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Research Article

Manifestations of Severe Malaria among the Under-five Children Attending Kampala International University Teaching Hospital, Bushenyi, Western Uganda: Pilot Study

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Abstract: The clinical spectrum of severe malaria has not been described in Bushenyi, hence; this study was carried out to document the prevalence, major clinical features, contributing factors and immediate outcome of this number one killer disease of under-five children, at Kampala International University Teaching Hospital (KIUTH). This is a pilot study. Study design was retrospective; carried out in the records department of KIUTH; the study population were files of children, 5 years of age and below who attended KIUTH between August and October 2009, sample size was 100 using systematic random sampling. Ethical clearance and permission were obtained. Data was collected using checklist, entered into Epi-Info version 3.2 and analysed with SPSS 16 statistical software. Prevalence of complicated malaria was 29.8%. Male: female ratio was 1.33:1. Peak age was 3years, 78% of the children had no wasting and 62% slept under treated bed nets. The three most common presentations were febrile multiple convulsions (69%), hyperparasitemia (67%) and circulatory shock (59%), prolonged coma was the least presentation (30%). The infants most commonly present with severe anaemia (60%), while the older ones manifest usually with febrile multiple convulsions (76.9%). Mortality rate was 14%, higher in the malnourished (27.3%), boys (19.3%), age 5year bracket (23.1%), with hypoglycaemia (18.8%), respiratory distress (17.9%) and multiple febrile convulsions (17.4%). The prevalence and mortality from severe malaria was high. The most common presentations were multiple febrile convulsions, hyperparasitaemia and circulatory shock. Immediate outcome was significantly affected by the nutritional status. A larger study will be done in future for a more complete picture of this problem.

Keywords: Bushenyi, KIUTH, manifestations, severe malaria, under fives, Uganda

INTRODUCTION

Malaria is endemic in 95% of Uganda. The remaining 5%, areas in the highlands of the southwest and east, are epidemic-prone. (Talisuna, 1999; Idro, 2001) According to a recent report from the World Health Organization, Uganda has the world's highest malaria incidence, with a rate of 478 cases per 1000 population per year (Idro, 2001; Namboze, 1997; National Malaria Control Policy Formulation Task Force, 1997).

In Uganda, malaria accounts for the highest disease burden in the country and is the leading cause of under-five morbidity and mortality (Idro, 2001). Malaria is responsible for 25 to 40% of all outpatient visits, 20-25% of all hospital admissions and about 14% of all hospital deaths ((Idro, 2001; Namboze, 1997; National Malaria Control Policy Formulation Task Force, 1997; Ministry of Health, 2000). These percentages have increased even with improved anti-malarial use and remain a serious illness requiring hospitalization (Namboze, 1997; National Malaria Control Policy Formulation Task Force, 1997). In 2009, according to WHO statistics, only 10% of our under-fives sleep under mosquito nets (Ministry of Health, 2008).

In highly endemic areas, most cases of severe malaria occur among children of age's 1-3 years except cerebral malaria which is less common in infancy but is mostly seen after one year of age (Idro, 2001).

The life threatening manifestation of malaria (complicated/severe malaria), is defined as the detection of p falciparum in the peripheral blood, in the presence of any of the clinical or laboratory features (singly or in combination) listed below (Idro, 2001):

- Prostration (inability or difficulty to sit upright, stand or walk without support in a child normally

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able to do so, or inability to drink in children too young to sit)
- Alteration in the level of consciousness (ranging from drowsiness to deep coma)
- Cerebral malaria (unarousable coma not attributable to any other cause in a patient with falciparum malaria)
- Respiratory distress (acidotic breathing)
- Multiple generalized convulsions (2 or more episodes within a 24 h period)
- Circulatory collapse (shock, septicaemia)
- Pulmonary edema
- Abnormal bleeding (Disseminated Intravascular Coagulopathy)
- Jaundice
- Haemoglobinuria (black water fever)
- Acute renal failure-presenting as oliguria or anuria.
- Severe anaemia (Hb <5g/dl or Hct<15%)
- Hypoglycaemia (blood glucose level<2.2.mmol/l)
- Hyperparasiteamia (parasitaemia of >200,000/μL- in high transmission area, or, 100,000/μL in low transmission area)
- Hyperlactataemia

Of these manifestations, prostration, followed by severe anaemia was by far the most common manifestation of severe malaria in all age groups in several studies in Uganda (Idro, 2001; Idro *et al*., 2005). The two most common causes of death from severe P.falciparum infection are severe anaemia and cerebral malaria (Idro, 2001). Severe anaemia tends to occur in a younger age group compared to cerebral malaria. Cerebral malaria (which is the most severe form) is less common in infancy but is mostly seen after 1year of age (Idro, 2001). Among children presenting to the acute care unit of Mulago National Referral Hospital of Makerere University with severe malaria, cerebral malaria accounted for 29.2% (Idro, 2001). In Jos (Nigeria), cerebral malaria accounted for about 17.6% of all clinical complications of severe malaria (Idro, 2001; Angyo *et al*., 1996). In spite of treatment, mortality rates of 5-30% from cerebral malaria, have been recorded from various studies in Uganda and neurological sequelae occurs in 1.5-29% of the survivors (Idro, 2001; World Health Organization, 2000). Approximately 7% of children, with complicated malaria are left with permanent neurological problems (Idro, 2001). These include spasticity, blindness, speech problems, learning difficulties and epilepsy (Idro, 2001; Meremikwa *et al*., 1997).

In the first two months of life, children may not contract malaria or the manifestations may be mild with low-grade parasitemia, due to the passive immunity offered by the maternal antibodies and retarded growth of the parasites in old erythrocytes containing Haemoglobin F (Idro, 2001; Chiabi *et al*., 2009). In endemic and hyperendemic areas, the parasite rate increases with age from 0 to 10% during first three months of life to 80 to 90% by one year of age and the rate persists at a high level during early childhood (Idro, 2001). The mortality rate is highest during the first two years of life (Idro, 2001). By school age, a considerable degree of immunity would have developed and asymptomatic parasitemia can be as high as 75% in primary school children (Idro, 2001). Hence, congenital malaria and Neonatal malaria are very rare, in spite of significant maternal parasitemia and sequestration of the parasites in the placenta (Idro, 2001).

Malnutrition does not increase susceptibility to severe falciparum malaria. In fact, it has been observed that well-nourished children are more likely to develop severe disease than those with malnutrition. However, when severe malaria does occur, malnourished children have a higher morbidity and mortality (Idro, 2001).

Children with heterozygous sickle cell trait have lower parasite rates and less fatal infections compared to normal children (however, homozygous sickle cell disease does not protect against fatal infection, Idro, 2001). By observation, SCD is not a common condition, in Bushenyi.

The proportion of households with at least one net has doubled between 2000 and 2004 increasing from 13.2% to 25.9% (Idro, 2001; Ministry of Health, 2008; Chiabi *et al*., 2009; Kemble *et al*., 2006; Eliades *et al*., 2006; Eriksen *et al*., 2007; Mbonye *et al*., 2008; Kleinschmidt *et al*., 2007) and mechanisms are put in place to allow a rapid increase of net distribution in the future.

There is no published documentation on the presentation of severe malaria in Bushenyi and yet the knowledge of the manner of presentation of this problem, is important for planning, prompt and appropriate diagnosis and treatment, assessment of clinical problems that require further research, prevention of further complications, saving cost and the reduction of disease burden in the population. Hence, this study was carried out to describe the major clinical manifestations of severe malaria, among the under-fives that attend Kampala International University Teaching Hospital, Bushenyi.

Objectives:
- To determine the prevalence of complicated malaria in children five years and below attending KIUTH
- To determine the most common presentations of complicated malaria in children five years and below attending KIUTH
- To assess the correlation between the socio demographic data and complicated malaria
- To evaluate the outcome of complicated malaria after management.

METHODOLOGY

The study site was the Records Department of Kampala International University Teaching Hospital (KIUTH). Approval from the Institution Ethical Committee was obtained and permission was granted

by the Head of the Records Department. KIUTH is located in a rural area (Ishaka) in Bushenyi district of South-western Uganda. Bushenyi is one of the largest districts in Uganda, about 71 km from Mbarara Town, an area of medium to high endemicity for malaria transmission and often called the 'food basket' of the country. Most cases of malaria occur in lowland areas that have stable, high malaria transmission, like Bushenyi. The population (mainly Myankole by tribe) of Bushenyi Town is about 35,286 and their major occupation is farming (mainly on subsistence level) and the major health problem in the community is malaria. The hospital acts both as a primary care centre and receives referral patients from the surrounding health units. Most of the population the hospital serves are of low socioeconomic status mainly comprising of peasant farmers, casual labourers and small scale businessmen.

KIUTH is a very new (about 38months old) government-private health facility of about 1,500 bed spaces, dedicated to the teaching of various levels of health professionals and providing health care services. Our paediatric range is from birth to the age of 12years. The average number of paediatric visit per month is between 150-200, at least 90% of which comprises of children below the age of 5years. Most of these children come from families of low social class mainly the peasant farmers, the casual labourers and orphans who come to seek free treatment provided by KIUTH.

This was a retrospective study involving the records of all the children aged 5years and below that consecutively attended KIUTH between August and October 2009. These months were chosen because they are relatively dry seasons compared to the rest of the year and hence patient visit is likely to be at its peak in the hospital. Using the formula by Kish (1965), the sample size calculated was 100. There was a total of 766 attendances, from the registers (both in-and out-patients) over this period of 3 months and out of these, 228 files had a discharging diagnosis of severe malaria. Thirteen files had incomplete information and were excluded from the severe malaria collections. The remaining 215 files satisfied WHO criteria for severe malaria, by the presence of one or more of the life-threatening signs of severe malaria and laboratory evidence of p.falciparum infection. The laboratory diagnosis was by microscopy, which is the gold standard for confirming malaria. These 215 files were numbered according to the date and time of hospital visit, from the beginning of the study period and this was used as the sampling frame. The final selection of the study population was by systematic random sampling, with sampling interval of 2. The first study case on the first day of the study period was picked and subsequently, every other file was recruited until the sample size of 100 was reached. From the final selection of severe malaria files, the patients' data including the age (to the nearest year), gender, body weight (to the nearest kilogram), parent's occupation and discharge status were extracted using a data form. Their nutritional status was classified into: no wasting (≥80% of reference weight for age), some wasting (60-≤80% of reference weight for age) and severe wasting (≤60% of reference weight for age). The data was entered into the EPI Info version 3.2.2 and subjected to analysis using SPSS version 16. The results were presented in form of tables, charts and figures. The significance between the variables was determined using Chi-square and p-value less than 0.05 was considered significant.

RESULTS

This was a review of 100 cases of severe malaria in children, 5years of age and below, who attended KIUTH over a period of 3months, between August and October 2009. A total of 766 children attended KIUTH during the study period and out of these, 228 were complicated malaria cases.

The prevalence for severe malaria was 228 out of 766 (29.8%). The majority of the children were between 1-3years of age (20%, 22% and 26% respectively), Table 1. The boys outnumbered the girls in the ratio, 1.33:1 (57%:43%). None of the children was severely wasted and the majority had no wasting (78%), Table 1. The majority were discharged alive (86%), while the mortality rate was 14%, Table 1. Sixty-two percent of the children had the privilege of sleeping under insecticide-treated mosquito net, 30% do not sleep under mosquito net and 8% have non-treated or damaged mosquito nets, Table 1. Only 16% of the children had mothers, who were civil servants, 46% had self employed mothers and 38% mothers were unemployed, Table 1. The three most common clinical

Table 1: Characteristics of the under-five children with severe malaria

Age (years)	1 20(20%)	2 22(22%)	3 26(26%)	4 19(19%)	5 13(13%)
Gender	Male 57(57%)	Female 43(43%)			
Wasting	No wasting 78(78%)	Some wasting 22(22%)	Severe wasting 0(0%)		
Use of preventive measures	Yes 62(62%)	No 30(30%)	Not treated net/ Damaged 8(8%)		
Discharge status	Alive 86(86%)	Diseased 14(14%)			
Mother's Occupation	Self-employed 46(46%)	Unemployed 38(38%)	Civil servant 16(16%)		

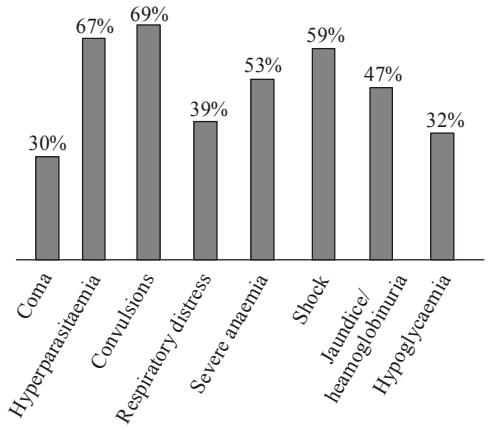

Fig. 1: Clinical presentation of sever malaria

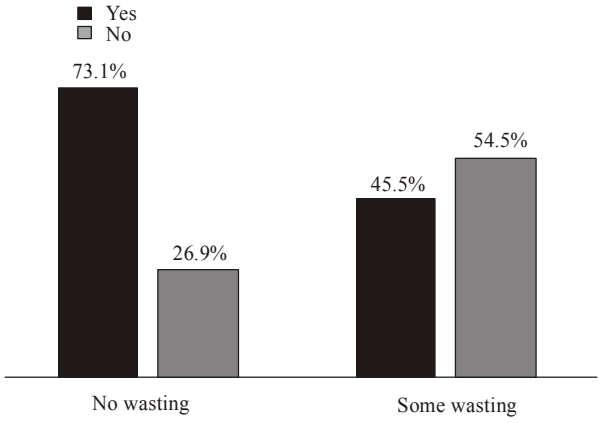

Fig. 2: Nutritional status and hyperparasitaemia. P.val-0.015

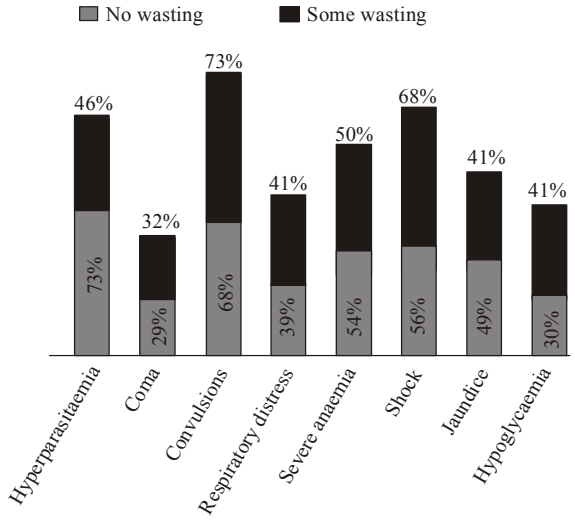

Fig. 3: Nutritional status and manifestations of sever malaria

presentation of severe malaria were multiple febrile convulsions (69%), hyperparasitaemia (67%) and circulatory shock (59%). The least common presentation was coma (30%), Fig. 1. Jaundice occurred

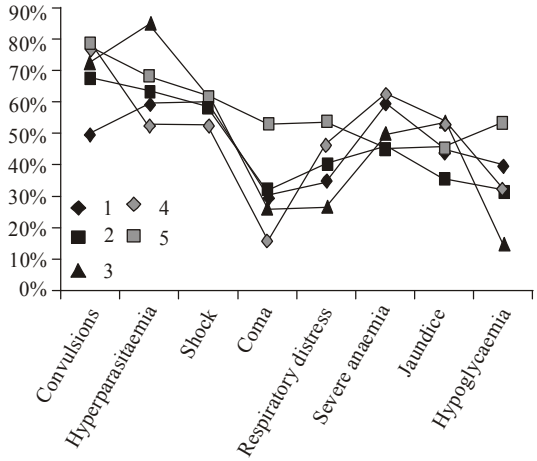

Fig. 4: Age and manifestations of sever malaria

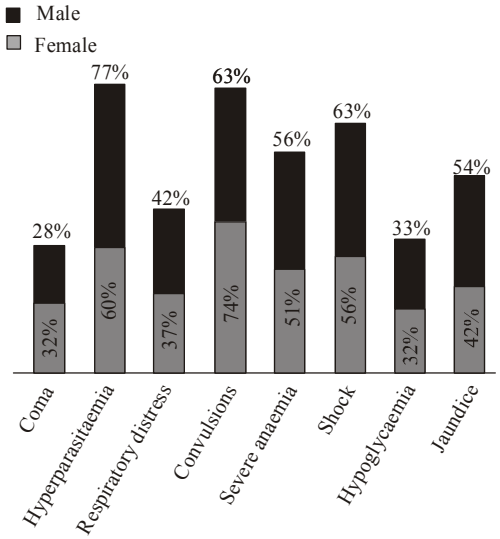

Fig. 5: Gender and manifestations of sever malaria

in 47% and respiratory distress was seen in 39% of the children. The majority of the children with no wasting had hyperparasitaemia (57/78, 73.1%), while the majority of those with some wasting had no hyperparasitaemia (12/22, 54.5%). The p.value was 0.015 and the Odds ratio was 3.257. Hence, the children with no wasting were 3.257 times more likely to develop hyperparasitaemia, than those with some wasting, Fig. 2. The children with some wasting presented mostly with convulsions (73%), Fig. 3. The infants presented mostly with severe anaemia (60%), those within the 2years old bracket and the preschool age group of 4 and 5years of age presented most commonly with convulsions (68.2%, 78.9% and 76.9% respectively) and the toddlers-3years old presented most frequently with hyperparasitaemia (84.6%), Fig. 4. Coma was seen most commonly among the 5 years old (53.8%, Fig. 4) and in boys (32% versus 28% for their female counterparts), Fig. 5. The boys presented

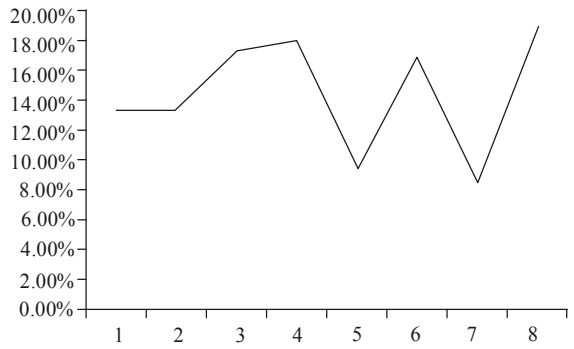

Fig. 6: Manifestations of sever malaria and case fatality rate 1: coma; 2: hyperparasitaemia; 3: multiple febrile onvulsions; 4: respiratory distress; 5: severe anaemia; 6: circulatory hock' 7: jaundice; 8: hypoglycaemia

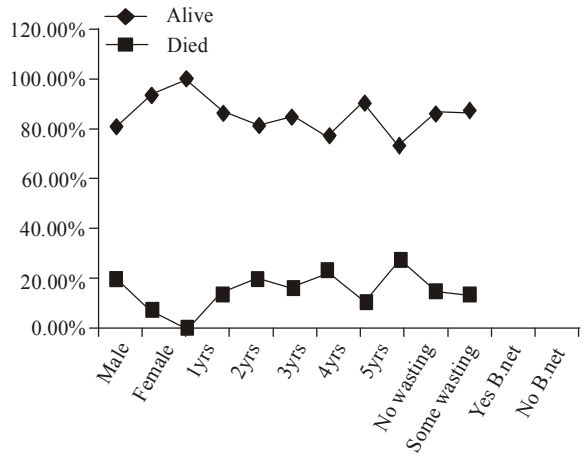

Fig. 7: Discharge status and gender, age nutritional state and use of bed net

mostcommonly with convulsions (74%), while the girls presented mostly with hyperparasitaemia (77%), Fig. 5. Mortality was highest amongst the children who presented with hypoglycaemia (6/32, 18.8%), followed by those with respiratory distress (7/39, 17.9%) and multiple febrile convulsions (12/69, 17.4%), Fig. 6. The best prognosis was amongst those who presented with jaundice (43/47, 91.5%). The fatality rate in cases with prolonged coma was 4/30, 13.3%, Fig. 6. There was a very significant relationship between the nutritional status of the patient and the discharge status with p.value of 0.042. The children with no wasting were 3.281 times (Odds ratio) more likely to be discharged alive than those with some wasting. Mortality was higher in the males than their female counterparts (19.3% versus 7%), age group of 5years (23.1%) compared to other age group, those with some wasting than those with no wasting (27.3% versus 10.3%) and slightly higher amongst those who sleep under insecticide treated bed nets than those who do not (14.5% versus 13.2%). Survival rate was highest amongst the infants (100%), Fig. 7.

DISCUSSION

This retrospective study was undertaken to determine the prevalence, clinical pattern and outcome among under-five children diagnosed with severe malaria over a period of 3 months (August to October 2009) in Kampala International University Teaching Hospital, Uganda. One hundred cases were reviewed out of a total of 228 files of severe malaria. There were 766 paediatric attendances during the study period. All the patients diagnosed with severe malaria were managed in the paediatric ward of KIUTH. The choice of under-fives as the participants for this study was because, 90% of the children who attend KIUTH were below 5years and also this is the most frequently presenting age group with severe malaria in the lowland areas of Uganda (Idro *et al*., 2005), where malaria endemicity is high and stable, as documented by many studies. In the highland areas of Uganda, where malaria transmission is unstable and epidemics occur, severe malaria often occurs in persons older than 5 years of age (Idro *et al*., 2005). The most frequently presenting age group in this study was between 1year to 3years (20-26%, peak age was 3years), consistent with Chiabi *et al*. (2009) findings, but in contrast to ages 0-8 years seen in the highland area (Idro *et al*., 2005). In this study, there was no child below the age of 6months, which is similar to the WHO's suggestion that, in parts of the world where endemicity of falciparum malaria is stable, severe malaria is mainly a disease of children from the first few months of life to the age of 5 years, because of acquisition of partial immunity (Idro, 2001; Chiabi *et al*., 2009). Late presentation could also account for this.

The prevalence of severe malaria at 29.8% in this study, is high, in comparison to the reported frequencies of 20-25% by the Uganda Ministry of Health (unpublished), 29.2% in Yaoundé Specialist hospital by Chiabi *et al*. (2009), 27% in eastern and mid-western parts of Uganda by Achan *et al*. (2011), 25% in Jos, Nigeria by Angyo *et al*. (1996) and 21% in Sudan by Zeidan *et al*., 2005. This higher rate could be because of a higher index of suspicion of attending doctors and the relatively dry season during which the study was carried out, just after the planting, wet months. The boys outnumber the girls by ratio, 1.3:1, consistent with Chiabi *et al*. (2009), report of 1.09:1 and Mulago study-1.22:1 (Idro, 2001). This may be explained by the fact that boys, being more active than their female counterparts are more likely to be exposed and bitten by mosquitoes and also the presence of double X-chromosomes in the female is protective against many diseases including malaria. None of our children was

severely wasted and the majority were well nourished (78%, similar to Mulago study, Idro, 2001) and sleep under mosquito net (62%). The observation that the well nourished children are more susceptible to severe malaria than those who are severely malnourished due to the presence of sufficient amount of nutrient PABA, which promote the growth and multiplication of malaria parasites in the well nourished child, might explain this (Chongsuphajaisiddhi, 1991). Also, the well nourished children usually come from families that can afford to purchase and use mosquito nets, hence they are usually protected and their immune system has not learned to fight off malaria effectively and prevent the life-threatening complications (Chongsuphajaisiddhi, 1991). This can be further supported by the fact that a larger proportion of the well nourished children compared to the malnourished ones (49/78-62.8% vs. 13/22-59.1%) and the boys compared to the girls (36/57-63.2% vs. 26/43-60.5%) in this study sleep under treated insecticide mosquito net. However, this idea is weakened by the fact that the majority of the children sleeping under treated mosquito nets in this study, were outside the peak ages of severe malaria (4years-68.4%, 5years-69.2% vs. 3years-53.8%, 2years-59.1% and 1year-65%). Also, the major users of mosquito nets were the unemployed-71.1% and the majority of the well nourished children in this study came from a larger proportion of mothers who were self-employed (82.6%) and unemployed (76.3%). Surprisingly, use of bed nets in this study is relatively high (70/100-70%), of which only 8/70-11.4% were untreated, compared to many African studies, with a range of 5 - 61% of which less than 20% were insecticide-treated, in fact 16% was documented in Younde Specialist Hospital (Idro, 2001; Ministry of Health, 2008; Chiabi *et al*., 2009; Kemble *et al*., 2006; Eliades *et al*., 2006; Eriksen *et al*., 2007; Mbonye *et al*., 2008; Kleinschmidt *et al*., 2007). This is mainly from the action programmes initiated by the Ministry of Health against malaria. When the malnourished child develops severe malaria, the mortality is usually higher with them than in the well nourished children which are exactly what we found in this study, where the majority of the children discharged alive were in the no-wasting group (89.7% versus 72.7%). The mortality rate in this study was high at 14%, in comparison to 1.7% (Kabale hospital, SW highland area of Uganda, Idro *et al*., 2005), 3.2% Jos, Nigeria, (Angyo *et al*., 1996), 11.2% in Northern Ghana (Mockenhaupt *et al*., 2004), however it is similar to reviews from other studies that reported 15-20% (Chiabi *et al*., 2009). This may be attributed to late presentation, poor management, lack of treatment facilities and delay in initiating treatment.

The specific clinical manifestations were age-related and are likely due to multiple factors, including differential parasite organ sequestration in younger children as compared with older children, low levels of complement regulatory proteins leading to increased red cell destruction and inadequate reticulocyte production in young children and possibly the need for exposure to specific strains in cerebral malaria (Idro, 2001; Chiabi *et al*., 2009). Febrile convulsions (69%), hyperparasitaemia (67%) and circulatory shock (59%) were the most common presentations overall, while the least was coma (30%). Multiple (two or more) manifestations of severe malaria were common. There was no abnormal bleeding and we did not include the assessment of the frequency of prostration, which was poorly described as ‘weakness’ in some of the records and hyperpyrexia was not supported often times with the body temperatures. This presentation is similar to the Jos study (Angyo *et al*., 1996), where febrile convulsions was the commonest manifestation of acute severe malaria, accounting for 49.7% of the cases seen in the Emergency Paediatric Unit, but differred in the highland of Uganda, where prostration (56.4%), respiratory distress (21.4%), severe anaemia (11.1%) were the most common and cerebral malaria, hyperparasitaemia and hypoglycaemia were very rare (Angyo *et al*., 1996). Hypoglycaemia occurred in 32% of our children. This figure could have been higher if the bedside random blood glucose was performed in all the participants on presentation, since the times when the glucometer was not available on the ward, this procedure was omitted. Our prolonged coma rate was definitely higher than what was found in the highland area, Mulago and Jos studies. This may be because of the level of parasitaemia and differential parasite organ sequestration or the presence of paucity of "cerebral malaria strains" of P. falciparum in high endemic areas and also could have contributed to the higher mortality rate documented here (Idro *et al*., 2005). In Northern Ghana, severe anaemia (55%), prostration (33%) and respiratory distress (23%) were the most frequent presentation (Mockenhaupt *et al*., 2004). Coma and convulsions were more frequent in older children, while severe anaemia was mostly seen in the infants. Strikingly obvious is the common occurrence of circulatory shock in this study, which is in contrast to several studies conducted in Africa (Idro, 2001). Circulatory collapse with hypotension has been attributed to Gram negative endotoxaemia even in the absence of demonstrable bacterial infection and its prevalence increases with increasing parasitaemia (Idro, 2001). The most likely reasons are a cross reaction between these endotoxins and malaria ‘toxins’ or absorption of endotoxin from the gut lumen following cytoadherence of parasitized RBCs in gut capillaries (Idro, 2001). The boys most commonly presenting with convulsions and the girls with hyperparasiteamia in this study, is poorly understood. Jaundice occurred in 47%

of the children. This was higher than the findings of previous studies where 6-10% had jaundice. It is not clear from this study why we had a very high number with jaundice. The prevalence of sickle cell gene in this area and glucose 6 phosphate dehydrogenises enzyme deficiencies is low from observation. Unfortunately, no determination of the sickle cell or G6PD enzyme status of the patients was done. However, none of the children was a known sickle cell patient nor had clinical evidence of the disease (Idro, 2001; Idro *et al*., 2005).

Mortality was highest in the children presenting with hypoglycaemia (18.8%), followed by those with respiratory distress (17.9%). The fatality rate in our children with prolonged coma was 4/30, 13.3%, which is high compared to the documented rate in the Mulago study for cerebral malaria (Idro, 2001), 7%. In fact, cerebral malaria accounted for 4/14, 28.6% of our over all fatality rate in this study. The infants, who most commonly presented with severe anaemia, had the highest survival rate. The nutritional status (some wasting) was the strongest factor that determined the discharge status among the variables tested (age, gender and use of bed nets), with mortality higher in the malnourished children, as in Ghana study (Mockenhaupt *et al*., 2004). Also, the children who sleep under treated bed net have slightly higher mortality than those who do not. This might be explained by the suggestion that the regular use of bed nets delays or hinders the development of immunity against malaria.

The findings of this study emphasize the importance of carefully defining clinical characteristics in areas of differing malaria transmission and provide important baseline information about how severe malaria presents in an area of medium to high malaria transmission level.

CONCLUSION

The prevalence and mortality rate of severe malaria was high at 29.8 and 14% respectively. Peak age was 3years. Male: Female ratio was 1.33:1. Use of treated bed nets was high at 70%. The three most common presentations were multiple febrile convulsions, hyperparasitaemia and circulatory shock. Mainly a disease of the well nourished, but fatality rate was higher with the malnourished, male gender, older children and presentations with hypoglycaemia, respiratory distress and multiple febrile convulsions. A larger study will be conducted in future to get a better picture of this problem in our community.

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