Clinical and epidemiological features of severe malaria in children in four hospitals in Sudan

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الملامح السريرية والوبائية للملاريا الوخيمة لدى الأطفال في أربعة مستشفيات في السودان

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الخلاصة: قام الباحثون في إطار هذه الدراسة بتقييم الملامح السريرية والوبائية لحالات الملاريا الوخيمة قبل الإدخال والمعالجة في المستشفى، وتقييم نتائج المعالجة والعوامل المرتبطة بها في أربعة مستشفيات في مختلف مناطق السودان، وذلك على مدى خمسة أشهر في عام ألفَيْن. وبلغ عدد الأطفال الذين أُدخلوا المستشفى 543 طفلاً، وهو ما يشكّل 21٪ من جميع حالات الأطفال الذين أُدخلوا المستشفيات. وكان ناصف median أعمار الأطفال 36 شهراً. وكانت المعالجة في المنزل هي أول إجراء اتَّخذته 57.5٪ من الأسر. وبلغت نسبة الإماتة بين الحالات 5 من كل ألف، وكان 93٪ من الأطفال الذين ماتوا دون التاسعة من العمر. وقد ارتبطت أعلى مخاطر الوفاة بالتباطؤ في التماس المعالجة وبمدى وخامة الملاريا قبل إدخال المريض في المستشفى. وبيَّنت الدراسة أن مستشفى أم درمان، في الخرطوم، كان أفضل المستشفيات من حيث مؤشِّر الأداء في معالجة الحالات المرضية بالمقارنة مع سائر المستشفيات.

ABSTRACT We assessed the clinical and epidemiological features of severe malaria cases before admission, management in hospital and outcome and associated factors in 4 hospitals in different areas of Sudan over a 5-month period in 2000. There were 543 children admitted representing 21% of all paediatric admissions. Median age was 36 months. Treatment at home was the first action taken by 57.5% of families. Case fatality rate was 5/1000 and 93% of the children who died were under 9 years. Highest risk of death was associated with delay in seeking treatment and severity of illness before admission. Omdurman Hospital in Khartoum had the best case-management performance index compared to the other hospitals.

Caractéristiques cliniques et épidémiologiques du paludisme grave chez des enfants dans 4 hôpitaux au Soudan

RÉSUMÉ Nous avons évalué les caractéristiques cliniques et épidémiologiques des cas de paludisme grave avant l'admission à l'hôpital, la prise en charge hospitalière et les résultats ainsi que les facteurs associés dans 4 hôpitaux de différentes zones du Soudan sur une période de 5 mois en 2000. Il y avait 543 enfants hospitalisés représentant 21 % de toutes les hospitalisations pédiatriques. L'âge médian était de 36 mois. Le traitement à domicile était la première mesure prise par 57,5 % des familles. Le taux de létalité s'élevait à 5 pour 1000 et 93 % des enfants qui sont décédés avaient moins de 9 ans. Le risque de mortalité le plus élevé était associé au retard dans le recours aux soins et à la gravité de la maladie avant l'admission à l'hôpital. L'hôpital Omdurman de Khartoum avait le meilleur index de performance pour la prise en charge des cas par rapport aux autres hôpitaux.

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Introduction

A severe malaria patient is defined by the World Health Organization (WHO) as a febrile patient with falciparum malaria with some complications of no other obvious causes who requires emergency hospitalization treatment [*1*]. Out of 1.5 to 2.7 million deaths that occur in the world every year as a result of malaria, 1 million are children [*2*]. In Africa, malaria kills 1 child in every 20 under the age of 5 years [*3*].

In Sudan, malaria remains a major public health problem, with a case prevalence of 93 per 1000 in 2002 [*4*]. It represented 25% of hospital admission in children.

Although severe malaria is life-threatening to children, there is limited information available on the severity of the disease, management, deaths and associated factors in Sudan; therefore there is an urgent need for reliable clinical and epidemiological information on severe malaria as a killing disease in children.

The objective of this study was to assess the clinical and epidemiological features of the disease before and on admission to hospital, management in hospital, outcome of the disease and associated risk factors for death.

Methods

We conducted a cross-sectional study in 4 district paediatric hospitals in Sudan in the 5-month period of the rainy season August to December 2000. The hospitals were located in Omdurman in Khartoum state, Wad Medani and Sennar in central Sudan and Gedaref in eastern Sudan. They are located in areas with a wide range of endemicity, from urban in Omdurman to mesoendemic and hyperendemic in Wad Medani, Gedaref and Sennar.

Omdurman is largest city in the country. It had an estimated total population of 4 million in 2002. The majority of the people in Omdurman are workers in the government and informal sectors. Omdurman has 2 major camps for displaced persons around the city with a population of 1 million, who have come mainly from the south and west of Sudan due to war and desertification. Wad Medani city is in Gezira State, which is located in the middle of the country. It is the main agricultural area of the country. Wad Medani has an estimated total population of 3.5 million people, the majority of whom are farmers. Sennar is located to the south-east of the country. It is also an agricultural area that has one of the main dams in the country which irrigates the Gezira agricultural scheme. Sennar has an estimated total population of 1.2 million people, the majority of whom are farmers. Gedaref is also an agricultural area located in the east of the country. The agriculture in Gedaref is based mainly on rain irrigation. It has an estimated population of 1.5 million. As it is located on the border with Ethiopia in the east of Sudan, Gedaref has witnessed a great influx of refugees from Ethiopia due to drought and war. The refugees are scattered in many camps around the town. The majority of people in Gedaref are also farmers [*4*].

Children under 15 years of age of both sexes admitted to the above-mentioned hospitals with severe malaria, based on WHO criteria, were included in the study [*5*]. The daily records of paediatric admissions to the 4 selected hospitals and of children admitted because of malaria were reviewed. Those of the children diagnosed as severe malaria were checked.

Interviews with the mothers or carers of the children admitted and diagnosed as severe malaria during the study period were conducted and a questionnaire completed.

Clinical information and procedures that were relevant to the cases and case management of severe malaria in children were recorded. Data on age, sex, occupation of father, educational level of parents, accessibility to care at the local level, early symptoms and signs, action taken before admission, treatment before and after admission, duration of illness and clinical presentation were collected. Diagnostic tests (blood film, parasite count, haemoglobin count, blood glucose, white blood count, haemoglobin in urine, cerebrospinal fluid analysis, and outcome (hospital case-fatality rate of severe malaria in children) were analysed.

Hospital management performance was compared between the study hospitals using a scoring system developed by the authors using 6 essential criteria which are considered optimum care performance for severe malaria in children. These criteria were: performance of thick and thin blood film for malaria, white blood count, haemoglobin count, blood glucose, lumbar puncture and administration of intravenous quinine.

Data were analysed using *SPSS*, version 10. Mean, standard deviation (SD), median, percentiles, proportions, percentages, tables and figures were used to summarize the data. Relative risk and attributable risk were used to assess the risk factors for death; 95% confidence intervals and chi-squared test were used to assess significant differences.

Results

Total malaria load compared to total paediatric admission among the 4 hospitals was 21.3% (4462/20944). Severe malaria load from the total malaria outpatient attendance among children was 12.2% (543/4462).

Most of the severe malaria cases in children (304 cases, 56.0%) were reported in Sennar followed by Wad Medani 99 cases (18.2%), Omdurman 75 cases (13.8%) and Gedaref 65 cases (12.0%).

Table 1 summarizes the important epidemiological features with regard of the cases in the selected hospitals. Of the cases, 56% were males and 44% were females. The median age of children with severe malaria was 36 months, 75th percentile was 72 months. The median age of children who died of severe malaria was 66 months, 75th percentile was 108 months.

A total of 34.8% of the cases reported availability of health units at the local level in all areas, while only 23.8% reported availability of pharmacies at their local level. Of the children for whom early action was taken, the majority 195/339 (57.5%) had received treatment at home before admission. Wad Medani reported the highest percentage for those who took action at home before admission, 63/81 (77.8%), followed by Sennar 124/183 (67.8%), Gedaref 7/37 (18.9%) and Omdurman 5/37 (13.5%). There was a significant difference between taking action at home in the capital (Omdurman) compared to the districts Wad Medani, Sennar and Gedaref ($\chi^2_1 = 43.4, 38.5$ and 17.4 respectively, $P < 0.05$).

The majority of actions taken at home were taken by the mothers. The commonest antimalarial used at home was chloroquine. The main source of drugs at home before admission were health units 108/195 (55.4%), followed by grocery shops (*canteens*) 58/195 (29.7%), pharmacies and drug sellers 23/195 (11.8%), and neighbours 6/195 (3.1%). Only 7 children were given quinine before admission at the local health facility and it was given only in 2 areas (Sennar and Gedaref); however, all of these children recovered.

Median time to reach the hospital from all areas by bus or any other form of public transport was 30 minutes, 75th percentile

Table 1 **Characteristics and treatment-seeking practice of cases with severe malaria**

Variable	Omdurman (*n* = 75)	Wad Medani (*n* = 99)	Sennar (*n* = 304)	Gedaref (*n* = 65)	Total (*n* = 543)
Median age of cases (75th percentile) (months)	36 (72)	36 (72)	36 (60)	60 (96)	36 (72)
Median age of cases who died (75 percentile) (months)	–	60 (144)	60 (96)	72 (108)	66 (108)
Sex (%)					
Male	67	62	54	48	56
Female	33	38	46	52	44
Father's occupation (%)					
Government employee	47	50	43	42	44
Farmer	15	35	40	42	48
Other	38	15	17	16	8
Illiteracy level (%)					
Father	32	39	52	63	48
Mother	60	51	72	89	69
Season (% of cases)					
August	9.3	17.2	10.9	13.8	12 (CFR% 7.4%)
September	29.3	25.3	23.7	26.2	25 (CFR% 1.4%)
October	17.3	27.3	36.8	40.0	32.8 (CFR% 1.2%)
November	17.3	30.3	21.1	20.0	22.1 (CFR% 4.2%)
December	26.7	0	7.6	0	7.9 (CFR% 0%)
Health units available at local level (%)	52.0	25.3	34.2	32.3	34.8
Median time to reach health unit (75% percentile) (minutes)	1 (15)	15 (30)	15 (30)	15 (30)	15 (30)
Availability of pharmacy at local level (%)	30.7	68.7	4.5	28.5	23.8
Early action taken before admission	38/75 (50.7%)	81/99 (81.8%)	183/304 (60.2%)	37/65 (56.9%)	339/543 (62.4%)
Action taken at home	5/38 (13.2%)	63/81 (77.8%)	120/183 (65.6%)	7/37 (18.9%)	195/339 (57.5%)
Antimalarials given at home	4/5 (80.0%)	39/63 (61.9%)	69/120 (57.5%)	1/7 (14.3%)	113/195 (57.9%)
Medium time to reach the hospital by vehicle (hours)	1.5	1	1	0.5	2

CFR% = case-fatality rate%.

was 1 hour for all areas. Mean duration of malaria in children before admission was 4.46 (SD 2.57) days.

History of fever was reported in 528/543 (97.2%) of the cases. On admission, 480 had temperature of whom 16 (3.3%) developed hyperprexia (body temperature > 40 °C). Most of the children (95.7%) had a normal weight for age. Convulsions were reported in 255 children (47.0 %), anaemia (Hb count < 7 g/dL) in 337 (62.1%) and severe anaemia (Hb < 5 g/dL) in 90 (16.6%). Parasite count in leukocytes was carried out for 302 patients (55.6%). Heavy parasitaemia (number of parasites > 10 000/μL) was found in 218 cases (72.2%) (95% CI: 67%–72%). Heavy parasitaemia was the cause of anaemia in 131/187 cases (70.1%) (95% CI: 63%–77%). A total of 198 (36.5%) children presented with severe malaria and coma. Cerebral malaria was the commonest complication found in 453/543 (83.4%) children. Splenomegaly was found in 199 (36.6%) children and hepatomegaly in 122 (22.5%). Eleven children developed jaundice and only 1 with dark black urine died. Tests for thrombocytopenia were not done. Leukocytosis was found in 31/144 of cases (21.5%) (95% CI: 17%–30%) (Table 2).

Different clinical presentations were observed in different areas: Sennar had the largest presentation with coma 133/198 (67.2%), anaemia 200/337 (59.3%), and convulsions 148/255 (58.0%) (Table 3).

Omdurman hospital had the highest management performance index (80.2%) followed by Gedaref (54.5%), Wad Medani (52.3%) and Sennar (45.8%) (Table 4). Omdurman hospital reported the highest percentage (93%) in prescribing quinine as a first-line drug for severe malaria compared to Sennar (57%), Gedaref (46%) and Wad Medani (36%).

Table 2 **Symptoms, signs and laboratory data for all cases with severe malaria**

Variable	No. (%) (*n* = 543)
Symptoms	
Fever	528 (97.2)
Vomiting	222 (40.9)
Signs	
Anaemia (Hb < 7.5 g/dL)	337 (62.1)
Jaundice	11 (2.0)
Hepatomegaly	122 (22.5)
Splenomegaly	199 (36.6)
Coma	198 (36.5)
Convulsion	255 (47.0)
Laboratory abnormalities	
Haemoglobin < 5 g/dL (***n*** = 337)	90 (26.7)
White blood cell count > 11 000/mm^3 (***n*** = 144)	31 (21.5)
Haemoglobinuria	14 (4.2)
Blood sugar < 60 g/mL (hypoglycaemia)	113 (21.0)

In all, 14 out of 543 of the children died from severe malaria; total case fatality rate was 5 deaths per 1000 cases of children per month. Cerebral malaria was the commonest cause of death (11/14, 78.6%). Most of the children (93%) who died were under 9 years old: the risk of dying in children under 9 years was 4 times as high as in children over 9 years. Risk factors associated with high mortality were age under 9 years (RR = 4.8, 95% CI: 3.4–14.8), delay in seeking medical care (RR = 13.4, 95% CI: 9.1–20.6), coma (RR = 4.4, 95%CI: 1.2–13.3) (Table 5).

Discussion

Based on the results of this study, severe malaria in children was a disease of young

Table 3 **Distribution of the commonest clinical presentation of cases with severe malaria**

Clinical presentation	Sennar (n = 304) No. (%)	Wad Medani (*n* = 99) No. (%)	Gedaref (*n* = 65) No. (%)	Omdurman (*n* = 75) No. (%)	Total (*n* = 543) No. (%)	*P*-value
Convulsions	148 (58.0%)	36 (14.1%)	29 (11.4%)	42 (16.5%)	255 (100%)	0.02
Coma	133 (67.2%)	16 (8.1%)	30 (15.2%)	20 (10.01%)	198 (100%)	0.05
Anaemia	200 (59.3%)	76 (22.6%)	27 (8.0%)	34 (10.1%)	337 (100%)	< 0.0001

children where median age was 4 years; 75% of the children were under 6 years of age. Most deaths occurred in children under 9 years of age. This result is in line with previous studies done by Imbert and colleagues and Luxemburger and colleagues [*6,7*], both of whom reported that severe malaria cases and deaths decreased with increasing age. Similar results were also reported by Sodiomon in Burkina Faso who found the mean age of children with severe malaria was 4.33 (SD 3.03) years [*8*]

We found normal nutritional status in the children with severe malaria which is similar to the results of Esamai and colleagues in western Kenya [*9*] who reported that the majority of children with severe malaria (95.7%) had a normal weight for age.

Different distributions of cases were obtained in the different hospitals in our study. The majority of cases were found in Sennar (56.0%), an area of hyperendemicity located south-east of Khartoum and characterized by heavy rains. The clinical presentation of severe malaria was different in the different hospitals (Table 3). This result indicates that the epidemiological context influences the occurrence, presentation and mortality associated with severe malaria in different areas. The same results were also obtained by Sodiomon, who analysed severe malaria presentation in Ouagadougou university hospital compared to Sourou and Nayala district hospitals [*10*].

Severe malaria is a disease associated with low socioeconomic status, poverty and illiteracy. The majority of fathers and mothers were illiterate and did not act early against the disease nor seek treatment early. Delay in seeking treatment was a significant

Table 4 **Management performance index for optimum care of severe malaria in the children by hospital**

Hospital	BF	WBC	Hb	Blood glucose	Lumber puncture	Intravenous quinine	Total score	Management performance index (%)
Omdurman	0.95	0.95	1	0.97	0.01	0.93	4.81	80.2
Gedaref	0.89	0.40	0.78	0.72	0.02	0.46	3.27	54.5
Wad Medani	0.96	0.40	1	0.40	0.02	0.36	3.14	52.3
Sennar	0.98	0.11	0.14	0.95	0	0.57	2.75	45.8
Maximum score	1	1	1	1	1	1	6	100

BF = performance of thick and thin blood film for malaria; WBC = performance of white blood cell count; Hb = performance of haemoglobin count.

Table 5 **Risk factors for dying from severe malaria among the cases**

Risk factor	Died	Recovered	Total	Case-fatality rate (%)	RR (95% CI)	AR%
Age (months)						
1–108	13	382	395	3.3	4.8 (3.4–14.8)	79
> 108	01	144	145			
Delays						
Yes	12	46	58	20.7	13.4 (9.1–20.6)	93
No	2	128	130			
Coma						
Yes	10	188	198	5.1	4.4 (1.2–13.3)	77
No	4	341	345			

RR = relative risk; CI = confidence interval; AR = attributable risk.

risk factor associated with death due to severe malaria. The attributable risk percentage was 88% indicating that 88% of deaths could be avoided if delay was avoided. Ejov and colleagues from Myanmar, in a hospital-based study of severe malaria, reported that the proportion of deaths increased with longest duration of illness before admission [*11*].

Almost two-thirds of patients' families reported a lack of health units available at the local level. Strengthening local health systems is an important component of the WHO Roll Back Malaria programme and this needs the urgent attention of policymakers at the Federal Ministry of Health. The provision of proper disease management cannot be expected in the absence of formal health services as stated by WHO and it should always be a priority of government to improve the access of malaria patients to good quality care [*12*].

Early treatment before admission took place at home in the district hospitals (Sennar, Wad Medani and Gedaref) while in Omdurman city the first action was to visit the hospital. The commonest antimalarial used was choloroquine; this result is similar to what had been reported by Thera et al., who found that 75.8% of mothers in southern Mali managed their child's malaria at home and used both traditional and modern medicine [*13*]. These results highlight the importance of educating mothers on home treatment of malaria and when to seek medical help.

The clinical features of severe malaria in children included the occurrence of cerebral malaria (coma + convulsions) and severe anaemia. These were observed with various frequencies among the children in the different hospitals. Cerebral malaria was a contributory factor in 78.6% of the 14 deaths. No deaths occurred in Omdurman which had the highest management performance index (80.2%). This may be attributed to the high proportion of children receiving parenteral treatment initially in Omdurman.

Conclusion and recommendations

Severe malaria is a disease of small children and the deaths decreased by age. The occurrence and severity of the disease are affected by seasonality and it differs with

different areas and different epidemiological context. Age below 9 years, delay in seeking treatment and severity of the illness at admission are the major risk factors of disease mortality. Disease management performance index is better in the Omdurman compared with the district hospitals. In view of this, we consider that malaria severity could be reduced by improving peripheral health facilities, educating mothers on malaria home management and providing appropriate education to communities to avoid delay in seeking treatment. The malaria control strategy should consider the different epidemiological context in different states in Sudan.

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