

Prevalence and Case-Control Study of Cerebral Malaria in Limbe of the South-West Cameroon

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SUMMARY

A study was carried out in Limbe and its environs to determine the prevalence of cerebral malaria vis-à-vis uncomplicated malaria, and to assess the importance of parasitaemia level, packed cell volume and hypoglycaemia as predictors of cerebral malaria. Data were obtained using a questionnaire administered to 650 people aged between 6 months and 70 years, and by a case-control study on 90 people (30 cases and 60 controls) aged between 6 months and fifteen years. The results of the questionnaire study revealed uncomplicated malaria prevalence rate of 50.9% as against 7.1% for cerebral malaria. The highest prevalence of these infections occurred in the 0-5 years age group, dropping in people aged 16 years and above. The case-control study revealed high parasitaemia (100,000 – 500,000 parasites/mm³ of blood) in uncomplicated malaria patients and hyperparasitaemia (>500,000 parasites/mm³ of blood) in cerebral malaria patients. Patients with uncomplicated malaria had either normal haemoglobin (PCV>33%) or were mildly anaemic (PCV 18-32%). Cerebral malaria patients suffered from severe anaemia (PCV<18%). Hypoglycaemia (<40mg glucose/dl) was recorded in 12.9% of cerebral malaria patients, but in none of the patients with uncomplicated malaria.

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Introduction

In African children severe complicated malaria presents most frequently as severe malaria anaemia (<5g Hb/dl) or as cerebral malaria. Cerebral malaria accounts for 80% of all fatal malaria cases admitted to hospital [1]. Despite the availability of effective anti-malarial drugs, mortality from cerebral malaria remains high, with an estimated case fatality rate of 10-30% among hospital admissions [2, 3].

It is now known that differences exist in the clinical manifestation of the disease in different regions of the world [4, 5]. More so, it has been extremely difficult to control malaria as a whole and cerebral malaria in particular due to administrative, economic, technical and socio-cultural factors, insecticide and drug resistance, and lack of

effective vaccine [6, 7, 8]. As such, a lot of work remains to be done to find ways and means of combating this disease.

The present study was designed to determine the prevalence rate of cerebral malaria vis-à-vis uncomplicated malaria in Limbe and its environs, and to assess the importance of parasitaemia level, packed cell volume and hypoglycaemia as predictors of cerebral malaria.

Materials and Methods

Study Site:

The work was carried out in Limbe town and its environs between June 1998 and February 1999. Limbe is a coastal town, about three metres above sea level, situated on the Amba Bay of the Atlantic Ocean at the foot of Mount Fako.

It has high temperatures with an annual average of 24⁰c, and abundant rainfall with an annual average of 405cm [9]. The dry season extends from mid-November to mid-March and the rainy season from mid-March to mid-November.

Study Subjects and Methods:

A questionnaire was administered to inhabitants of the town and its environs to rapidly assess the prevalence of cerebral malaria vis-à-vis uncomplicated malaria. A total of 650 people aged between six months to 70 years, constituting about 1% of the population, were interviewed. People were interviewed in houses chosen at random. For babies and toddlers, their older relations were interviewed. Fifty people were interviewed in each of the following age groups: 0-5, 6-10, 11-15, 16-20, 21-25, 26-30, 31-35, 36-40, 41-45, 46-50, 51-55, 56-60, and >60 years.

A case-control study on cerebral malaria patients (cases) and patients with uncomplicated malaria (controls) was carried out in the provincial hospital at Limbe. Thirty cases ranging in ages from 6 months to 15 years were recruited based on the following criteria:-

- (a) Convulsions or history of multiple convulsions in the last 48 hours.
- (b) Coma or history of coma prior to presentation.
- (c) Fever (temperature >38⁰c) or a history of fever in the last 72 hours.
- (d) Delirium.
- (e) Anaemia with PCV<32%.
- (f) Parasites in peripheral blood films.

Sixty control patients with mild uncomplicated malaria were recruited from the same hospital as the cerebral malaria cases.

Diagnosis was confirmed by demonstration of parasites in the blood smears. The controls were selected in such a manner as to keep their number with

respect to sex and age in proportion to the number of cases. Only patients who gave their consent or whose guardians consented were recruited.

The blood obtained from patients was processed for determination of parasitaemia level, using white blood cell count and parasite count from blood film slides. The number of parasites per mm³ of blood was calculated using the formula below [10]:

$$\text{(WBC count of patient X No. parasites per 100 WBC)/100}$$

Packed cell volume (PCV) was determined by microcentrifugation of blood samples in capillary tubes [11]. PCV was considered to be normal when it was $\geq 33\%$, low when it was between 18-32%, and very low when it was <18%. Blood glucose concentration was determined by the orthotoluidine method [11], employing fluoride oxalate as anticoagulant to prevent destruction of glucose in blood.

Results

Prevalence of uncomplicated and cerebral malaria:

Out of the 650 people interviewed, 331 (50.9%) had uncomplicated malaria while 46 (7.1%) had cerebral malaria. Fig.1 reveals that the prevalence of uncomplicated and cerebral malaria was different in the various age groups studied. Generally, the prevalence rate of both types of infection was age-dependent; the number of subjects with the infection decreased significantly ($\chi^2 = 72.9, P < 0.001$) as age increased. The occurrence of cerebral malaria was rarely reported in subjects 45 years old and above. The highest prevalence of this infection occurred in the 0-5 years age group (30%), while from 16 years and above, the prevalence rate dropped to less than 10% (Fig.1)

Overall, more males (53.1%) than females (48.8%) suffered from uncomplicated malaria, whereas the reverse was the case with cerebral malaria where more females

(8.2%) than males (5.9%) suffered from this infection. However, there was no significant correlation between the two types of malaria and sex of the subject ($\chi^2 = 1.22, P > 0.05$).

Table 1. Distribution of uncomplicated and cerebral malaria in subjects by sex and age group.

Age Group (Years)	Distribution of subjects by sex					
	Cerebral Malaria			Uncomplicated Malaria		
	Male (%)	Female (%)	Total (%)	Male (%)	Female (%)	Total (%)
0-5	10(76.9)	15(88.2)	25(83.3)	23(79.3)	25(80.7)	48(80.0)
6-10	1(7.7)	2(11.8)	3(10.0)	3(10.4)	5(16.1)	8(13.3)
11-15	2(15.4)	0(0)	2(6.7)	3(10.4)	1(3.2)	4(6.7)
Total	13	17	30	29	31	60

Table 2. Parasitaemia count in the study population.

Age Group (Years)	Cerebral Malaria				Uncomplicated Malaria			
	No. Examined	Parasite Count			No. Examined	Parasite Count		
		Low	High	Hyper		Low	High	Hyper
0-5	25	0	6	19	48	0	47	1
6-10	3	0	1	2	8	2	6	0
11-15	2	0	2	0	4	0	4	0
Total	30	0	9	21	60	2	57	1

Key

- Low parasitaemia = <100,000 parasites/mm³ of blood
- High parasitaemia = 100,000-500,000 parasites/mm³ of blood
- Hyperparasitaemia = >500,000 parasites/mm³ of blood

Table 3. Packed cell volume (PCV) of cerebral and uncomplicated malaria patients within different age groups.

Age Group (Years)	No. of Cerebral Malaria Patients with PCV Levels			No. of Uncomplicated Malaria Patients with PCV levels		
	Very low	Low	Normal	Very low	Low	Normal
0-5	7	18	0	3	38	3
6-10	0	3	0	0	6	0
11-15	0	2	0	1	2	0
Total	7	23	0	4	46	3

Key:

Very Low = PCV < 18% (severe anaemia)
 Low = PCV 18 – 32% (mild anaemia)
 Normal = PCV > 32%

Table 4: Blood glucose level of cerebral and uncomplicated malaria patients

Infection	No. Examined	No. of Patients with Blood Glucose Level		
		75-110mg/dl	40-74mg/dl	<40mg/dl
Cerebral Malaria	15	3	8	4
Uncomplicated Malaria	16	11	5	0
Total	31	14	13	4

Key:

75-110mg/dl = Normal range
 40-74 mg/dl = Intermediate range
 <40 mg/dl = Hypoglycaemia

Case-Control Study:

The distribution of uncomplicated and cerebral malaria in subjects by sex and age group is shown in Table 1. Twenty-five (83.3%) of the children with cerebral malaria were in the 0-5 years age group as compared with those above 5 years ($\chi^2 = 32.41, P < 0.001$). Sex, on the other hand, did not appear to be a significant factor.

Parasitaemia Level:

The parasitaemia levels of the subjects examined within the different age groups are shown in Table 2. Twenty-one (70%) of the cerebral malaria cases had hyperparasitaemia (>500,000 parasites/mm³ of blood). A comparison of the parasitaemia levels in the three age groups revealed that patients in the 0-5 and 6-10 years age groups were most at risk of having high and hyperparasitaemia ($\chi^2 = 32.41, P < 0.001$).

In the uncomplicated malaria patients, only one (1.67%) of them had hyperparasitaemia while 57 (95%) had high parasitaemia. There was a significant difference in the level of hyperparasitaemia in uncomplicated and cerebral malaria ($\chi^2 = 50.56$, $p < 0.001$).

Packed Cell Volume

The packed cell volume in the two groups of patients is shown in Table 3. In the cerebral malaria cases, severe anaemia (PCV < 18%) was observed only in the 0-5 years age group, and was significantly more common in this group than in the uncomplicated malaria patients ($\chi^2 = 32.41$, $p =$

Hypoglycaemia:

The blood glucose level of both cerebral malaria and uncomplicated malaria patients in the study is shown in Table 4 and Fig. 3. 12.9% of the patients were hypoglycaemic (< 40 mg/dl) while 45.2% had normal blood glucose levels ($\geq 74 - 110$ mg/dl). All of the hypoglycaemic patients were cerebral malaria cases (26.7%) while none of the patients with uncomplicated malaria was hypoglycaemic. However, there was no significant relationship between hypoglycaemia and severity of infection ($\chi^2 = 2.81$, $P > 0.05$).

Discussion

The prevalence rates obtained by using a questionnaire were 50.9% for uncomplicated malaria and 7.1% for cerebral malaria. Several factors contribute to the endemicity of malaria in Limbe. These include climatic, ecological and environmental factors which favour the breeding of the vector. The high temperatures (average 24°C) favour the rapid development of the mosquito from egg to adult stage, as well as the development of the parasitic stages within the mosquito. Abundant rainfall throughout most months of the year (with an annual average of 405 cm) allows the mosquito larvae to develop during a greater portion of the year [12].

The lush vegetation around the town and the presence of water-retaining crops planted close to dwelling areas (e.g. plantains, bananas, flowers) provide ideal breeding sites for the insidious *Anopheles* mosquito. It has been noted that the

prevalence of malaria is usually higher in rural agricultural areas than in urban areas. This is due to the fact that the *Anopheles* mosquitoes generally do not breed in polluted water as is often the case in towns [13].

In the sub-Saharan Africa both types of malaria are common in the 0-5 years age group [14, 15]. This is closely linked to the development of immunity to malaria. Immunity to malaria, unlike in many other infectious diseases, develops only after several acute malaria attacks. Unfortunately, such immunity is only partial, requiring constant immunological boosting with live parasite challenge [16, 17].

Uncomplicated malaria was found to be more frequent in males than in females, although the difference was not statistically significant. Other workers [18, 19] also reported a higher parasite density in males than in females. The greater susceptibility of males is alleged to be dependent on the male sex hormone, testosterone, which has been known to increase host susceptibility to other parasitic diseases. Females are said to have increased immunity to malaria and other parasitic diseases because of genetic and hormonal factors [20].

The parasitaemia levels of the cerebral malaria patients ranged from high (10,000 – 500,000) parasites/m³ of blood) to hyper levels (> 500,000 parasites/mm³ of blood), whereas in the uncomplicated malaria patients, mainly high parasitaemia levels were recorded. This is to be expected in endemic areas where people tend to have high parasite burdens while being asymptomatic, as a result of malaria tolerance [21]. The high rate of parasitaemia recorded in the 0-5 years age group reflects their yet poorly developed immunity as immunity develops with age and numbers of acute malaria attacks [22].

Anemia which results from the haemolysis of parasitised and non-parasitised erythrocytes is a common complication of all but the most benign malaria infections [17]. The severe anemia (< 18% haematocrit) recorded mostly in children of 0-5 years age group

correlated with the hyperparasitaemia

Hypoglycaemia is a common and serious clinical problem in cerebral malaria in some countries. It occurs as a result of the increase glucose requirement of parasitised erythrocytes [23]. It was recorded in 26.7% of the cerebral malaria cases, and in none of the uncomplicated malaria patients. Although the difference was not statistically significant, hypoglycaemia remains a criterion that justifies the need for prompt and appropriate treatment of cerebral malaria.

Conclusion

The 0-5 years age group was more at risk of malaria attacks than other people. The indicators of cerebral malaria included coma, convulsion, severe anemia, hypoglycaemia and hyperparasitaemia. Patients presenting with any of these indicators should be treated promptly for malaria to avert case fatality.

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