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In-hospital mortality attributable to severe anaemia and associated clinical signs in children admitted at hospitals in Bushenyi district

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Abstract

Severe anaemia is one of the important causes of admissions and deaths among children in majority of African countries, especially in Sub-Saharan Africa. East Africa is one of the regions that have the highest burden of anaemia in the world. In Uganda, severe anaemia complicates one third of hospital admissions and with associated increased mortality. Many of the studies on severe anaemia which have done in Uganda are community based and on specific populations like HIV infected children. This study described the in-hospital mortality attributable to severe anaemia and associated clinical signs among children admitted at all hospitals in Bushenyi district. This was a cross sectional descriptive and analytical study that consecutively enrolled 225 children aged 2 months to 12 years admitted at hospitals in Bushenyi district, Kampala International University Teaching Hospital, Comboni Hospital and Ishaka Adventist Hospital from April 2017 to December 2017. Data was collected using a structured questionnaire and analyzed using STATA version 14. We determined the proportion of children who had severe anaemia and died in the course of admission and the clinical signs at admission that were associated with mortality using bivariate and multivariate logistic regression. The proportion of severely anaemia children who died was 8.4%. The clinical signs at admission that were independently associated with mortality were coma [aOR=5.97, (95%CI, 1.94-18.36), p=<0.002] and tachypnea [aOR=6.02, (95%CI, 1.44-25.14), p=<0.014]. The in-hospital mortality attributable to severe anaemia among children admitted to hospitals in Bushenyi district is high. The clinical signs at admission that were significantly associated with mortality were tachypnea and coma. We therefore recommend that clinicians should routinely do hemoglobin concentration screening for all admitted children and give the appropriate emergency and long term management. Clinicians may use coma and tachycardia to triage severely anaemic children.

Keywords: Severe anaemia; Attributable clinical signs; In-hospital mortality

1. Introduction

Anaemia is defined as hemoglobin or hematocrit level below normal for the age, sex, altitude and physical state of an individual(Kliegman et al., 2015). It is not a diagnosis, but it is a sign of a severe underlying disease. Severe anaemia is hemoglobin concentration less than 7 g/dl in children 2 - 59 months and 8.0 g/dl for children 5 – 12 years (WHO, 2011). It is a global public health problem affecting 43% of young children under five years of age and 25% of children 5–15 years with Africa being most affected with a prevalence of 62.3%(WHO, 2015). It is the second leading nutritional cause of disability associated with poor health, physical and mental development, reduced academic achievement and national economic growth (WHO, 2015). Severe anaemia is among the leading causes of death in children admitted to hospitals in Sub-Saharan Africa with a prevalence ranging from 8% to 29% and case fatality rate of 9-18 % in hospital-based studies (Biemba et al., 2000). In East Africa, severe anaemia complicates one third of childhood admissions with

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associated increased mortality particularly in Uganda where the prevalence is 33% and a case fatality rate of 15.4% (Kiguli et al., 2015). The clinical presentation at admission, underlying cause, availability and timing of treatment intervention was found to determine the treatment outcome (Adegoke et al., 2012).

In East Africa particularly Uganda, where severe anaemia complicates one third of hospital admissions and with associated increased mortality, many of the studies done are community based and on specific populations like HIV infected children. Therefore, this study described the in-hospital mortality attributable to severe anaemia and associated clinical signs among children admitted at hospitals in Bushenyi district.

2. Material and methods

2.1. Study Design, Site and Study Population

This was a hospital based cross-sectional descriptive and analytical study that determined the mortality attributable to severe anaemia and its associated clinical signs among severely anaemic children aged 2 months to 12 years admitted at hospitals in Bushenyi district. The study was carried out in the pediatric wards of hospitals in Bushenyi district which include Kampala International University Teaching Hospital, Ishaka Adventist Hospital and Comboni Hospital and they are the only health facilities in the district offering blood transfusion services.

Kampala International University Teaching Hospital is the teaching hospital of Kampala International University. It is situated in Ishaka town, Bushenyi district in western Uganda, about 58 Km along Mbarara-Fortportal high way. Kampala International University-Teaching Hospital is a specialized teaching hospital and it receives patients from the community and health units in and around Bushenyi district. It is a private for profit hospital and it admits about 3793 pediatric patients per year, has a pediatric ward bed capacity of about 100 and admits on average 10 patients per day. The hospital offers free efficient blood transfusion services and blood is usually available for patients. The blood bank is about 100 metres from the pediatric ward and it operates 24 hours a day. The ward is run by six specialists, seven senior house officers, five intern doctors, four intern nurses and 11 qualified nurses. The laboratory offers basic hematological investigations like complete blood count, grouping and cross matching, peripheral blood film, blood smear for malaria parasites and iron studies. Ishaka Adventist hospital is a private for profit hospital located in Ishaka town, Bushenyi district, about 60 Km along Mbarara-Fortportal high way. The pediatric ward has a capacity of 10 beds and admits on average 2 patients per day and about 700 patients per year. Comboni hospital is a private not for profit(PNFP) hospital located 80km from Mbarara town along the Mbarara-Kasese high way, 15Km from Bushenyi district headquarters and 2 Km from the Mbarara Kasese high way. The pediatric ward has a bed capacity of 25 beds and admits on average 3 patients per day and 900 patients per year.

The sample size was calculated using the Kish and Leslie formula. Children aged 2 months to 12 years who were admitted to these hospitals with severe anaemia from April 2017 to December 2017 and met the inclusion criteria were consecutively enrolled until the sample size of 225 was attained.

2.2. Study Procedure

All children aged 2 months to 12 years admitted to the pediatric wards through accident and emergency and outpatient departments were assessed for eligibility using hemoglobin concentrations obtained by auto-hematology analyzer (Midrey BC 3000 plus and Sysmex kx-21.n models). Those who had severe anaemia (Hb < 7g/dL for children below 5 years and Hb < 8g/dL for children 5-12 years of age), their caregivers got a full explanation of the purpose of the study and were requested to sign a written informed consent statement or use a thumb print for those who couldn't write in order to participate in the study. After which thorough history and physical examination was done. All the study participants were followed up for treatment outcome within the first 48 hours of admission. The treatment outcome was taken after 48 hours because most severe anaemia attributable mortality occurs within this period.

2.3. Data management

Data from pre-coded and completed questionnaires were entered using statistical computer package software Microsoft excel 2016, it was cleaned, checked for errors, corrected and was then exported to STATA version 14, for analysis and summarized in frequency tables. The in-hospital mortality was calculated by obtaining the proportion of those who died among the severely anaemic children. The clinical signs associated with mortality were obtained by preforming bivariate and multivariate logistic regression analysis. Factors with a p-value less than 0.2 on bivariate logistic regression analysis were subjected to multivariate logistic regression. Factors with p-value of less than 0.05 were considered to be statistically significant.

2.4. Ethical considerations

Approval was sought from the Research and Ethical committee of Kampala International University and Mbarara University of Science and Technology Institutional Review Committee and from the departments of pediatrics of the hospitals in Bushenyi District where the research was carried out.

An informed consent form was signed by parents/care takers before conducting the study. All children were assessed for eligibility and enrolled into the study after the reason for hospitalization was taken care of.

3. Results

3.1. Description of the study participants

A total of 2808 children aged 2 months to 12 years were admitted at the study sites in the period between April 2017 and December 2017, Kampala International University Teaching Hospital, Comboni Hospital and Ishaka Adventist Hospital. See figure 1 below for details.

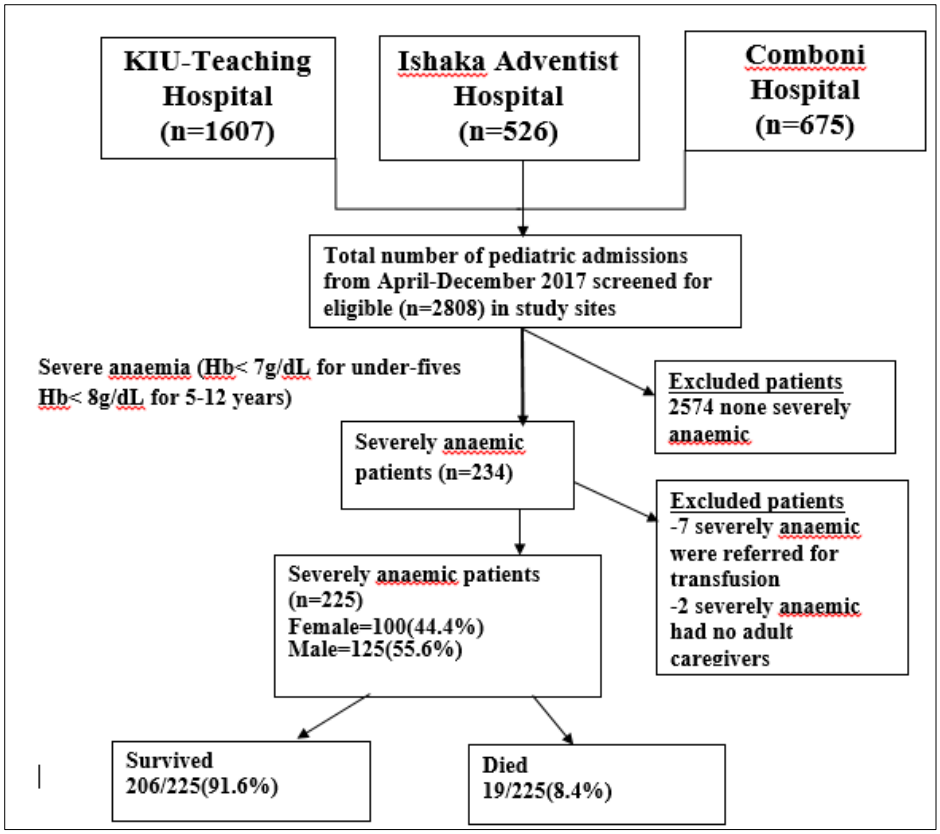

Figure 1 Flow chart of the distribution of patients in the study

3.2. Socio-demographic characteristics of the study population and their caregivers

Majority of the children (71.6%) were under-fives and 55.6% were males. Majority of the caregivers were biological parents (97.3%), Banyankole (79.1%), and came from Bushenyi district (42.2%) and Rubirizi district (31.1%). They were mainly peasant farmers (72.9%), married (89.9%) and only 6.7% had attained tertiary level of education.

3.3. Clinical symptoms of the study participants

The patients had at least one symptom at admission. Majority of the children had fever (85.3%), vomiting (60.9%), cough (46.2%) and difficulty in breathing (46.2%). Other symptoms included general body weakness (36.0%), irritability (24.0%), convulsions (27.6%), headache (17.3%), dizziness (16%), loss of consciousness (12.0%), cola urine (12.9%), body swelling (6.7%), and 4.0% had pica.

3.4. Clinical signs of the study participants

The patients had at least one clinical signs at admission. Majority of the children had respiratory distress (47.1%), tachypnea (47.1%), tachycardia (33.8%), gallop rhythm (29.8%), hepatomegaly (29.3%), jaundice (27.1%), coma (15.6%) and hypothermia (10.2%). A small number of the children had angular stomatitis (6.2%), pedal edema (4.9%), koilonychia (2.2) and atrophic glossitis (1.8%).

3.5. Proportion of children with severe anaemia

Out of the 2808 screened children, 225(8.1%) had severe anaemia. Majority of the patients were under-five years (71.6%).

3.6. Mortality attributable to severe anaemia

Of the 225 severely anaemia children, 19 (8.4%) died. Out of the 19 deaths, 8(42.1%) occurred before blood transfusion and 13(68.4%) of them occurred within the first 24 hours of admission. The medical conditions diagnosed among the deaths were; complicated malaria 11(57.9%), severe sepsis 3(15.8%), severe pneumonia 4(21.0%) and liver cirrhosis 1(5.3%)

3.7. Clinical signs associated with mortality

Table 1 Binary logistic regression analysis of the clinical signs associated with mortality among severely anaemic children aged 2 months to 12 years admitted in hospitals in Bushenyi district from April to December 2017

Variable	No death n=206	Death n=19	cOR (95% CI)	P value
Age in yrs				
5.00-12.00	63(98.44)	1(1.56)	1.00 (-)	-
1.10- 4.99	105(93.75)	7(6.25)	4.2(0.50-34.94)	0.18
≤ 1.00	38(77.55)	11(22.45)	18.24(2.26-146.90)	**0.006**
Hypothermia				
No	186(92.04)	16(7.96)	1.00	0.41
Yes	20(86.96)	3(13.04)	1.73(0.46-6.47)	
Jaundice				
No	150(91.46)	14(8.54)	1.00	0.94
Yes	56(91.80)	5(8.20)	0.96(0.33-2.78)	
Coma				
No	178(95.70)	8(4.30)	1.00	**0.001**
Yes	28(71.79)	11(28.21)	8.74(3.23-23.62)	
Under nutrition				
No	16(90.96)	16(9.04)	1.00	0.54
Yes	45 (93.75)	3(6.25)	0.54(0.19-2.40)	
Tachycardia				
No	146 (97.99)	3(2.01)	1.00	**0.001**
Yes	60(78.95)	16(21.05)	12.98(3.65-46.18)	
Tachypnea				
No	116(97.48)	3(2.52)	1.00	**0.008**
Yes	90(84.91)	16(15.09)	6.87(1.94-24.32)	
Respiratory distress				

No	110(97.35)	5(2.65)	1.00	
Yes	96(85.71)	14(14.29)	6.11(1.73-21.61)	**0.005**
Fine crepitations				
No	181(92.36)	15(7.65)	1.00	
Yes	25(86.21)	4(13.79)	1.93(0.59-6.28)	0.27
Jugular venous pressure				
No	157 (95.15)	8(4.85)	1.00	**0.003**
Yes	49(81.67)	11(18.3)	4.41(1.68-11.57)	
Gallop rhythm				
No	152(96.20)	6(3.80)	1.00	
Yes	54(80.60)	13(19.40)	6.10(2.21-16.84)	**0.001**
Hepatomegaly				
No	166(94.86)	9(5.14)	1.00	
Yes	40 (80.00)	10(20.00)	4.61(1.76-12.10)	**0.002**

cOR= Crude odds ratio. CI=Confidence interval.

Table 1 above shows binary logistic regression analysis of the clinical signs that were associated with mortality among severely anaemic children aged 2 months to 12 years admitted to hospitals in Bushenyi district from April to December 2017. The clinical signs that were significantly associated with mortality were infancy, tachycardia, tachypnea, respiratory distress, gallop rhythm, hepatomegaly, and coma. Children below 1 year of age were 18.24 times more likely to die compared to those who were above 1 year of age (cOR 18.24, 95%CI 2.26-146.90, p=0.006). Those with coma were 8.74 times more likely to die compared to conscious children (cOR 8.74, 95%CI 3.23-23.62, p=0.001). The presence of cardio-respiratory signs like tachypnea, features of respiratory distress, tachycardia, gallop rhythm, and hepatomegaly increases the likelihood of dying by 6.87 (cOR 6.87, 95%CI 1.94-24.32), p=0.008), 6.11 (cOR 6.11, 95%CI 1.73-21.61, p=0.005), 12.98 (cOR 12.98, 95%CI 3.65-46.18, p=0.001), 6.10 (cOR 6.10, 95%CI 2.21-16.84, p=0.001) and 4.61(cOR 4.61, 95%CI 1.76-12.10, p=0.002) respectively.

Table 2 Multivariate analysis of the clinical signs associated with mortality among severely anaemic children aged 2 months to 12 years admitted in pediatric wards of hospitals in Bushenyi district from April to December 2017

Variable	**aOR(95% CI)**	**p-value**
Coma		
No	1.00	-
Yes	5.97(1.94-18.36)	**0.002**
Tachycardia		
No	1.00	-
Yes	6.02(1.44-25.14)	**0.014**
Tender hepatomegaly		
No	1.00	-
Yes	2.41(0.77-7.48)	0.129
Raised JVP		
No	1.00	-
Yes	1.72(0.18-9.10)	0.806
Tachypnea		

No	1.00	-
Yes	1.63(0.22-11.83)	0.629
Respiratory distress		
No	1.00	-
Yes	1.28(0.55-5.37)	0.349

aOR= Adjusted odds ratio. CI=Confidence interval.

Table 2 below shows the clinical signs that were independently associated with mortality among severely anaemic children aged 2 months to 12 years admitted in pediatric wards of hospitals in Bushenyi district from April to December 2017. All the clinical signs at bivariate logistic regression analysis that had a p value of less than 0.2 were together considered for multivariate logistic regression analysis. The clinical signs which were independently associated with mortality were coma and tachycardia. Children with coma 5.97 times more likely to die compared to the conscious ones (aOR 5.97, 95%CI, 1.94-18.36, p=0.002) and those who had tachycardia were 6.02 times likely to die compared to those with normal heart rate (aOR 6.02, 95%CI 1.44-25.14, p=0.014).

4. Discussion

4.1. Mortality attributable to severe anaemia

The proportion of severely anaemic children who died was 8.4%. (Biemba et al., 2000) found the case fatality attributable of severe anaemia in Sub-Saharan Africa at 9-18 % which is similar to the proportion we got in our study. Nigerian studies by (Muoneke & Chidiibekwe, 2011) and (Adegoke et al., 2012) also found similar study findings. This could be because most of the areas Sub-Saharan Africa are endemic to malaria which is the commonest cause of severe anaemia due to acute hemolytic anaemia. An East African study by (Kiguli et al., 2015) found a case fatality rate of 15.4% which is about two times the proportion we got in this study. The difference could be because they carried out the study among very sick febrile children who had an increased risk of death, but we studied all severely anaemic children irrespective of their state of health.

4.2. Clinical signs associated with mortality

At bivariate logistic regression, the clinical signs that were associated with mortality were infancy, tachycardia, gallop rhythm, tender hepatomegaly, tachypnea and respiratory distress and coma. However, at multivariate logistic regression, the clinical signs that were independently associated with mortality were tachycardia and coma. Similar clinical signs were found to be associated with mortality in Nigerian studies by Adegoke et al., (2012) and (Muoneke & Chidiibekwe, 2011). The similarity could probably be because of the similar study settings. The area in Nigeria were the studies were conducted are endemic for malaria which is the case for our study site. Patients in our study and their studies presented with fever, convulsions, loss of consciousness and features of acute hemolysis which was attributed to severe malaria.

In this study, severely anaemic children who died were significantly younger than the survivors. Under-fives, particularly infants were more likely to die compared to children 5 years and above. This could be because younger children, particularly infants, toddlers and preschool, tend to develop severe anaemia more rapidly during acute hemolytic processes because of their low iron stores secondary to high iron demands for rapid growth and poor immune response to P. falciparum infection. Low iron stores also result from poor weaning practices like early mixed feeding and use of inappropriate feeds like large volumes of cow milk during infancy.

Majority of the study participants had fever, jaundice and cola colored urine which are features of acute hemolysis that led to rapid fall in hemoglobin concentration and features of cardiac failure like tachypnea, tachycardia, gallop rhythm, respiratory distress and hepatomegaly. The presence of these features increased case fatality rates of severely anaemic children by more than 5 times. These clinical signs could result from the low oxygen carrying capacity of blood due to low hemoglobin concentration which leads to tissue hypoxia, lactic acidosis and metabolic acidosis.

The presence of coma as a presenting sign increased the case fatality rate of severely anaemic children by more than 6 times. Children with severe anaemia may present with coma owing to metabolic acidosis due to lactic acidosis and hypoxia secondary to rapid reduction of hemoglobin concentration and decreased oxygen carrying capacity of blood. Coma could also be attributed to acute central nervous system infections like cerebral malaria, meningitis and

encephalitis that may cause cerebral edema, hypoxia, cerebral thrombosis, electrolyte imbalance (especially sodium) and metabolic disorders like hypoglycemia.

5. Conclusion

Mortality attributable to severe anaemia in Bushenyi district hospitals is very high. The clinical signs that were independently associated with mortality in children with severe anaemia were tachycardia and coma in Bushenyi district hospitals.

We therefore recommend that clinicians should routinely do hemoglobin concentration screening for all admitted children and give the appropriate emergency and long term management. Clinicians may use coma and tachycardia to triage severely anaemic children.

Compliance with ethical standards

Acknowledgments

I want to acknowledge and thank Dr. Kalubi Peters and Prof. Melvis Bernis for supervising my research. I also thank the caregivers who allowed their children to participate in the study.

Disclosure of conflict of interest

All authors declare that they have no competing interests.

Statement of ethical approval

Approval was sought from the Research and Ethical committee of Kampala International University and Mbarara University of Science and Technology Institutional Review Committee and from the departments of pediatrics of the hospitals in Bushenyi District where the research was carried out.

Statement of informed consent

A written informed consent was obtained from all individual participants (parents/care takers) included in the study.

Availability of data and materials

Important data for this paper are contained in the manuscript. Individual patient data are not shared in this work due to ethical reasons.

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