Factors associated with severe malaria among children below ten years in Mutasa and Nyanga districts, Zimbabwe, 2014-2015

Faith Mutsigiri-Murewanhema1, Patron Trish Mafaune2, Gerald Shambira1, Tsitsi Juru1*, Donewell Bangure1, More Mungati1, Notion Tafara Gombe1, Mufuta Tshimanga1

1Department of Community Medicine, University of Zimbabwe, Harare, Zimbabwe, 2Ministry of Health and Child Care, Manicaland Province, Zimbabwe

*Corresponding author: Tsitsi Juru, Department of Community Medicine, University of Zimbabwe, Harare, Zimbabwe

Key words: Severe malaria, risk factors, Mutasa, Nyanga, Zimbabwe

Received: 13/10/2016 - Accepted: 01/05/2017 - Published: 10/05/2017

Abstract

Introduction: Severe malaria is a rare life threatening illness. Only a small proportion of patients with clinical malaria progress to this medical emergency. On reviewing 61 malaria death investigation forms submitted to the provincial office in 2014, 22(36%) were children below ten years who succumbed to severe malaria. Mutasa and Nyanga Districts reported 73% of these deaths. This study was conducted to determine factors associated with severe malaria so as to come up with evidence based interventions to prevent severe malaria and associated mortality.

Methods: A 1:2 unmatched case control study was conducted. A case was defined as a child 10 years and below, who was admitted at Hauna (Mutasa) or Nyanga District Hospitals between September 2014 and May 2015 with a primary diagnosis of severe malaria. Controls were children of similar age with uncomplicated malaria. Permission to conduct the study was sought and granted by the Medical Research Council of Zimbabwe (Approval number B/874), Joint Research Ethics Committee, Health Studies Office and the Manicaland Directorate Institutional Review Board. Written informed consent was sought from all caregivers of enrolled children. Interviewer administered questionnaires were used to ascertain exposures.

Results: A total of 52 cases and 104 controls were enrolled into the study. The median age of cases was 4 years (Q1=3, Q3=9) and 6 years for controls (Q1=3, Q3=8). The Case Fatality Rate among cases was 28.8%. The independent risk factors for severe malaria were; distance >10km to the nearest health facility [Adjusted Odds Ratio (aOR)=14.35, 95% CI=1.30, 158.81], duration of symptoms before seeking medical care >2 days [aOR=9.03, 95% CI=2.21, 36.93], having comorbidities [aOR=5.38, 95% CI=1.90, 15.19], staying in a house under construction [aOR=4.51, 95%CI=1.80, 11.32] and duration of illness before receiving antimalarial medicines >24 hours [aOR=3.82, 95% CI=1.44, 10.12]. Owning at least one ITN in the household [aOR=0.32, 95% CI=0.11, 0.95] and having a mother as a caregiver [aOR=0.23, 95% CI=0.09, 0.76] were independently protective of severe malaria. Being undernourished [Odds Ratio (OR)=10.13, 95% CI=1.04, 98.49] and being female [OR=0.27, 95% CI=0.08, 0.96] were associated with mortality owing to severe malaria. Conclusion: Factors associated with severe malaria and mortality owing to severe malaria identified in this study are consistent with other studies. Caregiver healthcare seeking behaviours, patient related factors and health system related factors are important determinants of severe malaria among children. There is need for regular health education campaigns emphasizing on malaria prevention, signs and symptoms and benefits of seeking medical care immediately for sick children.

Pan African Medical Journal. 2017; 27:23 doi:10.11604/pamj.2017.27.23.10957

This article is available online at: http://www.panafrican-med-journal.com/content/article/27/23/full/

© Faith Mutsigiri-Murewanhema et al. The Pan African Medical Journal - ISSN 1937-8688. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/2.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.
Introduction

Malaria is among the world's commonest and life threatening tropical diseases. Malaria is caused by Plasmodium parasites which are transmitted through the female Anopheles mosquito's bite which occurs mainly between dusk and dawn [1]. In humans, malaria is caused by 4 parasites namely; Plasmodium falciparum, Plasmodium vivax, Plasmodium malariae and Plasmodium ovale. P. falciparum and P. vivax are the commonest [1], however, P. falciparum remains the single most important threat to public health at a global scale since it is the most deadly. It accounts for more than 90% of the world's malaria mortality [2]. Malaria is endemic in most tropical regions and about 3.4 billion people worldwide are exposed to malaria annually and 1.2 billion are at high risk [1]. Although preventable and curable, malaria causes significant morbidity and mortality especially in regions with limited resources [3]. An estimated 300-500 million people suffer from malaria every year and 1.5-2.7 million deaths occur [4,5]. Sub-Saharan Africa is the most affected region [3] contributing over 80% of global malaria deaths [6]. Although half of the world's population is at risk of malaria, and whilst anyone living or visiting a malaria endemic area may be at risk, vulnerability is higher in certain groups, particularly pregnant women and children. Malaria is a leading cause of death among children less than 5 years, who represent 77% of all global malaria deaths [7,8]. In Africa a child dies every minute from malaria [1]. Children are mostly affected because their immune systems are not yet fully developed to fight severe forms of disease [7,8]. Pregnant women have a reduced immunity hence they have increased risk of infection with malaria, severe disease and ultimately increased risk of death [9,10].

Malaria remains one of the top three causes of child mortality in sub-Saharan Africa, including Zimbabwe. It is a major public health problem in Zimbabwe with almost half of the population at risk. Approximately 1 in 12 children in Zimbabwe die before their 5th birthday due to malaria [11], this translates to 84 deaths per 1000 live births [12]. Plasmodium falciparum accounts for 97% of cases seen in health facilities in Zimbabwe [13]. If not treated within 24 hours, P. falciparum malaria can progress into fatal severe illness [1]. Early malaria diagnosis and treatment reduces disease, prevents deaths and can contribute to the reduction of malaria transmission. Mild cases of malaria are easily treatable with complete recovery using relatively inexpensive and widely available first line drugs. However, treatment is complicated and expensive for severe malaria. Mortality is also higher among children who present with severe malaria than among those with mild/ uncomplicated disease. On reviewing 61 malaria death investigation forms submitted to the provincial office in 2014, it was noted that 22(36%) were children below ten years who succumbed to severe malaria and of these, 14(64%) were under-fives. Mutasa and Nyanga Districts contributed the majority of these deaths with 16 of the 22 deaths (73%) reported from these two districts. Malaria morbidity and mortality remains high despite scaling up of the implementation of malaria control interventions by the national malaria control programme in the country. A major question of concern is why only a small proportion of infected individuals progress to severe and life-threatening illness. The objective of this study was to assess the factors associated with severe malaria among children below ten years.

Methods

An unmatched 1:2 case control study was conducted in Mutasa and Nyanga Districts, Manicaland Province, Zimbabwe. A case control study design was chosen because severe malaria is a rare disease and study participants were recruited on the basis of the disease status. The study design enabled determination of multiple exposures for a single outcome at once.

Study Setting: The study was conducted in health facilities and communities in Mutasa and Nyanga Districts of Manicaland Province.

Study Population: The study population were children under-ten years diagnosed of simple malaria and severe malaria between September 2014 and May 2015, their parents/caregivers and medical records.

Working definitions: For the purposes of this study, cases and controls were defined as follows;

Case: A child 10 years and below who was admitted at Hauna (Mutasa) or Nyanga District Hospitals in Manicaland Province between September 2014 and May 2015 with a primary diagnosis of severe malaria (defined by the presence of microscopy detected P. falciparum parasites together with at least one of the following features: convulsions before/during admission, severe anaemia (haemoglobin <5g/dl), cerebral malaria (impaired consciousness), prostration and/or respiratory distress (deep breathing and/or chest in drawing).

Control: A child 10 years and below who had uncomplicated malaria, defined by the presence of a fever (axillary temperature >37.5°C) and a positive Rapid Diagnostic Test result for malaria parasites, but without any features of severe malaria between September 2014 and May 2015, and also residing in the same area with a case.

Inclusion criteria: Child below 10 years with a primary diagnosis of WHO-defined severe malaria and was admitted at Hauna or Nyanga District Hospitals. (Cases); exclusion of other common known causes of any of the manifestations of severe malaria e.g meningitis. (Cases); child below 10 years with simple malaria diagnosed at a health facility which serves the areas where cases came from,(Controls); a patient who was resident in Mutasa or Nyanga District as confirmed by the patient's usual address recorded in the hospital records. During follow up of study participants to their homesteads, their parents/guardians also confirmed the residence status; informed consent was obtained from the child's caregiver for inclusion in the study.

Exclusion criteria: A patient who was visiting Mutasa or Nyanga District as confirmed by the patient's usual address recorded in the hospital records; a child whose caretaker denied to consent for participation in the study.

Sample size determination: Sample size was calculated using the Stat Calc function of Epi info version 7, using a confidence level of 95% and power of 80%. Based on a study by Imani et al “Human immunodeficiency virus infection and cerebral malaria in children in Uganda: a case-control study,” assumptions were that age under-five years (0-59 months) was a significant risk factor for severe malaria (Odds Ratio of 2.47). The prevalence of exposure among controls was 37.2% [14]. Based on this information, to conduct a 1:2 unmatched case control study the required minimum sample size was 65 cases and 130 controls.

Sampling procedure

Sampling of cases: A sampling frame of all children who had severe malaria and were hospitalized at Hauna and Nyanga District hospitals in Manicaland Province between September 2014 and May 2015 was developed. All the 52 children who had severe malaria
and satisfied the inclusion criteria after reviewing medical records were enrolled into the study. The children were traced to their homes using addresses on the patients' admission notes and their caregivers were interviewed.

**Sampling of controls:** Following recruitment of each case, two controls who resided in the same area with a case were recruited. Systematic sampling was used to randomly select controls from children who were attended for simple malaria at a health facility that serves the area where a case resided from September 2014 to May 2015. The clinic's daily attendance register was the sampling frame for controls. Selection of controls was limited to those who resided in the same area with a case. Children who were chosen to participate in the study were then traced to their homes using addresses in the admission and outpatient registers and their caregivers were interviewed.

**Permission to conduct study and ethical considerations:** Permission to conduct the study was sought from the Manicaland Provincial Medical Directorate Institutional Review Board, District Medical Officers for Mutasa and Nyanga and the Health Studies Office. Clearance to conduct the study was obtained from the Joint Research Ethics Committee (JREC) and the Medical Research Council of Zimbabwe (Approval number B/674). The aim of the study was explained to all the parents/guardians of potential study participants and all were assured that they were free to withdraw from the study at any time and no penalty would be imposed on them or their child if they decided to do so. Informed written consent was sought from caregivers of enrolled children. Confidentiality was assured and maintained throughout the study. Caregivers of children selected to participate in the study answered the questions. In the event that the child was deceased the caregivers were told to be prepared for emotional disturbance before the interview and those who required professional counselling were referred.

**Data collection:** Pretested interviewer administered questionnaires were used to collect data on socio-demographic characteristics, household related factors, patient related factors, health system related factors and caregiver healthcare seeking behaviour factors. Patients' medical records at the health facility were also reviewed to assess eligibility for participation in the study. Parents/caregivers of cases and controls were interviewed in the community.

**Data analysis:** Data were analysed using Epi info version 3.5.3 to calculate frequencies, proportions and means. The same statistical package was used to calculate measures of association and their 95% confidence intervals. Stepwise forward logistic regression was done for all variables that were significantly associated with severe malaria at the p=0.25 level on bivariate analysis to determine the independent factors associated with severe malaria.

**Results**

A total of 52 cases and 104 controls were enrolled into the study. The majority of both cases and controls were female; 55.8% and 52.9% respectively. The highest proportion of controls, (58.7%), were aged above five years old, whilst the majority of cases, 51.9%, were aged 5 and below. The median age of cases was 4 years (Q1=1; Q3=9) and 6 years (Q1=3; Q3=8) for controls. Fifty-one (98.1%) cases and 100 (96.2%) controls resided in rural areas. The majority of the cases, 35 (67.3%) presented with convulsions. The least common manifestation of severe malaria was severe anaemia, only 1 (1.9%) case presented with it. The Case Fatality Rate among cases was 28.8%. Table 1 summarizes the factors associated with severe malaria among children below ten years in Mutasa and Nyanga Districts. Caregiver factors associated with severe malaria among children were; having at least secondary education [Odds ratio (OR) =0.73, 95% CI=0.37, 1.43] being the mother of the child [OR=0.41, 95% CI=0.18, 0.91] and female caregiver [OR=0.36, 95% CI=0.07,1.66]. Environmental factors that were significantly associated with severe malaria were; staying in house under construction [OR=3.89, 95% CI=1.927.88>7.88], staying in a house with open eaves or poorly covered windows [OR=2.09, 95% CI=1.06, 4.12], stagnant water within 10 meters from household [2.08, 95% CI=1.01, 4.28] and having received IRS 12 months preceding child's illness [OR=0.39, 95% CI=0-20, 0.77]. Household related factors that were significantly protective of severe malaria were; sleeping under mosquito net net every night [ OR=0.33, 95% CI=0.16, 0.70] and owning at least one ITN in the household [OR=0.23, 95% CI=0.10, 0.51]. Patient related factors associated with severe malaria were; HIV positive status [OR=4.69 95% CI=1.73, 12.60], having comorbidities [OR=3.44, 95% CI=1.59, 7.44], undernutrition [OR=3.40, 95% CI=31.24, 9.34] and history of malaria illness [ OR=0.48, 95% CI=0.24, 0.96]. Health system factors that were significantly associated with severe malaria among children were; distance between home and nearest health facility >10km [OR=10.96, 95% CI=1.25, 96.41], delayed diagnosis [OR=5.24, 95% CI=1.29, 21.18] and having received antimalarial medications at initial visit to a health facility [OR=0.19, 95% CI=0.05, 0.77].

Children who were managed by a VHW were 1.53 times more likely to have severe malaria than those who were not. However this finding was not statistically significant [95% CI=0.74, 3.20]. Caregiver healthcare seeking behaviors that were significantly associated with severe malaria were; duration of child's symptoms before seeking medical care >2 days [OR=14.30, 95% CI=4.57, 45.36], duration of illness before child received antimalarial >24hrs [OR=0.59, 95% CI=0.27, <11.68] medication at home >24hrs [OR=0.35> administering medication at home before seeking medical care [OR=3.55, 95% CI=1.69, 7.43] and first action taken when child got sick was seeking medical care [OR=0.28, 95% CI=0.13, 0.58]. Of the 52 children with severe malaria, 15 died and 37 recovered. A sub-analysis was done to determine factors associated with mortality due to severe malaria. Table 2 summarizes the factors that were associated with mortality due to severe malaria among children below ten years in Mutasa and Nyanga Districts. The patient related factors that were associated with mortality were; undernutrition [OR=10.13, 95% CI=1.04-98.49], age <5 years [OR=2.35, 95% CI=0.67, 8.24] and HIV positive status [OR=1.22, 95% CI=0.22, 6.73]. Caregiver healthcare seeking behaviour factors that were associated with mortality due to severe malaria were; duration of child's symptoms before seeking medical care >2 days [OR=2.70, 95% CI=0.79, 9.29] and first action taken was seeking medical care [OR=0.45, 95% CI=0.13, 1.55] though not statistically significant. The independent risk factors for severe malaria were; distance >10km to the nearest health facility [Adjusted Odds Ratio (aOR)=14.35, 95% CI=13.0, 158.81], duration of symptoms before seeking medical care >2 days [aOR=9.03, 95% CI=2.21, 36.93], having comorbidities [OR=5.38, 95% CI=1.90, 15.19], staying in a house under construction [aOR=4.51, 1.80, 11.32] and duration of illness before receiving antimalarial medicines >24 hours [aOR=3.82, 95% CI=1.44,10.12]. Owning at least one ITN in the household [95% CI=0.11, 0.95] and having a mother as a caregiver [aOR=0.23, 95% CI=0.09, 0.76] were independent protective factors for severe malaria Table 3.

**Discussion**
Distance of more than 10km to the nearest health facility was an independent risk factor for severe malaria. Time spend travelling to a health facility was an independent risk factor for severe malaria. The decision to seek treatment early for malaria and therefore result in delayed diagnosis and treatment as caregivers opt for initial treatment at home. In a study by Malik et al in 2006 in Sudan, the choice of treatment for sick children among caregivers was highly dependent on accessibility and availability of health facilities [15]. Most people in rural areas live further away from health facilities. To address the issue of long distances between communities and health facilities which may result in delayed diagnosis and treatment, Zimbabwe introduced community case management of malaria by Village Health Workers (VHWs) in 2012. VHWs were introduced to bring essential health services closer to the people, hence they should have adequate malaria commodities at all times if their existence is to make a difference. Duration of symptoms before seeking medical care for the sick child of more than 2 days was an independent risk factor for severe malaria. Duration of illness >24 hours before receiving antimalarial medicines and delayed diagnosis were also significantly associated with severe malaria in children. This was consistent with findings in a study by Byakika-Kibewa et al (2009) in Uganda [16]. Malaria is an emergency because of its capability to progress to severe, fatal illness if not treated appropriately and promptly [17]. Quite a number of children die because of malaria within 24-72 hours of onset of symptoms [18]. Timeous diagnosis and treatment is therefore crucial to prevent progression of disease to severe form and ultimately lower mortality. Presumptive treatment with antimalarial medicines of all fevers in children who live in malaria endemic areas is the main strategy for reducing malaria related child morbidity and mortality [19].

Having comorbidities was found to be independently associated with severe malaria. Similar findings were reported in several studies [20-22]. Co-infection with plasmodium parasites and HIV infection is of importance. HIV infection and was found to be a risk factor for severe malaria. Infection with HIV suppresses the immune system hence increases the individual’s susceptibility to many other infections. HIV infection also decreases response to antimalarial medicines, thereby increasing the burden of the diseases [14]. Similar findings were also reported in studies in Kenya, Uganda and South Africa were HIV infection was found to be associated with severe malaria in children [14, 23-25]. Staying in a house under construction was an independent risk factor for severe malaria among cases in this study. A partially complete house with windows or a roof or with other openings may facilitate frequent and repeated exposure to parasite infected mosquitoes because mosquitoes gain access to the inside of the house through these openings thereby exposing the habitants to infective bites. Complete and good house construction is a barrier to malaria transmission because it limits access of mosquitoes to the household. Sir et al (2010) reported similar findings in Kenya, however the results were not significant on multivariate analysis [26]. Owning at least one ITN in the household was an independent protective factor against severe malaria. Sleeping under a mosquito net every night was also significantly protective of severe malaria. Bed net use offers personal protection from getting mosquito bites. Widespread ITN use has been seen to reduce malaria morbidity and mortality in Kenya and Nigeria [27, 28]. Having a mother as a caregiver was independently protective of severe malaria. Mothers tend to seek care immediately for their sick children and they pay particular attention to their children’s needs. It therefore makes it easier for a mother to notice that their child is not feeling well. In rural settings most mothers are not employed, they spend most of their time at home if not treating appropriately and promptly a child, hence children are most likely to tell their mother if they are not feeling well and the mother takes prompt action thereby decreasing chances of disease progression to severe form. Since child care is normally done by mothers, we suspect that having a caregiver who was not the mother may mean that the child is orphaned and this may lead to late identification of signs of disease and late presentation to health facilities for medical care.

Under-nutrition was a significant risk factor for severe malaria and associated with mortality in children. In a study by Caulfield et al in 2004, improved nutritional status was seen to reduce malaria related deaths because it lessens the severity of malaria episodes [29]. Undernutrition reduces functionality of all systems of the body. This has great consequences especially in young children [29]. Underweight children have increased susceptibility to malaria through impairment in the function of the immune system. Undernourished children may be incapable to mount appropriate immune response to parasites causing malaria because of reduced T-lymphocytes, impairment of antibody formulation and atrophy of the thymus and other lymphocyte tissues [30]. History of malaria illness prior to the recent illness was significantly associated with reduced odds of severe malaria. Similarly, in a study by Phillips history of malaria was seen to be protective of developing severe disease, probably through acquired immunity [31]. Related findings suggest acquiring some form of protection following at least one infection [32]. The CFR was high in this study. This can be attributed to the fact that the majority of the cases, were from rural areas. It has been noted that about 50% of those who develop severe malaria especially in remote areas die. This is because health services are faraway and are not well equipped to manage complications caused by the diseases [33, 34]. The CFR was higher (28.8%) compared to that in a study in Ghana by Mockenhaupt et al in 2004 (11.2%) [35]. In this study the high CFR can be attributed to convulsions which was the commonest manifestation of severe malaria among cases in this study. The CFR of severe malaria is dependent on the predominant manifestations that also have implications on the treatment [35].

Limitations: The required minimum sample size was not achieved because most children who were admitted with a diagnosis of severe malaria did not suit the WHO case definition. The study sample came from a population who sought treatment at the health facilities, therefore the findings from this study cannot be generalized regarding the health care seeking behaviours of every caregiver. There was a possibility of recall bias because some cases and controls risk recruited months after their illness. The study may also have been prone to under-reporting and over-reporting especially of healthcare seeking behaviours of caregivers because it was partly based on self-reporting. Retrospective record review may risk misclassification of cases and controls.

Conclusion

Severe malaria was characterized by a high proportion of convulsions and the CFR was high in this study. The factors associated with severe malaria and mortality due to severe malaria was identified. There is need for prompt treatment with antimalarial medicines of all high risk patients like undernourished children and those infected with HIV to avoid further progression of disease to severe form. There is need for stronger program linkages e.g. Malaria, HIV and Nutrition. There is need for training of health workers on manifestations of severe malaria to avoid over diagnosis. Scaling up community health education and promotion campaigns emphasizing on consistent and correct use of preventive strategies like ITNs is essential. A Prospective study is necessary to address some of the limitations of this study.
What is known about this topic

- Malaria due to plasmodium falciparum is the third leading cause of mortality among children in Zimbabwe;
- Approximately 1 in 12 children in Zimbabwe die before their 5th birthday due to malaria;
- Mortality and complications due to malaria can be prevented by early seeking of appropriate health care.

What this study adds

- This study corroborates findings from previous studies that the following are risk factors for severe malaria in children; HIV coinfection, undernutrition and delay in seeking medical care;
- There is need to integrate malaria, HIV and Nutrition programs in order to minimize complications associated with comorbidities of these diseases;
- Having a mother as the primary caregiver is protective of severe malaria.

Competing interests

The author declare no competing interest.

Authors’ contributions

Faith Mutsigiri-Murewanhema designed the study protocol, collected data, analysed data and wrote the manuscript. Patron Trish Mafaune assisted in designing the study protocol and manuscript writing. Gerald Shambira assisted with technical guidance during the designing of the study protocol, analysis of data and manuscript writing. Tsitsi Juru, Donewell Bangure, Notion Tafara Gombe and Mufuta Tshimanga helped with technical guidance throughout the study up to the writing of the manuscript. The manuscript was read and approved by all authors.

Acknowledgments

We wish to express our sincere gratitude to the University of Zimbabwe (UZ) Department of Community Medicine academic and non-academic staff for the unwavering support and guidance they provided to us throughout the conduct of this study. Our gratitude also goes to the Health Studies Office (HSO), Centres for Disease Control and Prevention, Zimbabwe (CDC) and Manicaland Provincial Health Executive for their unwavering support. Many thanks go to all the study participants who consented to participate in the study. Lastly, we would like to thank our families for their support throughout the implementation of the project.

Tables

Table 1: Factors associated with severe malaria among children below ten years, Mutasa and Nyanga districts, Zimbabwe, 2014-2015

Table 2: Factors associated with mortality due to severe malaria among children below ten years, Mutasa and Nyanga districts, Zimbabwe, 2014-2015

Table 3: Independent factors associated with severe malaria among children below ten years, Mutasa and Nyanga districts, Zimbabwe, 2014-2015

References

1. WHO. World Malaria Report 2014. Geneva, Switzerland Available on (Accessed on March 03, 2015). Google Scholar

2. Snow RW, Gilles HM. The epidemiology of malaria. Essential malariology. 2002;4:85-106. Google Scholar

3. Centres for Disease Control and Prevention. Malaria. (Accessed on March 03, 2015). PubMed | Google Scholar

4. Muettener P, Schlagenhauf P, Steffen R. Imported malaria (1985-95): trends and perspectives. Bull World Health Organ. 1999; 77: 560-566. PubMed | Google Scholar

5. Sachs J, Malaney P. The economic and social burden of malaria. Nature. 2002; 415: 680-685. PubMed | Google Scholar

6. Murray C J, Rosenfeld L C, Lim S S, Andrews K G, Forement K J, Haring D, Fullman N, Naghavi M, Lopez A D. Global malaria mortality between 1980 & 2010: a systematic analysis. Lancet. 2012; 379:413. PubMed | Google Scholar

7. World Health Organisation. World Malaria Report 2013. Geneva, Switzerland. Accessed (March 05, 2015). PubMed | Google Scholar

8. Tanner M, de Savigny D. Malaria Eradication Back on the Table. Bull World Health Organ. 2008; 86(2): 82. PubMed | Google Scholar

9. Dellicour S, Tatem A J, Guerra CA, Snow RW, ter Kuile FO. Quantifying the Number of Pregnancies at Risk of Malaria in 2007: A Demographic Study. PLoS Med. 2010 Jan 26;7(1):e1000221. PubMed | Google Scholar

10. WHO. Malaria in Pregnancy. (Accessed on March 03, 2015). PubMed | Google Scholar

11. Zimbabwe National Statistics Agency and ICF. Zimbabwe Demographic and Health Survey 2010-2012 Zimbabwe National Statistics Agency and ICF. March 2012. PubMed | Google Scholar

12. Ministry of Health and Child Care. Malaria. Indicator Survey. 2012. PubMed | Google Scholar

13. Taylor P. The Malaria Problem in Zimbabwe epidemiology. Central African Journal of Medicine. 1985 Sep; 31(9): 163-6. PubMed | Google Scholar

14. Imani PD, Musoke P, Byarugaba J, Twumwike JK. Human immunodeficiency virus infection and cerebral malaria in children in Uganda: a case-control study. BMC Pediatrics. 2011; 11: 5. PubMed | Google Scholar
15. Malik EM, Hanafi K, Ali SH, Ahmed ES, Mohamed KA, Malar J. Treatment-seeking behaviour for malaria in children under-five years of age: Implication for home management in rural areas with high seasonal transmission in Sudan. Malaria Journal. 2006; 5: 60. PubMed | Google Scholar

16. Byakika-Kibwika P, Ndezei G, Kamya MR. Health care related factors associated with severe malaria in children in Kampala, Uganda. Afr Health Sci. 2009 Sep; 9(3): 206-210. PubMed | Google Scholar

17. Trampuz A, Jereb M, Muzlovic I, Prabhu RM. Clinical Review: Severe Malaria. Critical Care. 2003; 7: 315-323. PubMed | Google Scholar

18. Ilohe GUP, Ofoedu JN, Njoku PU, Amadi AN, Godswill-Uko EU. The magnitude of under-five emergencies in a resource-poor environment of a rural hospital in Eastern, Nigeria: Implications for strengthening the house-hold and community-integrated management of childhood illnesses. North Am J Med Sci. 2012; 4: 344-349. PubMed | Google Scholar

19. Olaleye BO, Williams LA, D’Alessandro U. Clinical predictors of malaria in Gambian children with fever or history of fever. Trans R Soc Trop Med Hyg.1998; 92: 300-304. PubMed | Google Scholar

20. Bruneel F, Hoquetouls L, Alberti C, Wolff M, Chevret S, Bédos JP, Durand R, Le Bras J, Régnier B, Vachon F. The clinical spectrum of severe imported falciparum malaria in the ICU: Report of 188 cases in adults. Am J Respir Crit Care Med. 2003; 167: 684-689. PubMed | Google Scholar

21. Blumberg L, Lee RP, Lipman J, Beards S. Predictors of mortality in severe malaria: a two year experience in a non-endemic area. Anaesth Intensive Care. 1996; 24: 217-223. PubMed | Google Scholar

22. Schwartz E, Sadetzki S, Murad H, Raveh D. Age as a risk factor for severe Plasmodium falciparum malaria in nonimmune patients. Clin Infect Dis. 2001; 33: 1774-1777. PubMed | Google Scholar

23. Grimwade K, French N, Mbathá DD, Zungu DD, Dedicoat M, Gilks CF. HIV infection as a cofactor for severe falciparum malaria in adults living in a region of unstable malaria transmission in South Africa. AIDS. 2004; 18(3): 547-54. PubMed | Google Scholar

24. Grimwade K, French N, Mbathá DD, Zungu DD, Dedicoat M, Gilks CF. Childhood malaria in a region of unstable transmission and high human immunodeficiency virus prevalence. Pediatr Infect Dis J. 2003; 22(12): 1057-63. PubMed | Google Scholar

25. Berkley J, Bejon P, Mwangi T, Gwer S, Maitland K, Williams T et al. HIV infection, malnutrition, and invasive bacterial infection among children with severe malaria. Clin Infect Dis. 2009;49(3): 336-43. PubMed | Google Scholar

26. Siri JG, Wilson ML, Murray S, Rosen DH, Vulule JM, Slutsker L, Lindblade KA. Significance of Travel to Rural Areas as a Risk Factor for Malarial Anaemia in an Urban Setting. Am J Trop Med Hyg. 2010; 82(3): 391-397. PubMed | Google Scholar

27. Hawley W A, Terkuile F O, Steketeet R S. Implications of the western Kenya permethrin-treated bed net study for policy, program implementation and future research. Am J Trop Med Hyg. 2003;68(4):168-17. PubMed | Google Scholar

28. Nwankwo B O, Okafor J O. Effectiveness of insecticide treated bednets in malaria prevention among children aged 6 months to 5 years in a rural community in Ifo state, Nigeria. International Journal of Tropical Medicine. 2009; 4(1): 41-49. PubMed | Google Scholar

29. Caulfield LE, Richard SA, Black RE. Under nutrition as an underlying cause of malaria morbidity and mortality in children less than five years old. Am J Trop Med Hyg. 2004 Aug; 71(2): 55-63. PubMed | Google Scholar

30. Scrimshaw NS, San Giovanni JP. Synergism of nutrition, infection, and immunity: an overview. Am J Clin Nutr. 1997;66:477S-477S. PubMed | Google Scholar

31. Phillips A, Bassett P, Szeki S, Newman S, Pasvol G. Risk Factors for Severe Disease in Adults with Falciparum Malaria. Clin Infect Dis. 2009; 48(7): 871-878. PubMed | Google Scholar

32. Gupta S, Snow RW, Donnelly CA, Marsh K, Newbold C. Immunity to non-cerebral severe malaria is acquired after one or two infections. Nat Med. 1999; 5: 340-3. PubMed | Google Scholar

33. Marsh K. Malaria-a neglected disease. Parasitology. 1992;104:S53-S69. PubMed | Google Scholar

34. Greenwood BM, Bradley AK, Greenwood AM, Byass P, Jamme K, Marsh K, Tulloch S, Oldfield FSJ, Hayes R. Mortality and morbidity from malaria among children in a rural area of the Gambia, West Africa. Trans R Soc Trop Med Hyg.1987;81:478-486. PubMed | Google Scholar

35. Mockenhaupt FP, Erhardt S, Burkhardt J, Bosomtwe SY, Laryea S, Anemana SD et al. Manifestation And Outcome Of Severe Malaria In Children In Northern Ghana. Am J Trop Med Hyg. 2004; 71(2): 167-172. PubMed | Google Scholar
Table 1: factors associated with severe malaria among children below ten years, Mutasa and Nyanga districts, Zimbabwe, 2014-2015

| Variable                                      | Cases n (%)  | Controls n (%) | OR (95% CI)     | p-value |
|----------------------------------------------|--------------|----------------|-----------------|---------|
| At least secondary education                 | 28(53.8)     | 64(61.5)       | 0.73 (0.37-1.43)| 0.36    |
| Being mother of the child                    | 36(69.2)     | 88(84.6)       | 0.41 (0.18-0.91)| 0.02    |
| Female caregiver                             | 48(92.3)     | 101(97.1)      | 0.36 (0.07-1.66)| 0.17    |
| Staying in a house under construction        | 35(67.3)     | 36(34.6)       | 3.89 (1.92-7.88)| <0.01  |
| Staying in a house with open eaves or poorly covered windows | 31(59.6) | 43(41.3) | 2.09 (1.06-4.12) | 0.03 |
| Stagnant water within 10 meters from household | 20(38.5) | 24(33.6) | 2.08 (1.01-4.28) | 0.04 |
| Received IRS 12 months preceding child's illness | 22(42.3) | 68(65.4) | 0.39 (0.20-0.77) | 0.01 |
| Own at least 1 ITN in household              | 32(61.5)     | 91(87.5)       | 0.23 (0.10-0.51)| <0.01  |
| Child sleeps/slept under mosquito net every night | 13(25.0) | 52(50.0) | 0.33 (0.16-0.70) | <0.01 |
| Positive HIV status                          | 16(53.3)     | 10(19.6)       | 4.69 (1.73-12.69)| <0.01  |
| Having comorbidities                         | 20(38.5)     | 16(33.3)       | 3.44 (1.59-7.44)| <0.01  |
| Under nutrition                              | 17(54.8)     | 6(18.2)        | 3.40 (1.24-9.34)| 0.02    |
| History of malaria illness                   | 20(38.5)     | 59(56.7)       | 0.48 (0.24-0.96)| 0.04    |
| Distance between home and the nearest health facility >10km | 5(9.6) | 1(1.0) | 10.96 (1.25-96.41) | <0.01 |
| Delayed diagnosis                            | 7(13.5)      | 3(2.9)         | 5.24 (1.29-21.18)| 0.01    |
| Child managed by a VHW                       | 17(32.7)     | 25(49.0)       | 1.53 (0.74-3.20)| 0.35    |
| Received antimalarial at initial visit to a health facility | 45(86.5) | 101(97.1) | 0.19 (0.05-0.77) | 0.01 |
| Duration of symptoms before seeking medical care >2 days | 19(36.5) | 4(3.8) | 14.30(4.57-45.36) | <0.01 |
| Duration of illness before child received antimalarial >24hrs | 38(73.1) | 34(65.4) | 5.59 (2.67-11.68) | <0.01 |
| Administered medication at home before seeking medical care | 23(44.2) | 19(38.5) | 3.55 (1.69-7.43) | <0.01 |
| First action taken when child got sick was seeking medical care | 28(53.8) | 84(80.8) | 0.28 (0.13-0.58) | <0.01 |
### Table 2: factors associated with mortality due to severe malaria among children below ten years, Mutasa and Nyanga districts, 2014-2015

| Variable                                      | Category | Died n (%) | Recovered n (%) | OR(95%CI)          | p-value |
|-----------------------------------------------|----------|------------|-----------------|--------------------|---------|
| Child undernourished                          | Yes      | 9(90.0)    | 8(47.1)         | 10.13(1.04-98.49)  | 0.03    |
|                                               | No       | 1(10.0)    | 9(52.9)         |                    |         |
| Delayed Diagnosis                             | Yes      | 3(20.0)    | 4(10.8)         | 2.75(0.49-15.53)   | 0.24    |
|                                               | No       | 12(80.0)   | 33(89.2)        |                    |         |
| Duration of child’s symptoms before seeking medical care >2 days | Yes | 8(53.3) | 11(29.7) | 2.70(0.79-9.29) | 0.11 |
|                                               | No       | 7(46.7)    | 26(70.3)        |                    |         |
| Age <5 years                                  | Yes      | 10(66.7)   | 17(45.9)        | 2.35(0.67-8.24)    | 0.18    |
|                                               | No       | 5(33.3)    | 20(54.1)        |                    |         |
| HIV Status                                    | Positive | 4(57.1)    | 12(52.2)        | 1.22(0.22-6.73)    | 0.82    |
|                                               | Negative | 3(42.9)    | 11(47.8)        |                    |         |
| Having comorbidities                          | Yes      | 6(40.0)    | 14(37.8)        | 1.10(0.32-3.74)    | 0.89    |
|                                               | No       | 9(60.0)    | 23(62.2)        |                    |         |
| First action taken was seeking medical care    | Yes      | 6(40.0)    | 22(59.5)        | 0.45(0.13-1.55)    | 0.20    |
|                                               | No       | 9(60.0)    | 15(40.5)        |                    |         |
| Sex                                           | Female   | 5(33.3)    | 24(64.9)        | 0.27(0.08-0.96)    | 0.04    |
|                                               | Male     | 10(66.7)   | 13(35.1)        |                    |         |

### Table 3: independent factors associated with severe malaria among children below ten years, Mutasa and Nyanga districts, 2014-2015

| Variable                                      | AOR     | 95%CI       | Coefficient | p-value |
|-----------------------------------------------|---------|-------------|-------------|---------|
| Distance between home and nearest health facility >10km | 14.35   | 1.30-158.81 | 2.66        | 0.03    |
| Duration of child’s symptoms before seeking medical care >2 days | 9.03 | 2.21-36.93 | 2.20 | <0.01 |
| Having comorbidities                         | 5.38    | 1.90-15.19  | 1.68        | <0.01   |
| Staying in a house under construction        | 4.51    | 1.80-11.32  | 1.51        | <0.01   |
| Duration of illness before child received antimalarial >24hrs | 3.82 | 1.44-10.12 | 1.34 | <0.01 |
| Own at least 1 ITN                           | 0.32    | 0.11-0.95   | -1.14       | 0.04    |
| Having mother as a caregiver                 | 0.23    | 0.09-0.76   | -1.36       | 0.01    |
| Constant                                     | +       | +           | -1.15       | 0.12    |