparum malaria in African children (AQUAMAT): an open-label, randomised trial. *Lancet*. 2010; **376**:1647-1657.′
40. Caulfield LE, Richard SA, Black RE. Undernutrition as an underlying cause of malaria morbidity and mortality in children less than five years old. *Am J Trop Med Hyg*. 2004; **71**:55-63.
41. Caulfield LE, de Onis M, Blössner M, Black RE. Undernutrition as an underlying cause of child deaths associated with diarrhea, pneumonia, malaria, and measles. *Am J Clin Nutr*. 2004; **80**:193-198.
42. Ferreira E, Alexandre MA, Salinas JL, de Siqueira AM, Benzecry SG, de LacerdaMVG, et al. Association between anthropometry-based nutritional status and malaria: a systematic review of observational studies. *Malar J.* 2015; **14**:346.
43. Oldenburg CE, Guerin PJ, Berthé F, Grais RF, Isanaka S. Malaria and nutritional status among children with severe acute malnutrition in Niger: A Prospective Cohort Study. *Clin Infect Dis*. 2018; **67**:1027-1034.