ABSTRACT

Objective: The objective of this case control, hospital-based, prospective study is to determine the influence of severe malaria on blood glucose and haemoglobin concentrations and oxygen saturation in young children admitted to Wad Medani Children Teaching Hospital, Gezira state, central Sudan.

Methods: A hundred children with age ranges between 1-10 years were recruited, 50 children as cases and another 50 as age and sex matched controls. The case group had severe malaria defined according...
to WHO classification of severe malaria. The general information was recorded and clinical examination was performed on admission. Thin and thick blood films for malaria were performed. Blood glucose level, haemoglobin concentration and oxygen saturation were done. Ethical issues were respected.

**Results:** Anaemia was found to be the most predominant complication (74%) of severe malaria among young children, followed by convulsions (26%), and hypoglycaemia (8%). The highest prevalence of the disease (28 out of 50 patients) was observed in age group of ≤5 years. Glucose and haemoglobin concentrations and oxygen saturation were found significantly decreased in patients when compared with healthy children.

**Conclusions:** This study gave evidence that anemia, hypoglycemia and low oxygen saturation are most common complications associated with severe malaria in children. The use of pulse oximetry to estimate oxygen saturation for all patients with severe malaria especially children, is recommended. Further studies to investigate the pathophysiology and prognostic significance of acidosis in children with severe malaria are highly suggested.

**INTRODUCTION**

Malaria remains a major cause of morbidity and mortality, especially among children. It is endemic throughout most parts of the tropics, but readily transmitted in sub-Saharan Africa. About 350–500 million clinical malaria episodes were estimated annually and approximately half of the world’s population is at risk of malaria.1 In areas of high malaria transmission, severe malaria mainly affects children under five years of age and pregnant women.2,3 In other areas, all age groups are at risk of developing severe malaria.2,4

Sudan is the largest country in sub-Saharan Africa and malaria is a leading cause of morbidity and mortality. Virtually the whole population of Sudan is considered to be at risk of malaria, and the whole country is now considered endemic, with variable degrees of endemcity.5

Malaria is an important cause of anemia, a leading cause of child morbidity.6 In malaria-endemic areas, the incidence and age pattern of severe anemia are strongly dependent on the intensity of Plasmodium falciparum transmission.7 Severe anaemia has also been associated with respiratory distress secondary to lactic acidosis and/or hypoxia.8 The pathogenesis of malarial anaemia is complex and includes the process of haemolysis, sequestration of red cells, and dyserythropoiesis.9

Hypoglycemia ‘blood glucose ≤40 mg/dL (or <2.2 mmol/L),10,11 is a common complication in acute falciparum malaria, associated with a high morbidity and mortality and poor prognosis.12 It may develop in patients with severe untreated malaria and particularly among those with hyperparasitaemia.13 Convulsions associated with hypoglycaemia are common, particularly in children under 3 years of age, with febrile convulsions and hyperparasitaemia.14,15 Hypoglycemia may complicate the course of treatment with parental quinine.16

Blood oxygen saturation may be used to assess the ability of blood to carry oxygen to the tissues.17 Normal oxygen saturation at sea level in a child is 95-100%. Hypoxia (the percentage of the total hemoglobin presents as oxyhaemoglobin) is defined as arterial O2 <90% and measured by a pulse oximetry.2 The relative shortage of oxygen in tissues occupied by sequestered parasites diverts the biochemical pathways not dependent on oxygen, this results in metabolic lactic acidosis.18 Acidosis is the best independent predictor of death in patients with severe malaria, in both adults and children.19

Hypoxia associated with severe malaria is an important detrimental factor, correlates with disease severity.20 Mortality was significantly more common amongst children in whom impaired consciousness was associated with hypoxia.21

This study aims to determine the impact of severe malaria on glucose and haemoglobin concentrations and oxygen saturation in young children admitted to Wad Medani Children Teaching Hospital, Gezira state, central Sudan.

**METHODS**

This is a hospital based; prospective case-control
study was conducted at Wad Medani Children Teaching Hospital, in the period between October 2008 and February 2009. Wad Medani is the main town of Gezira state in central Sudan, located on the western bank of the Blue Nile River. It lies about 184 kilometers south to Khartoum, the capital of Sudan. Geographically the town is located in the Sudanese poor savannah belt and it is one of the main agricultural areas of the country. The population in Gezira state was estimated to be 4.2 millions according to the latest census done in 2008. Anopheles arabiensis is the sole malaria vector in this area. Wad Medani Children Teaching Hospital is the main referral hospital in Central Sudan. It serves the Gezira state and other neighbouring states.

Fifty children less than 10 years of age including 27 females and 23 males, with a gender ratio of 1:1.2 and of mean age 5.24±2.34 years, were recruited for the study. Children were admitted to Wad Medani Children Teaching Hospital, with severe malaria, based on the WHO criteria of severe malaria. Another fifty, age and sex matched children who were admitted to the hospital for elective surgery, check up or other problems excluding children presented with mixed malaria infections, pneumonia, asthma and chronic bronchitis were selected as a control group. The mean age for the control group was 5.14±2.33 years.

An ethical clearance was obtained from the local research ethical committee before commencement of the study and an informed consent was obtained from the parents or a child guardian.

On admission, patients and controls were interviewed using a structured designed questionnaire to investigate the demographic data and symptoms. All children in both groups were succumbed to comprehensive assessment, including hydration status and other complications of Plasmodium falciparum malaria. The level of consciousness was also assessed using of the Blantyre coma scale.22

Thin and thick blood films were prepared and stained following the procedures outlined in Basic Malaria Microscopy, Part 1,23 using 10% Giemsa stain at pH (7.2). one hundred fields of thin films fixed with methanol and then examined for parasite morphology and for the exclusion of mixed infections. Parasitaemia was variably quantified using either the scanty to heavy or the plus (+) system. Random blood glucose level using glucose oxidase methods and haemoglobin concentration using cyanmethemoglobin methods were measured calorimetrically. Oxygen saturation for each child was assessed using the pulse oximeter. Patients were treated with intramuscular or intravenous quinine under strict supervision.

Statistical analyses of data were performed using computer program software (SPSS), version 13.0. Data was expressed as mean±SD. Student’s t-test was applied to compare the differences between the two groups (patients and controls), p-values ≤0.05 were considered significant.

RESULTS AND DISCUSSION

In this study fever was a prominent symptom observed in all patients (100%) (Table 1); Similar result was obtained from an endemic zone in West Africa reported by Waller D et al.24 In four hospitals in Sudan study, history of fever was reported in 528/543 (97.2%) of children with severe malaria.25

<table>
<thead>
<tr>
<th>Symptoms and signs</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>50 (100%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>37 (74%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>14 (28%)</td>
</tr>
<tr>
<td>Chills</td>
<td>35 (70%)</td>
</tr>
<tr>
<td>Cough</td>
<td>23 (46%)</td>
</tr>
<tr>
<td>Pallor</td>
<td>21 (42%)</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>04 (08%)</td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>02 (04%)</td>
</tr>
<tr>
<td>Convulsions</td>
<td>13 (26%)</td>
</tr>
<tr>
<td>Severe malarial anemia</td>
<td>03 (06%)</td>
</tr>
<tr>
<td>Hypoglycaemia</td>
<td>04 (08%)</td>
</tr>
</tbody>
</table>

Table 1. Symptoms and signs of study patients.

A cut-off level of haemoglobin stated by the WHO and UNICEF is less than 11 g/dl for children 6-59 months and less than 11.5 g/dl for children 5-11 years is
used to define anemia. In this study, 74% of patients were anemic, 6% of them had severe anemia, 32% had moderate anemia and 36% had mild anemia, conforming to Obonyo CO, et al results from Kenya.

The patients in this study had significantly lower hemoglobin concentration (p=0.0003) as compared to the control group. These results are in agreement with previous studies done in Kenya and Gabon, as they found that severe malarial anemia is a leading cause of pediatric morbidity, hospitalization and mortality. Severe anaemia is correlated with very young age group. The haemoglobin concentrations was lower in the age group ≤5 than that of age >5 (Table 3), but the difference was not significant. This could be similar to observations in Kenya where young age was strongly associated with severe malarial anemia.

Splenomegaly and hepatomegaly are important malarial epidemiological indicators; both are commonly reported in young children with malaria due to their low immunity. In this study splenomegaly was found in 8% of the patients and 4% had hepatomegaly. These results were lower than reported results in Sudan before. Study done in Mali, showed that splenomegaly was found in 25% of patients and hepatomegaly in 92%. Our results demonstrated that, patients with splenomegaly had significantly lower haemoglobin concentration (p=0009). Similar results were obtained by Giha et al., where the spleen size was found to be significantly inversely correlated with haemoglobin.

Children are the most vulnerable group to hypoxia, severe anaemia and hypoglycaemia as complications of falciparum malaria. This study showed that 8% of children were significantly hypoglycaemic on admission, although all patients showed lower blood glucose as compared to the control group (p=0.0001).

These results were consistent with a previous study which reported prevalence of hypoglycemia in children with severe malaria, ranging from 8% to 34%.

Measurement of blood oxygen saturation assesses the ability of blood to carry oxygen to the tissues. Hypoxia is a common complication of childhood infections and is a recognized risk factor for death and correlates well with the disease severity. Hypoxia is strongly associated with inpatient death. The mortality was significantly more common amongst children in whom impaired conscious was associated with hypoxia.

This study showed statistical decrease in oxygen saturation in patients as compared to the control group (p=0.0001). However, this decrease in oxygen saturation is of no clinical significance. None of the patients had oxygen saturation less than 90% or hypoxic on admission. This may be due to the small number of population of this study. Data reported from Kenya stated...
that hypoxia was found to be more common in children with severe malaria (31 children had unrecordable oxygen saturation on admission), especially in those with clinical evidence of convulsions.\textsuperscript{30}

The geometric mean of parasite density was found to be 82830/μl, (ranged 6400-497600). This may reflect the high transmission intensity in Gezira state. In Uganda, a similar result was observed in high transmission intensities region suggesting that heavy \textit{Plasmodium falciparum} parasitaemia may be important in the development of seizures, severe malarial anaemia and impaired consciousness in children below 5 years of age.\textsuperscript{34}

**CONCLUSIONS**

This study testifies that anemia, hypoglycemia and low oxygen saturation are most common complications associated with severe malaria in children. Pulse oximetry is essential, easy and non invasive method for detecting hypoxia so it is recommended to estimate oxygen saturation for all patients with severe malaria especially children. Further studies to investigate the pathophysiology and prognostic significance of acidosis in children with severe malaria are highly recommended.

**REFERENCES**


