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LABORATORY ASSESSMENT OF HYPOGLYCAEMIA DUE TO MALARIA IN CHILDREN ATTENDING GENERAL HOSPITAL KATSINA

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ABSTRACT
Early and accurate laboratory diagnosis of Plasmodium falciparum parasitaemia as well as assessment of its severity which include among other parameters; blood glucose concentration are very important in the management of children with complicated malaria. In this study, the conventional thick blood film examination was used to detect malaria parasitaemia, while enzymatic colorimetric glucose-oxidae technique was used to estimate blood glucose level. A total of (450) chlidren were assessed for malaria and hypoglycaemia due to malaria over a period of five months in paediatrics ward of General Hospital Katsina, Nigeria. From the results obtained, 380 (84.4%) children had primary diagnosis of malaria and 113 (25.1%) of the malaria positive children were hypoglycaemic on the first day of admission. Highest incidence of malaria and hypoglycaemia due to malaria were recorded in children between the age of 2-5 years with 37.3% and 9.3% respectively. Lowest incidence of malaria and hypoglycaemia due to malaria were recorded in children between the age of 11-15years with 9.3% and 3.3% respectively. Although apparently there was difference in the number of males and females found to be malaria positive as well as hypoglycaemic, chi-square (χ^2) test at $P \leq 0.05$ showed no significant difference. Questionnaire analysis in this study showed that high incidence of severe malaria leading to hypoglycaemia in children could be attributed to poverty, malnutrition, inadequate management of uncomplicated malaria in the health centres as well as late arrival at the hospital. Early laboratory and clinical diagnosis, correct treatment and improved quality management are key strategies for malaria control.

Key words: Hypoglycaemia, Malaria, Children

INTRODUCTION

Malaria is a major global threat to health, social and economic development (WHO, 1993). Almost half of the world's population is at risk of the disease (WHO, 1993). The poor and most under privileged part of population is severely affected. Each year it causes more than 2.5 million deaths and 300 – 500 million clinical illnesses, the majority being in sub-Saharan Africa (WHO, 1998 and Coosemans, and 'D' Alessandro, 2000).

Most deaths due to malaria in children occur shortly less than 24 hours after admission to hospital. Young children living in sub-Saharan Africa carry the largest part of malaria global burden (World Bank, 1993). Lactic acidosis complicates 35% of severe childhood malaria (Krishna *et al*, 1994) and hypoglycaemia is present in 20% of children with cerebral malaria (Newton and Krishna, 1998). Both acidosis and hypoglycaemia commonly coexist but each is considered separately as a cause of fatality in children and adults due to severe complicated malaria.

Hypoglycaemia is known to be an independent risk factor for death in both severe malaria (Molyneux *et al.*, 1989) and other severe childhood infections in the tropics (Kawo *et al.*, 1990). Despite its importance, its pathogenesis is not well understood (English *et al.*, 1998).

Hypoglycaemia is a medical term referring to a pathologic state produced by a lower than normal level of glucose in blood. Technically, hypoglycaemia is the clinical state due to low plasma glucose, usually less than 2.2mmol/l (Gray *et al.*, 1985).

Hypoglycaemia is associated with a poor prognosis in severe malaria (krishna *et al*, 1994). In African children with malaria, impairment in hepatic gluconeogenesis in the presence of adequate levels of precursors (glycerol) has been considered the most likely mechanism (White *et al.*, 1987). Irreversible coma may quickly develop if the condition is not effectively treated. The fasting and random blood plasma glucose levels are generally maintained within a range of 3.9 – 7.8mmol/l for healthy humans (Philip, 1997). Although defining the lower level of hypoglycaemia is debatable, the precise level of glucose considered low enough to define hypoglycaemia is dependent on (1) the measurement method, (2) the age of the patient, (3) presence or absence of effects and (4) the purpose of the definition (Cornblath *et al.*, 1990).

Severe malaria on the other hand, is defined as blood film positive *P. falciparum* plus one or more of the following complications; prostration (inability to sit or breast feed), coma, prolonged or recurrent seizures, respiratory distress, circulatory collapse, anaemia (haemoglobin <5g/dl), jaundice and hypoglycaemia (low blood glucose level <4.0mmol/l), (WHO, 2000 and Usman *et al.*, 2007).

Severe and complicated malaria should be diagnosed early and managed accordingly if one or more of the signs of complication are observed in patient with *P. falciparum* malaria. This condition is a medical emergency, and is usually a result of delayed and inadequate treatment of uncomplicated malaria.

Microscopic examination of thick or thin blood film is essential both to diagnose malaria and to quantify parasitaemia. Other important measures used in managing severe malaria in children on the bed side includes parenteral administration of quinine and fluids, frequent monitoring of vital signs (body temperature, respiratory rate, blood pressure and pulse rate) and blood glucose level (WHO, 2000).

Two most commonly used methods of measuring blood glucose are: glucose oxidase colorimetric method and glucose meter capillary method (Cheesbrough, 2004), but since according to the observation of English *et al.* 1998, the bed side glucose meter overestimates blood glucose measurement, and seriously over-estimates the frequency of hypoglycemia, glucose oxidase colorimetric method is considered the best and more accurate method.

One important measure taken in the management of hypoglycaemia is to treat the patient with 0.5ml/kg of 50% dextrose diluted in an equal volume of sterile water and given over 5 minutes. This should be immediately followed by the start of the 4% dextrose/0.18%. saline infusion (English *et al.*, 1998). Additional measurement of blood glucose level 2 hours after starting treatment should follow.

The objectives of this study are to assess the prevalence of malaria in children, to ascertain the degree of one of the complications of malaria (hypoglycaemia) leading to death in children and to provide suggestions in the management of children with severe malaria including blood glucose monitoring.

MATERIALS AND METHODS

Inclusion Criteria

Only children on admission in the paediatric ward with symptoms of severe malaria (coma, prostration, fever and respiratory distress) were selected in this study on the first day of admission before management commences, between May, 2006 to September, 2006. Only blood samples that are malaria positive were further tested for blood glucose level.

Questionnaire

A questionnaire was designed to provide detailed information about the patients. Parameters such as names, age, sex, address, socio-economic status, treatment at primary health Care and Score of symptoms presented by patients were recorded.

Sample collection

Venous blood samples (3.0ml) were collected aseptically using dry, sterile syringe and needle. The blood was withdrawn with a minimum stasis from a suitable vein in the arm after swabbing with cotton wool soaked in 70% alcohol. Part of each blood sample was used in thick blood film making while other part was slowly ejected into sodium fluoride containing sample bottles for glucose estimation.

All the 450 blood samples were collected at the paediatric ward of General Hospital Katsina, Nigeria on the first day of admission, and labeled appropriately (Usman *et a*l., 2007).

Preparation and Examination of Thick Blood Film

One thick blood film was prepared for each specimen and stained according to the method proposed by Cheesbrough (2004), using field's staining technique. Each of the thick blood films was dipped into field's stain A for 5 seconds, and excess stain was drained off. It was then washed gently for about 5 seconds in clean water and excess water was drained off. Each film was then dipped into field's stain B for 3 seconds, excess stain drained off, and washed gently in another clean water. It was allowed to air-dry and each slide was observed under the microscope using oil immersion objective.

Blood glucose estimation (Glucose – Oxidase Method)

All the thick film positive blood samples were further tested fro glucose level using glucose-oxidase colorimetric (enzymatic) principle as suggested by Cheesebrough (2004), and Baker *et al.,* (2001) but with strict compliance with Randox® manufacturers instructions. Three test tubes were arranged for each test, and glucose – oxidase reagent (0.1ml) was dispensed in each. Then distilled water (10µl) was pipetted into tube 1 (blank), standard solution (10µl) into tube 2 (standard) while patient plasma (10µl) was pipetted into tube 3 (Test). All the set ups were mixed and incubated in water bath at 37^{o}C for 10 minutes for colour development. The test tubes were then mixed and their absorbance read using spectrophotometer at 540nm. The glucose values were calculated and recorded in mmol/l.

RESULTS

The results obtained indicated that out of the four hundred and fifty (450) children admitted with symptoms of malaria, three hundred and eighty (84.4%) had primary diagnosis of malaria, as shown in Table 1. One hundred and forty (31.1%) were males while two hundred and forty (53.3%) were females (Table 2).

Out of the diagnosed malaria positive children, one hundred and thirteen (25.1%) were hypoglycaemic on the first day of admission (Table 1.) sixty (13.3%) were males while fifty three (11.8%) were females (Tables 2).

On the basis of age group, highest incidence of malaria and hypoglycaemia due to malaria were recorded in children between the age of 2 – 5 years with 37.3% and 9.3% respectively. Lowest incidence of malaria and hypoglycaemia due to malaria were recorded in age group. 11 – 15 years with 9.3% and 3.3% respectively (Table 3).

Although apparently there was difference in the number of males and females found to be malaria positive as well as hypoglycaemic, chi-square (χ^2) test at $P \leq 0.05$ showed significant difference.

Results of the questionnaire analysis in this study showed that high incidence of severe malaria leading to hypoglycaemia in children could be attributed to poverty, malnutrition, inadequate management of uncomplicated malaria in the health centres as well as late arrival at the hospital.

Table 1 Showing Malaria and hypoglycaemia due to malaria

Total No. of samples examined	No. of +ve samples	% of malaria +ve samples	No. of Hypoglycaemia +ve Samples	% of Hypoglycaemia +ve Samples
450	380	84.4	113	25.1

Key: +ve : Positive

Table 2 Showing Malaria and hypoglycaemia due to malaria by Sex

Sex	No. examined	No. of malaria positive	%of malaria positive	No of Hypoglycaemia +ve	% of Hypoglycaemia +ve
Males	170	140	31.1	60	13.3
Females	280	240	53.3	53	11.8
Total	**450**	**380**	**84.4**	**113**	**25.1**

Table 3 Showing Malaria and hypoglycaemia due to malaria by age groups

Age (years)	No. examined	No. of malaria positive	%of malaria positive	No of Hypoglycaemia +ve	% of Hypoglycaemia +ve
0 - 1	94	79	17.6	21	4.7
2 - 5	200	168	37.3	42	9.3
6 – 10	108	91	20.2	35	7.8
11 – 15	50	42	9.3	15	3.3
Total	**450**	**380**	**84.4**	**113**	**25.1**

Key: +ve : Positive

DISCUSSION

From the results of this study, a very high number of children with primary diagnosis of malaria (84.4%) was recorded, and it is noteworthy that other numerous uncomplicated cases were treated at the paediatric out patient department (POPD) and primary health centres. Only those children with severe illness were admitted and considered in this study to ascertain the severity of malaria.

Questionnaire analysis revealed that most of the children admitted with complicated malaria were from the rural areas and did not report to the hospital on time because the period during which malaria strikes hard is the rainy season when there is more breeding places for mosquitoes and the production season when the poor farmer can't afford to be absent from his farm and family due to seeding and harvesting.

Another reason why the incidence of malaria among children was very high is poverty. Child mortality rates are known to be higher in poorer households, and malaria is responsible for a substantial proportion of these deaths (Mwageni *et al.,* 2002). Poor families live in dwellings that offer little protection against mosquitoes and are less able to afford insecticide treated nets. Poor people are also less likely to be able to pay either for effective malaria treatment or for transportation to a health facility capable of treating the disease (WHO, 1998). To this effect, although some state governments in Nigeria including Katsina State have initiated free malaria treatment, due to poverty, it does not include free adequate malaria management for in-patients.

Higher incidence of malaria was recorded in children between the age of 2 – 5 years because at that age, most children have not yet acquired adequate clinical immunity, which makes early years particularly dangerous.

Hypoglycemia is very common in children under 3 years and in those with convulsions or hyperparasitaemia. It is the second complication of severe malaria after anaemia. Hypoglycaemia due to malaria is often overlooked clinically because the manifestations may be similar to those of cerebral malaria.

Although, glycerol appears to be an important precursor for gluconeogenesis in mild malaria (Dekker *et al.*, 1997), however English *et al* (1998) in their studies of hypoglycemia in Kenyan children with severe malaria suggested that limitation in supply of this substrate (glycerol) is not proved beyond reasonable doubt to be the cause of hypoglycemia in severe malaria.

CONCLUSION AND RECOMMENDATIONS

Malaria constitutes a major health problem in children especially in endemic areas. Complications such as severe anaemia and hypoglycaemia are responsible for many of the deaths in children. These complications can be prevented or managed without difficulty if adequate preparation is made to handle them. To decrease mortality, uncomplicated cases of malaria must be treated early and adequately. Patients must be managed in the nearest health centres. Many of the complications of malaria can be managed at the health centres that are well organized.

- Availability of simple, rapid and reliable laboratory test at health centres should be ensured, so as to assess and manage major complications like severe anaemia and hypoglycaemia.
- To avoid death due to hypoglycaemia in children with severe malaria closed nursing care as well as adequate supply of 50% dextrose and dextrose saline infusions must be ensured.
- Due to high poverty level, state governments in Nigeria should also incorporate free management of severe malaria along side with free malaria treatment.

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