Original article

Severe malaria among children in Gambella, western Ethiopia

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Abstract

Background: Most of the malarial morbidity and mortality occur in children and pregnant women. Annually 1-2 million children die of malaria in Africa. The information on the epidemiology of severe malaria among children in Ethiopia is scanty.

Objective: To assess the pattern of clinical features of severe malaria and their association with mortality.

Methods: A prospective study was conducted in the pediatric ward of Gambella hospital between June 1998 and November 1999. There were a total of 127 children with severe malaria. Demographic, clinical and laboratory data were collected using structured questionnaires.

Results: The mean age of the children was 36.7 months. The mortality rate was 22% and most deaths occurred in the first 24 hour (60.7%). The most common findings were anaemia (hematocrit <33%), nasal flaring, grunting, chest indrawing, diarrhea and convulsion in decreasing order. Anaemia was significantly linked to mortality when any signs of respiratory distress were present. A child with any sign of respiratory distress, with or without auscultatory chest finding, is at higher risk of dying. No association between coma and mortality was found. Impaired consciousness, with or without convulsion, was significantly associated with mortality.

Conclusion: A child with severe signs of respiratory distress and/or impaired consciousness is at increased risk of death. Hence they need prompt and early detection with effective management. [*Ethiop. J. Health Dev.* 2002;16(1):61-70]

Introduction

Malaria continues to be a major health problem in the world. Two billion people in the world are at risk of malaria infection, and each year 270 million people are infected. About 90% of affected people live in sub-saharan Africa, a region where malarial transmission is the highest in the world (1). There are about 1-2 million pediatric malaria deaths in Africa per annum(2).

Forty million people living in 75% of the land of Ethiopia are at risk from malaria. Four to five million people are affected annually. In Ethiopia, malaria transmission is unstable and seasonal which produces little immunity in the community; hence malaria epidemics are common and lead to high mortality and morbidity (4). Gambella is one of the areas of Ethiopia with high malarial endemicity. Hospital records indicate that in 1998, 20% of outpatient morbidity and 26% of deaths in this region were due to malaria.

Most of malarial morbidity and mortality occur in children and pregnant women. Children, particularly under-fives, are at risk of developing severe malaria due to their relatively less developed immunity to malaria and the decline of passively acquired immunity (5).

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The World Health Organization has proposed criteria of symptoms and signs for severe and complicated malaria. The manifestations of malaria for those living in endemic areas are more variable in infants and children. Many of them die of cerebral malaria, severe anaemia and repeated convulsions (6). Cerebral malaria and other severe manifestations occur most commonly between the ages of six months and three years in children living in endemic areas (7).

The clinical spectrum of severe malaria lies largely between cerebral malaria and severe anaemia. Impaired consciousness, respiratory distress, hypoglycemia and jaundice were identified as prognostic indicators of mortality in children. It was also shown that the World Health Organization criteria can be simplified to require bed side assessments of neurological involvement and respiratory distress for the purpose of identifying children at a higher risk of death (6).

The clinical features and patterns of severe malaria differ with respect to age and geographical location. It also varies with the intensity of malarial transmission. Cerebral malaria is a more common presentation of severe malaria in the Gambia while severe anaemia is the most common manifestation of severe malaria in children of Papua New Guinea. In adults with severe falciparum malaria, acute renal failure and pulmonary edema are the frequent causes of death. In contrast, children with this infection more commonly die of severe anaemia and lactic acidosis with hypoglycemia, although the exact cause of death is mostly unknown. Cerebral malaria, the most important severe manifestation, is associated with nearly 20% of mortality in different hospitals (7,8).

The purpose of this study is to assess the pattern of clinical features of severe malaria and their association with mortality, thereby identifying those children who are at increased risk of death. It also investigates socio-economic factors and health practices and their relation with the mortality.

Methods

Study design and area: A prospective study design was used to assess severe malaria in children. The study was conducted in Gambella Hospital, a regional hospital located in Gambella town, 777 kms from Addis Ababa. It is the only hospital in the region and serves nearly 200,000 people. Gambella is generally lowland, with an average altitude of 300-500m. Annual rainfall averages 1200mm. These environmental factors con-tribute to the endemicity of malaria in the region.

Study Period and Population: The study was conducted between June 1998 and November 1999 in the Pediatric ward of Gambella hospital. There were a total of 127 sick children who met the criteria for severe malaria used in this study.

Measurement and data collection: All mothers or guardians of children that participated in the study were interviewed and examined using structured questionnaires within at least twelve hours of their admission by the ward physician. All of the mothers or guardians were willing to participate in the study. Data on socio-economic characteristics, malaria prevention practices and clinical symptoms and signs were collected. Laboratory tests for blood film, blood cell count and hematocrit were performed within at least twelve hours of admission.

The duration of each symptom was measured in days except for convulsion and loss of consciousness which were taken in hours. The patient was examined for vital signs, sign of anaemia (pallor), signs of respiratory distress: nasal flaring, intercostal retraction, chest indrawing, auscultatory chest findings, hepatomegaly and splenomegaly. The level of consciousness was

assessed using the Blantyre Coma Scale. Any anti-malarial drugs that were given within 15 days prior to admission were recorded. Use of bed nets was confirmed if the child was sleeping under the bed net.

All children with assessment of severe malaria were treated with parentral quinine. Intrave-nous or rectal diazepam was given for convulsing children. Paracetamol was also given to febrile children with temperature of greater than 38.5^{o}C.

Data Analysis: Data was entered and analysed with the use of Epi Info Version 6 software. Continuous clinical variables were analysed using the Kruskal-Wallis test. Chi Square or Fisher's Exact test were used for categorical variables. Associations between severe features of malaria were also assessed using chi square in a two by two table. P-value was significant if it was less than 0.05.

Definitions :
Malaria - reported fever or temperature>37.5^{o}C and blood film revealing *Plasmodium falci-parum* asexual parasitemia (11).
Diarrhea - three or more loose stools in 24 hours.
Convulsion - reported or witnessed abnormal or generalized body movement (6).
Coma - a score of two or less in the Blantyre Coma Score (6).
Impaired Consciousness - a score of four or less in blantyre Coma Score.
Respiratory Distress - Presence of any of: nasal flaring, intercostal retraction, chest indrawing and grunting (8).
Chest Indrawing - a definite inward movement of the lower chest border on breathing in, and persistent (10).
Anaemia - Hematocrit <33% (10).
Severe Malaria - asexual parasitemia with at least one of the following (6).

- Coma
- Impaired consciousness
- Respiratory distress
- Convulsions > two in 24 hours
- Severe anaemia
- Renal failure
- Hypoglycemia
- Shock
- Spontaneous bleeding
- Hemoglobinuria
- Metabolic acidosis

Blantyre coma score for young children

Response	Score
Best motor response	
- Localizes painful stimuli	2
- withdraws limb from painful stimuli	1
- no response or inappropriate response	0
Best Verbal response	
- cries appropriately with painful stimulus or if verbal, speaks	2
- Moans or abnormal cry with painful stimulus	1
- no vocal response to painful stimulus	0
Eye Movement	
- watches or follows	1
- fails to watch or follow	0

Note - The Blantyre coma score is calculated by adding the scores for each response Max=5, Min=0

Result

From June 1998 to November 1999, a total of 127 children were found to have severe malaria according to the definition used in the study. Forty six percent of them were females. The majority of them were young children between the ages of 1-5 years. The mean age was 36.7 months. The mean number of live children was 2.5 per family. At least one child death was found in 22% of the families. Most of the children (74.8%) did not use bed nets. There was a 64.6% of chlo-roquine treatment and a 16.5% of sulfadoxine-pyrimethamine treatment prior to admission. Sixty six percent of children were treated with anti-fiver drugs before admission.

Table 1: **Age and sex distribution of deaths and survivors of the children, Gambella Hospital, June 1998-Nov. 1999.**

Age group (months)	Deaths		Survivors		Total
	M	F	M	F	
0-2	2	1	1	1	5
3-12	5	5	10	13	33
13-60	9	4	34	25	72
>60	1	1	7	8	17
Total	17	11	52	47	127

All children were reported to have fever of varying degrees. The major symptoms reported by the mother were in order of frequency: vomiting 82.7%, cough 52%, grunting 39%, convulsions 37.2% and diarrhea 32.3%. Only 23 mothers reported loss of consciousness in their child before admission. The mean duration of fever, vomiting, cough, grunting and convulsion were, 4.96, 2.23, 1.86, 0.69 (in days) and 5.03 (in hours) respectively. Loss of consciousness occurred in a mean duration of 8.5 hours.

The major findings observed were in the order of anaemia (78.8%), hepatomegaly (57.5%), flaring of ala nasi (56.7%), intercostal retraction (52.8%), splenomegaly (50.4%), and pale conjuctiva (49.6%). Most of the children were fully conscious with a Blantyre Coma Score of 5 (62.2%). Seventeen percent of children had a Blantyre Coma Score of 2 or less. The mean temperature and respi-ratory rate was 38.93^{0}C and 48.6/min respectively. The mean hematocrit was 36.7%. Anaemia was found in 79% of children while severe anaemia (hematocrit < 20%) was observed in 37.8% of children.

Table 2: **The distribution of Socioeconomic characteristics between survivors and deaths of the children, Gambella Hospital, Jun 1998-Nov. 1999**

Characteristics	Deaths	Survivors	Total	Chi-square	P-value
Maternal age (yrs)					
<20	5	9	14	3.47	NS
20-35	23	78	101		
>35	0	12	12		
Maternal education					
Illiterate	13	47	60	0.01	NS
1-6	8	23	31		
7-8	4	16	20		
9-12	1	8	9		
>12	2	5	7		
Family income (Birr per month)					
<100	10	32	42	0.17	NS
100-250	10	38	48		
250-500	8	24	32		
>500	0	5	5		

Table 3: **Distribution of preventive and treatment practices in deaths and survivors of the children, Gambella Hospital, Jun 1998- Nov. 1999.**

Prevention and treatment	Deaths	Survivors	Chi-square	Relative Risk	P-value
Bed net use					
No	6	26	0.27	1.24	0.63
Yes	22	95			
Chloroquine					
No	12	33	0.87	1.37	0.35
Yes	16	60			
Sulfadoxine Pyrimethamine					
No				5.35	
Yes	27	79	4.37		0.36
	1	20			
Antifever					
No	13	30	2.53	1.69	0.11
Yes	15	69			

The age distribution of different signs and symptoms was also evaluated. Cough was more common in the age group of 13 to 16 months, while grunting and vomiting were more common in infants. There were a total of 28 deaths with a mortality rate of 22%. Sixty percent of the deceased were males. The mean age at the time of death was 25.3 months, while the mean age of survivors was 37.8 months. Eighty two percent and 60.7% of the deaths occurred respectively within 48 and 24 hours of admission. The survivors stayed in hospital for a mean duration of 5.21 days.

Table 4: **The distribution of means of duration of symptoms between deaths and survivors of the children, Gambella Hospital, June 1998 - Nov 1999**

Symptoms	Deaths (X/SD)	Survivors (X/SD)	P-value
Fever	5.57(3.49)	7.78(3.01)	NS
Cough	3.21(3.57)	1.51(2.01)	0.01
Diarrhea	2.39(2.67)	0.84(1.63)	0.07
Vomiting	2.68(3.02)	2.10(2.54)	NS
Convulsion	5.72(8.63)	2.60(6.35)	0.01
Grunting	1.00(0.9)	0.59(1.67)	0.0006

The distribution of various characteristics, with their associations, was also analyzed between those who died and the survivors. No significant difference was seen between females and males. Generally, as the age increased above one year, the number of deaths increased significantly (chi-square for the trend=6.1, p-value<0.01). No statistical difference was seen in maternal age, family income and maternal education between the patients who died and the survivors. Additionally, no difference was found between those who used bed nets or received pre-treatment with chloroquine. However, children who were not treated with sulfadoxine-pyrimethamine prior to admission were

5 times more at risk of dying than those who were treated with sulfadoxine-pyrimethamine (RR= 5.37).

Grunting, diarrhea and convulsions were the most significant symptoms associated with mortality ($p<0.05$). Cough, vomiting and loss of consciousness were not significantly associated with mortality. As the frequency of convulsion increased, the risk of dying also

Table 5: **The distribution of clinical features between deaths and survivors of the children, Gambella Hospital, June- 1998 Nov. 1999**

Clinical Feature	%	Deaths	Survivors	Chi-square	Relative Risk	CI	P-value
Symptoms							
Vomiting	82.7	25	80				NS
Cough	52	19	47				NS
Grunting	39	19	31	12.21	3.25	1.6,6.6	0.0004
Convulsion	37.2	15	32	4.23	1.96	1.03,3.76	0.03
Diarrhea	32.3	16	25	10.14	2.8	1.46,5.35	0.01
Loss of consciousness	19	6	15				NS
Findings							
Temperature		38.9	38.8				NS
RR/min		55.5	46.7				0.04
Pale conjunctiva		15	48				NS
Nasal flaring		23	49	9.48	3.51	1.43,8.65	0.02
Intercostal retraction		24	43	15.65	537	1.98,14.6	0.0000
Chest indrawing		16	23	11.80	11.80	1.58,5.74	0.0006
Crepitations		9	20				NS
Hepatomegaly		19	54				NS
Splenomegaly		15	49				NS
Impaired consciousness		21	35	13.92	3.80	1.74,8.34	0.00019
Coma		7	16				NS
Hematocrit <33%		23	78				NS
Hematocrit <20%		13	27				NS

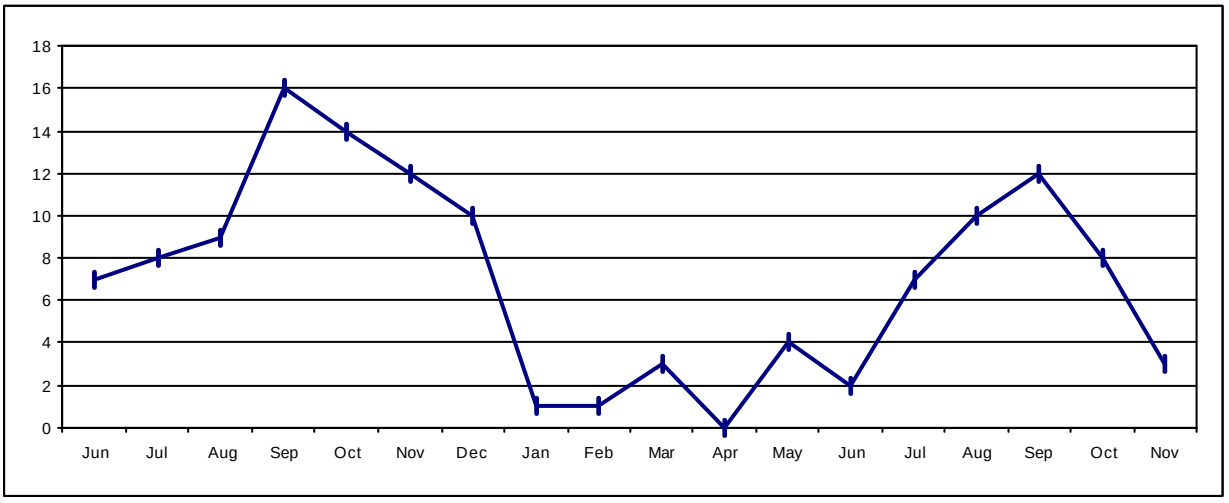

Figure 1: The seasonal pattern of severe malaria in children in Gambella hospital between June 1998-Nov.1999.

Table 6: **The associations among significant mortality associated clinical features of the study children, Gambella Hospital, June 1998 - Nov. 1999.**

	Convulsion	Diarrhea	Impaired consciousness	Respiratory distress
Severe anaemia	P=0.267	P=0.39	P=0.31	P=0.02
Respiratory distress	P=0.07	P=0.602	P=0.63	
Impaired consciousness	P=0.000	P=0.97		
Diarrhea	P=0.212			

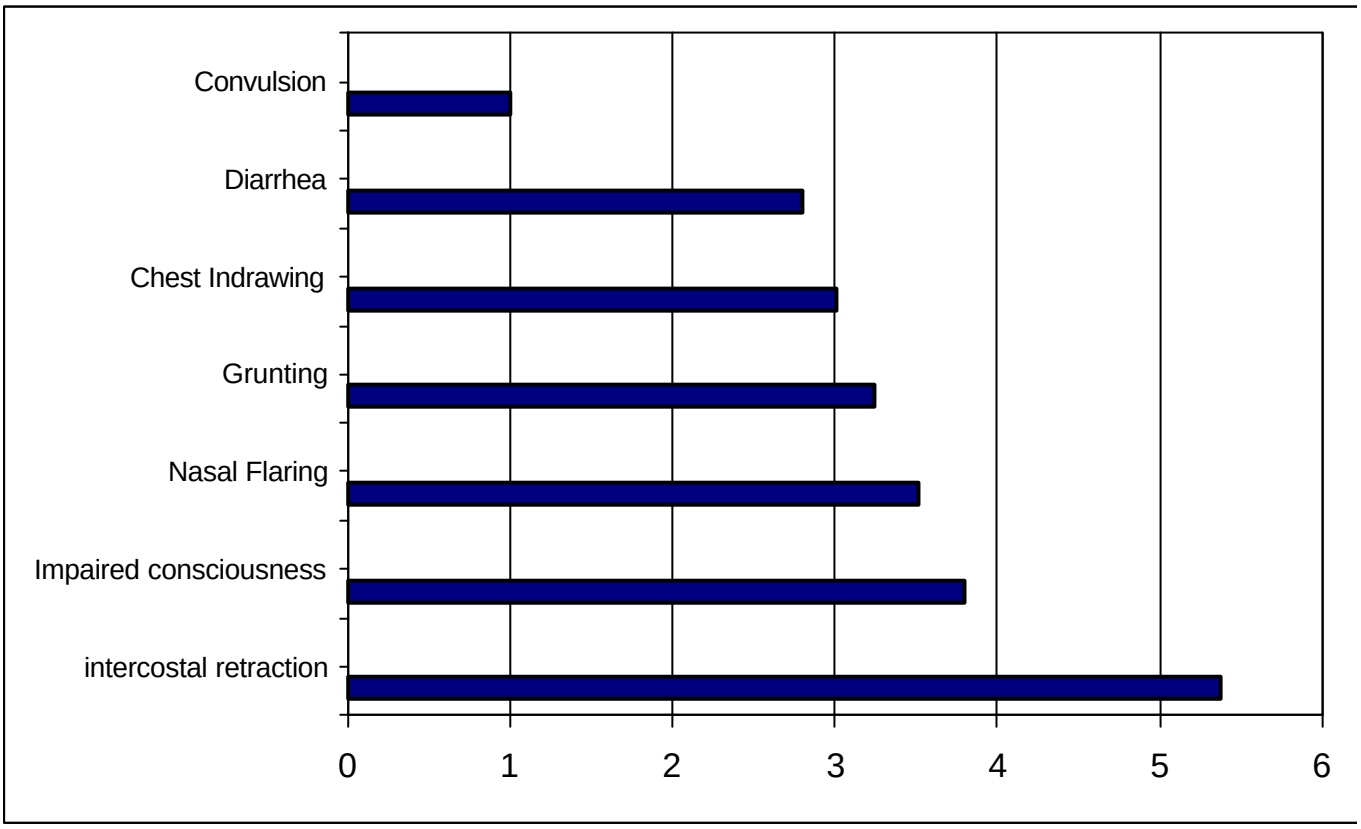

Figure 2: **The relative risks of the significant mortality associated clinical features of the study children, Gambella Hospital, June 1998- Nov. 1990**

increased significantly (chi square for trend =4.27). The difference of the durations of cough, diarrhea, convulsion and grunting between those who died and those who survived was statistically significant. The respiratory rate in the patients who died was greater than that of the survivors by a mean of 10 per minute ($p< 0.05$). No significant difference was observed regarding temperature between the two groups.

The most significant findings associated with mortality were intercostal retraction, impaired consciousness, chest indrawing and flaring of ala nasi, respectively. Neither hematocrit <33% (anaemia) nor hematocrit <20% (severe anaemia) were significantly associated with mortality. However, impaired consciousness was associated significantly with mortality, even when

excluding those who were comatose. The case fatality rates of coma, impaired consciousness, anaemia and respiratory distress were 7/23, 21/56, 23/01 and 24/64, respectively.

The association between the significant clinical features was also investigated. A statistical significant association was observed between severe anaemia and respiratory distress and between convulsion and impaired conscious-ness. The significant association observed between respiratory distress and mortality, disappeared when children with severe anaemia were excluded from those with respiratory distress ($p<0.05$). However, the association with mortality became extremely strong when children with both anaemia and respiratory distress were analyzed. Respiratory distress remained strongly associated with mortality, regardless of the presence or absence of aus-cultatory chest findings (crepitations). The seasonal variation of severe malaria is also shown in Fig 1.

Discussion

To the best of our knowledge, this is the first study to examine severe malaira in children in Gambella region. Malaria is one of the five leading causes of child mortality and morbidity in the Tropics (9). It is often life threatening among children and pregnant women whare it is severe and complicated (7). Severe malaria is a multi-system disease with a spectrum of various features. It accounts for 90% of mor-tality associated with *Plasmodium falciparum* worldwide. World Health Organization has def-ined a standard criteria for recognition and management of severe malarial disease. However, there have been clinical variations observed in African children. There may also be differences in age and level of endemicity (6). Our study tries to investigate the patterns of severe malaria with the association and risks of mortality in the study children. Though the common features of severe malaria in children are cerebral malaria and severe anaemia, the number of cases could have been more if more investigations were added.

The mortality rate in our study, 22% is not beyond expectation as the region is one of the high malaria endemic areas. The mortality rate was higher than that found in Kenya (10%). As the age of the child increases, the risk of dying also increases significantly (Chi-square for the trend=6.1). This could be due to the relative decline of passively acquired immunity. The study conducted in Kenya showed a fewer number of deaths that occurred within 2 days (27%) than that of our study (82%). This could indicate that the children were seriously ill when they came to hospital and it might have been too late to intervene. This is most likely in the 17 children who died on the day of admission (60.7%) (11).

The most common clinical features associated with death in another Kenyan hospital were impaired consciousness, respiratory distress, hypoglycemia and jaundice in their order of importance. In our study, however, respiratory distress, particularly intercostal retraction, impaired consciousness and convulsions were the prominent features associated with mortality.

Respiratory distress is gaining a prognostic importance in severe malaria although it received little attention in the past. It may potentially result from several underlying processes acting alone or in combination. In non-immune adults with severe malaria, respiratory distress is a grave sign, often ref-lecting pulmonary edema. This type of respiratory distress is uncommon in African children. It could be considered typical of heart failure due to severe malarial anaemia. Our finding that respiratory distress is significantly associated with severe anaemia may support this explanation. Furthermore, the significant association of respir atory distress with mortality disappears when those with either anaemia or severe anaemia are excluded from the analysis. Lactic acidosis, which is documented as a predictor of death in many studies, can also result in respiratory distress (6). Pneumonia coexisting with malaria may also result in respiratory distress. However,

regardless of the presence or absence of auscultatory chest findings, crepitations; respiratory distress maintains its strong association with mortality. A child with both respiratory distress and anaemia was 2.6 times at risk of dying than the others, indicating anaemia as a possible cause of respiratory distress in our study.

Anaemia is an important cause of morbidity and probably mortality in patients with acute *Plasmodium falciparum* infection and it is also one of the complications of malaria in endemic areas (11). In this study, any degree of anaemia alone, whether it is severe or not, was not associated with mortality. This was similar to a study done in the Gambia that indicated that anaemia alone was not a cause of death in patients with severe malaria (2). However, anaemia in combination with other severe features may result in death. Anaemia can worsen acidosis, thereby respiratory distress, by impairing tissue oxygenation (6). Although anaemia was the most common severe manifes-tation in the study in papua New Guinea, it was not a cause of death (8). This was similar to the findings in our study and the Gambian study. However, in Kenya, the risk of dying increased with anaemia and younger age (11).

The preventive and therapeutic measures taken by mothers depend on the level of education and family income. Although no association was found between anti-fever treatment and mortality in our study, systematic treatment of fever was attributed to a low mortality due to malaria in Congo-Brazzaville. The same study revealed the ineffectiveness of the use of untreated bed nets in reducing mortality (13). This keeps with our result that no association was observed between not using bed nets and mortality. However, it is known that impregnated bed nets can significantly reduce the child morbidity and mortality in malaria endemic areas. The finding that children unt-reated with sulfadoxine-pyrimethamine prior to admission have a five times greater risk of dying has some important implication. It shows the current level of effectiveness of the drug in line with its being the first line drug against uncomplicated falciparum malaria by the National Malaria Guideline of Ethiopia. Secondly, it might show that effective and prompt treatment of non-severe and uncomplicated malaria cases could result in reducing the mortality.

Conclusion

Some conclusions can be drawn from this study. A single criteria may not be appropriate or applicable to every child living in malarious areas, in order to detect life-threatening malaria. However, this study could have included some investigations to diagnose more features of severe and complicated malaria.

Regardless of the presence or absence of auscultatory chest findings, a child with a single sign of respiratory distress is at risk of dying and therefore should be managed promptly and effectively as a case of severe and life-threatening malaria. This does not depend on the variety of the sign: flaring of ala nasi, intercostal retraction, grunting and chest indrawing. However, conditions which may be associated with respiratory distress, such as hyperpyrexia, should also be taken into account.

Any level of impaired consciousness, with or without coma, warrants prompt intervention as a case of severe malaria. It alone indicates increased risk of dying and does not depend on the presence or absence of anaemia or convulsion. Any degree of anaemia combined with any sign of respiratory distress should be regarded as a sign of life-threatening malaria and deserves appropriate management. Cur-rently, the use of sulfadoxine-pyrime-thamine must be encouraged for those children with non-severe and uncomplicated malaria, as a failure to use it is associated with increased mortality as it is observed in our study.

It is known that malaria can result in diarrhea in children. Since the level of dehydration is not determined in our study, the association observed between diarrhea and mortality requires further investigation. There may also be a mere seasonal overlap between the two. Further studies are also needed to determine the relationship between the respiratory rate and severity of malaria at a level of cut-off point. Although our study vividly shows a strong association between respiratory distress and mortality, the cut-off respiratory rate was not determined. However, the mean res-piratory rate for those who died was greater than that of the survivors by 10/min. ($P<0.05$).

Health education should target mothers to bring their child to hospital as early as possible. This is shown by the fact that there was a significantly longer duration of symptoms, except fever, in those who died than the survivors. This could also be a reason for a rela tively higher case fatality rate of severe malaria (22%) in combination with the pitfalls in the overall care of the sick child. Detecting those at risk of dying, as shown above, as early as possible and particularly those who did not take sulfadoxine-pyri-methamine, will help in reducing the mortality through prompt and effective management. Integrated management of childhood illness should be implemented for it is sensitive and effective in early detection and treatment of common childhood diseases (12).

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