Journal of Pediatric Sciences

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Journal of Pediatric Sciences 2013;5:e189

How to cite this article:

Ansong D, Osei-Akoto A, Owusu SK, Boakye I, Nguah SB, Sambian DJ, Sylverken J, Arhin B. Haematological indices, nutritional assessment and mortality outcome of children presenting with severe malaria to a tertiary hospital in Ghana. Journal of Pediatric Sciences. 2013;5:e189

ORIGINAL ARTICLE

Haematological indices, nutritional assessment and mortality outcome of children presenting with severe malaria to a tertiary hospital in Ghana

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Abstract:

Background: *Severe malaria in children remains the commonest clinical disease in the paediatric emergency units of most hospitals in sub-Saharan Africa. Anaemia and nutritional deficiency are associated with severe malaria. The aim of the study was to describe the haematological indices, nutritional status and mortality among children admitted in a tertiary hospital in Ghana with severe malaria.* ***Methods:*** *We conducted a prospective cross-sectional study documenting the haematological, nutritional indices and mortality outcomes of children less than five years reporting to the Komfo Anokye Teaching Hospital with severe malaria.* ***Results:*** *The study recruited four-hundred-and-eight (408) children between April, 2005 and July, 2006. There were 231 males (57%). The median age was 21 months, (1QR: 4-54months). 36 (8.8%) patients had weight-for-age z-score <-3; 101 (24.7%) had z-score ≥-3 to < -2; 130 (31.9%) had z-scores ≥-2 to <-1 and 141 (34.6%) had z-scores ≥-1. The mean haemoglobin level was 6.2g/dl (SD=2.2, 95% CI: 6.0-6.4). The mean haemoglobin levels of children with normal, mild, moderate, and severe malnutrition were 6.5g/dl, 6.0g/dL, 6.0g/dL, and 6.0g/dL, respectively, p=0.15. The overall case fatality rate was 4.9%. Children with malnutrition (weight-for-age z-score ≤-2) had a significantly higher case fatality rate of 8.0% (11/126) compared to those with z-score > -2, 3.3% (RR=1.7, 95%CI: 1.1-2.6, P=0.038).* ***Conclusion:*** *Malaria in children under five remains a principal cause of morbidity and mortality. The study did not find any association between the haemoglobin levels and the nutritional status. However, Mortality was associated with malnutrition (weight-for-age z-score ≤-2) in this study.*

Keywords: *Malnutrition; Severe malaria; Haematological indices; Children*

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Introduction

Malaria kills about 750,000 people each year worldwide, and about 90% of these deaths occur in the sub-Saharan Africa(1). A significant proportion of these deaths (70%) occurs in children living in the rural areas of Africa, where access to health and medicine is poor (2).

Malnutrition and anaemia are two clinical conditions that are common in children living in the sub-Saharan Africa (3,4). They contribute significantly to the under-five mortality directly or indirectly by complicating diseases like malaria, broncho-pneumonia, and diarrheal diseases (2-5). Anaemia

presents alone or concurrently with malnutrition in infants and young children living in the sub-Saharan Africa and both conditions are associated with high morbidity and mortality (5). The Ghana Demographic and Health Survey in 2003 indicated that, three-quarters of Ghanaian children between 6 and 59 months have anaemia. Of these, 23% are mildly anaemic, 47% moderately anaemic, with 6% severely anaemic (6). Prevalence of anaemia among children is higher in rural areas (80%) than in urban areas (68%). The survey report further stated that 30% of children under five are stunted, 11% severely stunted, 7% of the children wasted, and 1% severely wasted (6). 22% are underweight, with 5% severely underweight (3,6,7). In Ghana, the high prevalence of anaemia and malnutrition together with malaria are major public health concerns (8). Anaemia and malnutrition potentially could impact on the outcome of children reporting to the emergency units with severe malaria. The present study sought to describe the haematological indices, nutritional status, and mortality outcomes of severe malaria in children reporting to the Paediatric Emergency Unit (PEU) of a tertiary hospital in Ghana.

Material and Methods

Study Design

A prospective cross-sectional study was conducted between April 2005 and July, 2006 in the Paediatric Emergency Unit (PEU) of the Komfo Anokye Teaching Hospital, Kumasi, Ghana. All children aged between 3 and 59 months diagnosed with Plasmodium falciparum malaria were eligible for inclusion in the study.

Study Site

The Department of Child Health of the Komfo Anokye Teaching Hospital has 200 beds with a bed occupancy rate between 80 and 120%. The average monthly admissions to the PEU is 450 children with about 40% of these cases being children under five years (KATH, Department of Statistics) (9). In the rainy season, about 48% of these children have laboratory-confirmed severe malaria. The most prevalent parasite is Plasmodium falciparum. Malaria transmission is perennial with peak transmission occurring during the rainy season. There are two main seasons: the wet season, which starts from April, and ends in October; and the dry season, which begins in November and ends in March.

Sample Size

A sample size of 408 children based on a 95% confidence interval with a power of 80% to detect a relationship between the nutritional status and the outcome of malaria, with margin of error of 5% was applied in this study

Study procedure

All children reporting to the PEU undergo screening for malaria parasitemia in their peripheral blood smear. Those with positive malaria smear (i.e. the presence of any malaria parasite load) and within the age 5-59 months and satisfied the WHO criteria for severe malaria were recruited after written informed consent had been signed by the parent or legal guardian (10). The weight measurements with age were converted to standard normal z-scores for the patients using Epi-Info 3.2.1. Weight-for-age z-scores were divided into four categories of nutritional status based on their z-scores: no malnutrition (normal), mild, moderate, and severe malnutrition as (>-1), (<-1 to -2), (<-2 to -3) and (<-3), respectively. Anaemia was classified as severe (haemoglobin level < 5.0g/dL), non-severe (haemoglobin level 5.1-9.3g/dL) and normal (haemoglobin above 9.4g/dL) (11). About 5mls of blood was used for Complete Blood Count (CBC) using a Sysmex Haematology analyzer. Thin and thick blood films were prepared for each patient using the Giemsa staining method. A 1:10 dilution of the Giemsa stain in buffered water (pH 7.2) staining was done for 15 minutes, slides dried and examined under a microscope using oil immersion, at 100X magnification objective. Malaria parasites were counted per 200 WBCs on the thick film and the result calculated per L after determining the actual WBC count on a Sysmex Haematology analyzer. The study outcome was mortality or survival during hospitalization.

Data Analysis

Data was exported from Epi-Info version 3.2.1 to Stata version-8 Intercool. Summary statistics of the baseline characteristics was conducted. Univariate analysis on baseline characteristics of the population of children used in the study was determined. Comparative descriptive analysis of outcome variables based on the presence of haemotransfusion and survival with the nutritional status was conducted using chi-square test. The mean and standard deviation with 95% confidence interval for the haematological indices were determined and

Table 1. Demographic and clinical Status with nutritional status

Characteristics	Nutritional Status				
	No Malnutrition n (%)	Mild n (%)	Moderate n (%)	Severe n (%)	p-value
Age					
<12	31(29.8)	40(38.5)	24(23.1)	9(8.7)	
12-23	36(31.9)	38(33.6)	29(25.7)	10(8.9)	
24-35	47(47.0)	24(24.0)	22(22.0)	7(7.0)	
36-47	17(32.1)	16(30.2)	12(22.6)	8(15.1)	
48-59	10(26.3)	12(31.6)	14(36.8)	2(5.3)	
Total	*141(34.6)*	*130(31.7)*	*101(24.8)*	*36(8.8)*	*0.20*
Sex					
Male	71(30.7)	86(37.3)	52(22.5)	22(9.5)	
Female	70(39.5)	44(24.9)	49(27.7)	14(7.9)	
Total	*141(34.6)*	*130(31.9)*	*101(24.7)*	*36(8.8)*	*0.04*

stratified according to the nutritional status. Median and range were used to describe skewed haematological distributions. ANOVA was applied to determine statistical significant difference. P-value of 0.05 used to determine the level of statistical significance.

Ethics

Authorization to conduct the study obtained from the Institutional Review Board (IRB) of the Kwame Nkrumah University of Science and Technology (KNUST) and the Komfo Anokye Teaching Hospital (KATH) Kumasi-Ghana.

Results

A total of four-hundred-and-eight (408) children were admitted to the study within the period, April, 2005 to July, 2006. The total number of males was 231, representing 57%, with a male-to-female ratio of 1.3:1 (Table 1).

About 8.8% had a weight-for-age z-score of <-3 representing Severe Malnutrition, and 24.8% had their weight-for-age z-scores between ≥-3 and <-2 representing moderate malnutrition. More than a third of the children presenting with severe malaria were classified as No Malnutrition (weight-for-age z-score ≥-1) (Table 2).

A mean haemoglobin level of 6.2g/dL (SD=2.2, 95% CI: 6.0-6.4g/dL) was observed. Haematocrit and red cell count were similarly low (Table 2). The median parasite density was 55,012.5/µL ranging between 120 and 1,224,068/µL in the study population (Table 3).

The mean MCV and the MCHC were within normal ranges with no statistically significant relationship on the nutritional status (Table 4). The mean (SD) haemoglobin levels of children with mild, moderate, and severe malnutrition was 6.0g/dL. There was no statistically significant difference (P=0.15) between the haemoglobin levels of children with severe malnutrition and children with mild and moderate malnutrition. Children with severe malnutrition had the lowest mean haemoglobin level. The mean MCH, MCHC, and MCV levels were within normal limits for all categories of the nutritional status (Table 4).

Table 2. The distribution of the weight-for-age categories of children aged 3-59 months admitted to the Paediatric Emergency Unit

Z-score category	Weight-for-Age Classification	
	n (%)	Classification
<-3	36 (8.8)	Severe
≥-3 to <-2	101 (24.8)	Moderate
≥-2 to <-1	130 (31.9)	Mild
≥-1	141 (34.6)	No malnutrition

The study showed that about 35.8% (n=139) had severe anaemia and only 7.7% (n=30) presented with no anaemia (Table 5).

The overall case fatality rate was 4.9% (20/408). Moderate and severe malnutrition (weight-for-age z-score ≤-2) had a significantly higher case fatality rate of 8.0% (11/137) compared to those who had no or

Table 3. Haematological indices of children aged 3-59 months admitted to the study

Statistic	Mean	SD	Range	95% CI
Haemoglobin (g/dl)	6.2	2.2	1.5-13.4	6.0-6.4
Pack cell volume	18.6	6.4	4.4-37.3	18.0-19.2
MCHC (g/dl)	2.0	33.3	24.6-39.5	33.1-33.5
MCV(fL)	73.7	8.6	47-110.5	72.9-74.6
MCH (pg)	25.0	4.3	15.1-37.7	24.5-25.4
RBC (/uL)	2.5	0.9	0.6-5.5	2.4-2.6
*Platelet count/x 10^9/L	81.5		2.6-611	
*Parasite density	55012.5		120-1244068	
*WBC x 10^9/L	11.65		1.9-57	

*Median values provided

Table 4. Relationship between the haematological indices of children aged 3-59 months and their nutritional status

	Nutrition Status				
Characteristics	Normal Mean(sd)	Mild Mean(sd)	Moderate mean(sd)	Severe Mean(sd)	p-value
Haemoglobin (g/dL)	6.5(2.2)	6.0(2.2)	6.0(2.3)	6.0 (1.9)	0.15
Haematocrit (%)	19.7(6.3)	18.52(8.1)	18.05(6.4)	18.03(5.8)	0.29
MCH (pg)	25.1(3.7)	25.34(5.7)	24.47(3.2)	24.52(2.6)	0.35
MCV (fl)	74.1(8.7)	73.65(8.7)	73.70(8.4)	72.74(8.4)	0.87
MCHC (g/d	33.5(2.8)	33.43(2.1)	33.02(1.9)	33.41(1.5)	0.44
RBC $X10^{12}$/L	2.6(0.9)	2.39 (0.9)	2.45 (0.9)	2.34 (0.7)	0.41
*Platelet count	67	101	85	66	0.07
*Parasite count	199803	124994	151843	130975	0.56
*WBC	11.1	1			

mild malnutrition (weight-for-age z-score ≥ -2) 3.3% (9/271) (RR=1.7, 95%CI: 1.1-2.6, P=0.038) (Table 6).

Discussion

Majority of the cases of severe malaria in children on admission in this study area was associated with anaemia, mean haemoglobin on admission of 6.17g/dL. This is an expected finding and similar to other studies of children with severe malaria (5,12–15,16). The development of anaemia in children with malaria has been well document in a review by Menendex C et al.

Potential contributing factors are the degree of parasitemia with the resultant splenic destruction of the parasitized and the non-parasitized red cells and the level of malnutrition (17). Hookworm infestation was not assessed in this study. It could be another key contributing factor in considering the source of anaemia in these children as been reported in other studies (18,19). The low levels of haemoglobin could be the result of repeated non-symptomatic and clinical malaria infections in the study subject as has been reported in other studies (20). The presence of high levels of Plasmodium falciparum parasitemia in healthy children is known and it contribution to

Table 5. Level of anaemia and nutritional status of children aged 3-59 admitted into the study

	Malnutrition (Weight-for age z scores)				
Level of anaemia	Normal n (%)	Mild n (%)	Moderate n (%)	Severe n (%)	Total n (%)
Severe anaemia	39 (29.1)	47 (37.4)	41 (43.2)	12 (36.4)	139 (35.8)
Non severe anaemia	81 (61.2)	70 (55.6)	48 (50.5)	27 (57.6)	219 (56.5)
Normal	13 (9.7)	9 (7.1)	6 (6.3)	2 (6.1)	30 (7.7)

Table 6. Survival status of children with no or mild malnutrition with moderate to severe malnutrition reporting with severe malaria

Characteristics	Nutritional Status		OR	95% CI	p-value
	Weight-for-Age z-score ≥ -2	Weight-for-Age z-score ≤-2			
Survival					
Died	9(3.2)	11(8.0)			
Survived	262(96.8)	126(92.0)			
Total	*271(100.0)*	*137(100.0)*	*1.7*	*1.1-2.6*	*0.038*

the development of anaemia (21–23). In a study done in northern Ghana, 22% of the individuals examined during the low transmission season had malaria parasites in their peripheral blood smear, and 68% had malaria parasites during the high transmission season (24). Similarly, a study conducted to determine the prevalence of malaria parasitemia in children living in an urban area in the Ashanti region of the study area demonstrated 37.8% asymptomatic parasitemia in children (25). The risk implication is that a significant proportion of children living in the malaria endemic area could have reduced baseline haemoglobin. These children could develop severe anaemia when they develop overt malaria.

It is evident from this study that malnutrition is a significant problem in children under five years reporting with malaria. Over 8% of the children reported with Weight-for-Age z-score <-3, and about 33.58% of the children at presentation had moderate-to-severe malnutrition using the WHO classification. This is slightly lower than the 60% prevalence of malnutrition in children living in rural communities of Ghana (26–29). The prevalence is higher in the part of Ghana. (26,30,31).

The case fatality of 4.9% observed in this study appears to be on the lower end of the range of mortalities reported elsewhere in Africa (32). A study conducted in northern Ghana found a slightly lower case fatality of 3.5% (26). In Africa, case fatality from severe malaria has marked variability depending on the clinical settings (20). Mortality from severe and complicated malaria can be extremely high in settings with limited facilities for diagnosis and treatment, whereas, in tertiary and specialized institutions, mortality is low mainly because of the specialized care. There was however, a statistical significant difference in the proportion of children who died and had weight-for-age z-score ≥ -2; (P=0.038). Similarly, studies have found that children with malnutrition weight-for-age in the lower quartile were more likely to die from malaria (OR: 2.1, 95% CI= 1.3-3.5) (26) (32).

The Study conducted within specific working hours (between 8.00am to 5.00 pm). Severely ill children brought to the hospital during late hours in the study setting were not included, and it could under estimate the clinical problem.

Conclusions

Low haemoglobin levels and malnutrition are essential clinical conditions associated with severe malaria in the study area. Moderate and severe malnutrition are risk factors associated with mortality in children with severe malaria in this study.

Acknowledgments

The following individuals supported the conduct of the study: Kofi Aikins, Debora Okyere Darko, Maxwell Owusu, David Ntiamoah Fosu, all of the Komfo Anokye Teaching Hospital.

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