RESEARCH PAPER

Factors Associated with Mortality in Under-Five Children with Severe Anemia in Ebonyi, Nigeria

VIVIAN U MUONEKE, ROLAND C IBEKWE, *HENRIETTA U NEBE-AGUMADU AND BEDE C IBE

*From the Department of Pediatrics, Ebonyi State University, Abakaliki, Ebonyi State; *Department of Pediatrics, University of Abuja, Abuja; and +Department of Pediatrics, University of Nigeria, Enugu Campus, Nigeria.*

Correspondence to: Dr Vivian Uzo Muoneke, Department of Pediatrics, Ebonyi State University, Abakaliki, Ebonyi State, Nigeria. vizym@yahoo.com

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Objective: To determine the risk factors associated with poor outcome among under-five children with severe anemia in sub Saharan Africa.

Design: Cross-sectional.

Setting: University Teaching Hospital, Nigeria.

Participants: Under-five children presenting with severe anemia (PCV ≤15%, Hb ≤5g/dL).

Methods: Between January and June 2006, children admitted with severe anemia were recruited. The biodata, socio-economic status, signs and symptoms were documented for each child after the initial stabilization. Laboratory investigations using blood, stool and urine samples were carried out. Data were analyzed using SPSS version 11.0.

Results: 140 out of the 1,450 patients admitted during the period of study had severe anemia (prevalence 9.7%). Malaria either alone or in combination was the most common cause of severe anemia [n=90 (64.3%)]. 117 patients (83.6%) recovered, while 4(2.8%) left against medical advice and 19 died (case fatality rate 13.6%). The variables associated with mortality were malnutrition (*P*=0.02), tachycardia (*P*= 0.03), coma (*P*<0.001), and absence of blood transfusion (*P*=0.001). On logistic regression analysis coma (*P*=0.002), not receiving blood transfusion (*P*=0.002) and female gender (P=0.04) predicted poor outcome.

Conclusions: The study revealed high mortality rates among under-five children with severe anemia. Coma, malnutrition, female gender and absence of blood transfusion were associated with higher mortality in severe anemia.

Key words: *Anemia, Causes, Death, Malaria, Nigeria.*

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Severe anemia is a common blood disorder in children from developing [1,2]. Mortality rates from severe anemia are high in these regions with high levels of poverty, infections and malnutrition in addition to the problems of inaccessible and poorly funded health facilities [3-6].

Urgent blood transfusion is generally the mainstay of treatment however, despite blood transfusion, a number of children with severe anemia still die [2,4,6-8]. We conducted this study to improve our understanding of the probable risk factors associated with poor outcome in children with severe anemia.

METHODS

This cross-sectional study was conducted at the Children's Emergency Unit and the Children's Outpatient Department of Ebonyi State University Teaching Hospital, Abakaliki, Ebonyi State, Nigeria. This hospital is a major referral center for other health institutions located within and around the Abakaliki metropolis. About 60,000 patients are seen annually in the hospital and children constitute about 10% of this population (unpublished hospital data).

The study area, Abakaliki, is the capital of Ebonyi State and is located in the South Eastern part of Nigeria, covering an area approximately 51 km^2, with an atmospheric temperature of 30^0C. It has an estimated population of 255,000 people who are predominantly small to medium-scale farmers, civil servants, and traders.

Between January and June 2006, a consecutive sample of children aged 6 to 60 months who presented at the Outpatient Department and the Children's Emergency Room with a primary diagnosis of severe anemia (defined

as a hemoglobin concentration of ≤5.0g/dL or PCV of ≤15%) [8,9] were recruited. A minimum sample size of 110 was obtained using the formula for calculating sample size in a finite population [9], based on severe anemia prevalence of 7% in under-5 African children [10], attrition rate of 10% and the number of under-5 presenting in the hospital in 2005 (5749). Children who had received blood transfusion within the previous 3 months were excluded. Recruited subjects with obvious life-threatening conditions were stabilized before history was taken. The study was approved by the ethics committee of the Ebonyi State University Teaching Hospital, Abakaliki, and an written informed consent was obtained from the parent or the guardian of each child.

A detailed history including socio-demographic data was collected from all patients; social class was determined using the highest educational qualification and occupation of both parents as suggested by Oyedeji [11]. Complete physical examination including vital signs and anthropometric assessment were Taken according to standardized procedure [12,13]. The nutritional status was assessed using Wellcome classification [14]. Presence of tachycardia, tachypnea, tender hepatomegaly, abnormal cardiac rhythm (gallop rhythm), with or without peripheral pedal edema (in the older children) were taken as indicators of congestive cardiac failure [12,13].

Samples of blood, urine, and stool were collected according to standard techniqueand sent to the laboratory for analysis within 24 h or refrigerated at temperatures between 4 and 8°C. 5mL of blood was collected from the median antecubital vein. Peripheral blood films were examined for determination of presence of asexual form of malaria parasites. Hematological parameters namely packed cell volume (PCV), hemoglobin concentration, white blood cell (WBC) count and hemoglobin electrophoresis were estimated for all children. PCV and hemoglobin were assessed using the micro-hematocrit technique and cyanmethemoglobin method respectively. Hemoglobin electrophoresis was carried out using the cellulose acetate electrophoresis method. The mean cell hemoglobin concentration (MCHC) was used as suggesting the presence or absence of iron deficiency. Iron studies were not done. Children with low MCHC were assumed to have iron deficiency anemia [15]. Biochemical and direct microscopic analysis of all stool and urine samples was done. Cultures of blood and urinewere done for selected subjects based on their presenting history, clinical condition and on the outcome of their initial laboratory tests. Blood culture was done according to standard methods [16] for only subjects with a history of fever, abnormal white cell count/differentials on admission and in other subjects who continued to have fever despite initial medical treatment. All study subjects with positive cultures were regarded as having septicemia.

Urine samples with positive dipstick findings (positive urine nitrate) and microscopic findings (high WBCs per high power field and presence of bacteria) qualified for urine culture using blood agar. All those with fever and positive urine cultures were regarded as having urinary tract infections. Stool culture was not done in any participant. All subjects were admitted and managed according to a standardized protocol. Outcome following treatment/blood transfusion was categorised as survived, died or left against medical advice.

The data collected were entered into the data editor of Statistical Package for Social Sciences (SPSS) software package version 11.0. Analysis was based on simple percentages, proportions, charts and tables. The influence of sex, age, socio-economic status of the parents, certain clinical findings and disease presence (malaria, septicemia, malnutrition and hemoglobinopathies) on the outcome of severe anemia was assessed. Differences in proportions were compared using the chi square statistic. Where figures in the table were too few for the chi square test, Yates correction test was used. Logistic regression was done to determine the factors that are predictive of poor outcome among the study population. Statistical significance was set at $P< 0.05$.

RESULTS

A total of 140 under-five children were enrolled. There were 76 (54.2%) boys. The mean age of the patients was 25.1±16.7 months with majority of the patients(89, 63.6%) below 2 years of age. Most patients (114, 81.4%) belonged to the lower social classes. The PCV levels ranged between 5-15 % with a mean level of 11.8±3.0%. Temperature ranged between 34.3°C with a mean of 38.12±1.0°C; 71.4% of patients (*n*=100) had pyrexia. Presenting features of enrolled children are depicted in ***Table* I**. 13 (9.3%) children were comatosed on admission. Based on the defined criteria, 74 (52%) children were in congestive cardiac failure on presentation. Antropometric assessment revealed that 104 patients (74.3%) had normal weight measurements, 33 (23.6%) were undernourished while 3 (2.1%) were severely malnourished. 126 (90.0%) children were transfused.

Malaria was the commonest condition causing severe anemia among the enrolled children (77, 55%) while 13 (9.3%) patients had malaria in combination with other

TABLE I CLINICAL FEATURES OF THE PARTICIPANTS WITH SEVERE ANEMIA (*n*=140)

Clinical features	*Frequency (%)*	
Symptoms		
Breathlessness	104	(74.3)
Fever	100	(71.4)
Weakness	45	(32.1)
Vomiting	26	(18.6)
Convulsion	19	(13.6)
Anorexia	15	(10.7)
Cough	11	(7.9)
Diarrhea	9	(6.4)
Signs		
Pallor	140	(100.0)
Hepatomegaly	114	(81.4)
Splenomegaly	78	(55.7)
Jaundice	21	(15.0)
Gallop rhythm	20	(14.3)
Pedal edema	3	(2.1)
Others	15	(10.7)

causes. Other common causes include sepsis 19 (13.6%), sickle cell anemia 13 (9.3%) and malnutrition/ iron deficiency anemia 10 (7.1%).

117 (83.6%) patients recovered, 4 (2.8%) were discharged against medical advice and 19 (13.6%) died. Fourteen of the 19 children (73.68%) died within 24 hours of admission. Severe malaria was the most common diagnosis in the deceased (*n*=11) septicemia (*n*=5). Next being 13 (68.42%) were tranfused while 6 (31.58%) did not receive blood transfusion. All the children that were not transfused died within 2 hours of presentation while those that were transfused survived for longer periods. ***Table* II** highlights the factors associated with poor outcome in children with severe anemia. Logistic regression analysis of factors with predictive influence on mortality in severely anemic children revealed that presence of coma (*P*=0.002), not receiving blood transfusion (*P*=0.002) and sex (*P*=0.04) increased the likelihood of mortality in severely anemic children.

TABLE II ASSOCIATION BETWEEN CLINICAL AND LABORATORY VARIABLES AND MORTALITY OF SEVE-RELY ANEMIC CHILDREN IN EBSUTH, ABAKALIKI

Variables	*Recovered (n=121)*	*Died (n=19)*	*P value*
Age (mths)			
< 24	67	12	0.53
>24	54	7	
Female sex	53	11	0.25
PCV (%)			
5-10	49	5	0.24
11-15	72	14	
Social class			
I	7	0	0.32
II	17	2	
III	52	6	
IV	45	11	
Malaria parasitemia			
Negative	24	2	0.33
Positive	97	17	
Fever	83	14	0.81
Hypothermia/subnormal	6	2	
Normal	28	3	
Respiratory distress	88	16	0.29
Tachycardia	77	17	0.03
Associated factors			
Malaria + combined	11	2	
Sepsis	7	5	
SCD	12	1	0.10
Malnutrition	10	0	
Others	11	2	
Helminthiasis	2	0	
Malaria	68	9	
Cardiac failure	62	12	0.33
Not in cardiac failure	59	7	
Blood transfusion			
Transfused	113	13	0.001
Not transfused	8	6	
Consciousness status			
Conscious	116	11	<0.001
Coma	5	8	
Splenomegaly	83	15	

DISCUSSION

The hospital case fatality rate of 13.6% in the present report is within the reported range in Africa [3,4,6,7,] but is higher than the 5.6% reported by Ojukwu [5] from this facility. This difference could be due to the differences in subjects' selections as their definition of severe anemia was packed cell volume of less than 20% and the age category was for children below 12 years, this postulation is supported by the finding that most of the deaths in that report occurred in children less than five years old.

Existing guideline in managing severe anemia highlight that mortality in children with severe anemia is high at hemoglobin lower than 4g/dL or the presence of respiratory distress at higher hemoglobin levels [17].

However, in this report, neither tachypnea nor hemoglobin level was found to have any influence on outcome. Tachycardia on the other hand was found to be significantly associated with poor outcome. In view of the lack of association between cardiac failure and outcome, how tachycardia alone leads to poor outcome is not clear.

The importance of blood transfusion in the management of childhood severe anemia is supported by the finding of increased fatality among untransfused children in the present report [7,8,17]. However, those who died without transfusion, died within two hours of presentation. This supports the contention of Lackritz, *et al*. [7] that these children were very ill and their deaths may not have been prevented by blood transfusion. With the risk of transmission of the human immunodeficiency virus type-I (HIV-I), the use of blood transfusion in the management of severe pediatric anemia has become an important clinical decision problem in Africa [18,19].

The association of the syndrome of severe anemia, respiratory distress and coma, and poor outcome in African children with severe malaria has been previously reported [20]. This is partly supported by the finding of a significant association between poor outcome and the presence of coma in the present report. Since most of the cases that presented in coma had malaria, they were likely to be cases of cerebral malaria which is known to be associated with poor prognosis [20,21].

Various studies in sub Sahara Africa report that about 50% of under-five deaths can be attributed to malnutrition and the contribution of malnutrition to mortalitly in children with diarrhea, pneumonia, measles and malaria has also been well documented [22]. It is imperative to further elucidate the contribution of the complex interplay of malaria, malnutrition and anemia in morbidity and mortality of children in sub-Sahara Africa [23-25].

Though more males presented with severe anemia, there were more female deaths. Previous studies from United States of America (Blacks) [26] and India [27] have confirmed this trend. In India, it was reported that due to cultural preference for males, female children were brought to health facilities in more advanced stages of illness than males, less money were spent on drugs for them, and they were taken to less qualified health practitioners [27,28]. There is a need to conduct local studies to elucidate if the same reasons are responsible for the gender difference in mortality in Nigeria.

Severe under-five anemia in this area is associated with significant fatality. Mortality appears to be worse when it is associated with coma, malnutrition, female gender and absence of blood transfusion. Health workers should therefore seek out these children for improved attention, so that if the high case fatality rate can be improved.

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