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Original Research Article

Etiological Profile of Severe Anemia Requiring Red Cell Concentrate Transfusion in a Pediatric Tertiary Care Center

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Abstract:
Objective: To determine the frequency of etiological factors leading to severe anemia requiring Red Cell Concentrate transfusion in children. ***Study Design:*** A descriptive cross-sectional study. ***Place and Duration of Study:*** Department of Paediatrics, Ayub Teaching Hospital, Abbottabad, Pakistan, from 12th May 2025 to 12th October 2025. ***Methodology:*** A total of 77 children aged 1 to 15 years with severe anaemia requiring at least one red cell concentrate transfusion were included through consecutive sampling. Children with trauma-related transfusion, malignancy or chronic kidney disease were excluded. Clinical assessment and relevant laboratory investigations were performed to identify the underlying causes. Categorical variables were presented as n (%) and quantitative variables as mean ± standard deviation. Chi-square test and Fisher exact test were used for association analysis, with p-value ≤0.05 considered significant. ***Results:*** The mean age was 8.86 ± 4.11 years and mean weight was 31.52 ± 11.48 kg. Males were 48 (62.3%) and females 29 (37.7%). Most children belonged to low socioeconomic status 42 (54.5%) and rural areas 50 (64.9%). Iron deficiency anaemia was the most frequent aetiology 28 (36.4%), followed by sepsis 12 (15.6%), thalassaemia 11 (14.3%), malaria 8 (10.4%) and sickle cell disease 5 (6.5%). Sepsis was associated with age ≤10 years (p=0.002), iron deficiency anaemia with younger age (p=0.003), and thalassaemia with age >10 years (p<0.001). Thalassaemia was also associated with male gender (p=0.045). ***Conclusion:*** Iron deficiency anaemia was the main cause of severe anaemia requiring transfusion, while socioeconomic and demographic factors showed important associations with some aetiologies.

Keywords: Anaemia, Children, Iron deficiency, Malaria, Red cell transfusion, Sepsis, Thalassaemia.

INTRODUCTION

Anemia is a common disorder in children characterized by a reduction in number of red blood cells or hemoglobin concentration of the blood, thus compromised tissue oxygen delivery.1 Anemia may be presented by such symptoms as fatigue, pallor, irritability, and growth retardation.2 Children's anemia has multiple different etiologies from deficiencies (iron, B12, folic acid deficiency) to chronic disease, hereditary diseases, and acute/chronic blood loss.3 The most frequent form of children's anemia is iron deficiency anemia, most often caused by a diet that is medically inadequate in iron intake or impaired absorption.4 Untreated, the condition can result in such complications as growth retardation, immune system failure, and in exceptionally rare scenarios, heart failure.5

Severe anaemia in children is likely to require urgent treatment, and treatment most commonly is the transfusion of Red Cell Concentrate (RCC).6 This is commonly indicated if hemoglobin levels fall very

low, perhaps as low as 7 g/dL, and/or if the presentation is extreme, such as with extreme weakness, tachycardia, dizziness, and even respiratory compromise.7 Transfusions of RCC are effective to quickly improve the oxygen-carrying capacity of the blood, especially in children who are not supported by oral or intravascular iron replacement therapy.8 It is particularly valuable in the setting of anaemia due to acute haemorrhage (for example, following trauma or surgery) as well as haemolytic or chronic anaemia with complicating background disease states such as in sickle cell disease or thalassemia.8

The etiologic profile of childhood severe anemia is multifactorial in nature and is commonly a result of a combination of both pathological as well as dietary factors.9 Iron deficiency anemia is the most common cause in limited-resource worlds, followed by excessive blood loss as a result of parasitic infestations such as hookworm infection or malaria.9 Hemolytic anemias such as sickle cell disease, hereditary spherocytosis, and thalassemia are common in populations with high genetic predispositions.10 Chronic inflammatory disorders, cancer, as well as bone marrow failure syndromes also cause severe anemia.11 In a small number of situations, acute blood loss from trauma or gastrointestinal bleeding may cause severe anemia.12

A large evidence gap has been reported in local studies on the etiologic profile of severe anemia requiring Red Cell Concentrate transfusion among children. Anemia is a very common condition globally, especially among children, yet no local studies were conducted systematically to study the local etiologic factors. It is essential to identify the etiologic factors of severe anemia to formulate targeted interventions, maximize the treatment plan, as well as avoid transfusion-related complications. The study endeavors to fill the gap in a lack of local studies and provide valuable information regarding local etiologic factors to ensure proper management as well as prevention of children's severe anemia.

METHODOLOGY

This cross-sectional study was conducted from 12th May 2025 to 12th October 2025 in the Pediatrics Department of Ayub Teaching Hospital Abbottabad. A total of 77 children were included in the study. The sample size was calculated by using WHO calculator with 95% confidence interval, 7% margin of error and expected frequency of sepsis as 11% from previous reference study.13 Children were selected through non-probability consecutive sampling technique.

Children aged 1 to 15 years of either gender were included. Those having severe anemia as per study criteria and who had received at least 1 blood transfusion documented in medical record were also included. Children with history of trauma-related transfusions, malignancies or chronic kidney disease were excluded.

Ethical approval was obtained from the ethical committee of Ayub Teaching Hospital, Abbottabad, under Ethical Certificate Ref. No. RC-EA-2025/88, before commencement of data collection. Written informed consent was obtained from parents or legal guardians before collection of data.

Demographic information was recorded including age, gender, weight, residency, socioeconomic status and parent's education. Detailed history was taken and clinical examination was performed during hospital admission and throughout hospital stay. Particular attention was given to symptoms and clinical findings related with severe anemia and its possible causes. Laboratory investigations were reviewed according to clinical requirement, including haemoglobin level, peripheral blood smear, serum ferritin, serum iron, total iron-binding capacity (TIBC), haemoglobin electrophoresis, blood culture and malaria diagnostic tests. The transfusion history was also checked from medical record, and children were followed during hospitalisation to identify the underlying etiological factors.

After completion of clinical assessment, laboratory investigations and hospital follow-up, severe anemia requiring Red Cell Concentrate transfusion was considered when haemoglobin level was below 7 g/dL with at least 1 clinical feature including pallor, fatigue, tachycardia, dyspnoea or signs of organ hypoperfusion. Pallor was considered when noticeable paleness of skin or mucous membrane was present, assessed mainly by conjunctival colour. Fatigue was considered when general weakness or tiredness affected daily activities and was assessed according to reported severity. Tachycardia was considered when heart rate was more than 100 beats/minute. Dyspnoea was considered when shortness of breath was present during usual physical activity. Signs of organ hypoperfusion included urine output less than 0.5 mL/kg/hour, altered mental status such as confusion or reduced consciousness and cold extremities.

The etiological factors leading to severe anemia requiring Red Cell Concentrate transfusion were assessed after the above evaluation. Malaria was considered when infection with Plasmodium species was confirmed by positive blood smear or rapid diagnostic test (RDT), with compatible clinical findings including fever above 38°C and chills. Sickle Cell Disease was considered when sickle-shaped red blood cells were identified with supportive peripheral smear findings and haemoglobin electrophoresis showed predominant HbS with HbA less than 2%. Sepsis was considered when blood culture

demonstrated growth of a pathogenic organism such as Escherichia coli, Staphylococcus aureus, Streptococcus pneumoniae or Klebsiella pneumoniae. Iron Deficiency Anemia was considered in children having severe anemia with serum ferritin below 12 ng/mL, serum iron below 50 mcg/dL , TIBC above 400 mcg/dL and microcytic hypochromic picture, with MCV below 70 fL in children aged 1 to 5 years and below 80 fL in children aged 6 to 15 years and MCH below 25 pg. Thalassemia was considered when microcytic hypochromic anemia was present with MCV below 70 fL in children aged 1 to 5 years or below 80 fL in children aged 6 to 15 years, MCH below 25 pg, and haemoglobin electrophoresis showed abnormal pattern with HbF above 2 % and HbA2 above 3.5 %.

Data was analysed by using IBM SPSS version 27. Categorical variables including gender, residency, socioeconomic status, parent's education, malaria, sickle cell disease, sepsis, iron deficiency anemia and thalassemia were presented as frequencies and percentages. Quantitative variables including age and weight were presented as mean ± SD

RESULTS

The mean age of patients were 8.86 ± 4.11 years and mean weight were 31.52 ± 11.48 kg. Regarding gender distribution, 48 (62.3%) patients was male and 29 (37.7%) was female. With respect to parental education, majority of parents was uneducated 30 (39.0%), followed by primary level education 22 (28.6%), secondary education 17 (22.1%) and higher education 8 (10.4%). Socioeconomic status revealed that most patients belongs to low socioeconomic group 42 (54.5%), followed by middle 27 (35.1%) and high 8 (10.4%). In terms of residential status, 50 (64.9%) patients was from rural areas whereas 27 (35.1%) was from urban areas (Table 1).

Table 1. Patient Demographics

Demographics	Mean ± SD / n (%)
Age (years)	8.86 ± 4.11
Weight (kg)	31.52 ± 11.48
Gender	
Male n (%)	48 (62.3%)
Female n (%)	29 (37.7%)
Parents Education	
Uneducated n (%)	30 (39.0%)
Primary n (%)	22 (28.6%)
Secondary n (%)	17 (22.1%)
Higher n (%)	8 (10.4%)
Socioeconomic Status	
Low n (%)	42 (54.5%)
Middle n (%)	27 (35.1%)
High n (%)	8 (10.4%)
Residential Status	
Rural n (%)	50 (64.9%)
Urban n (%)	27 (35.1%)

Regarding etiological profile, iron deficiency anaemia was the most common cause of severe anaemia requiring red cell concentrate transfusion, accounting for 28 (36.4%) of cases, followed by sepsis in 12 (15.6%), thalassaemia in 11 (14.3%), malaria in 8 (10.4%) and sickle cell disease in 5 (6.5%) patients (Table 2).

Table 2. Etiological Profile of Severe Anemia Requiring Red Cell Concentrate Transfusion

Etiology	Frequency	%age
Malaria	8	10.40%
Sickle Cell Disease	5	6.50%
Sepsis	12	15.60%
Iron Deficiency Anemia	28	36.40%
Thalassemia	11	14.30%

On stratified analysis, sepsis was significantly more common in patients aged ≤10 years 12 (26.1%) as compared to those aged >10 years 0 (0.0%) (p=0.002), whereas iron deficiency anaemia also shows significant association with younger age group (p=0.003). Thalassaemia was significantly more prevalent in older patients >10 years 10 (32.3%) versus 1 (2.2%) in younger group (p<0.001). Among gender, thalassaemia was significantly more frequent in male patients 10 (20.8%) as compared to female 1 (3.4%) (p=0.045). Socioeconomic status shows significant association with sepsis (p=0.001) and iron deficiency anaemia (p<0.001), with sepsis being more prevalent in middle socioeconomic group 10 (37.0%) and iron deficiency anaemia being highest in low socioeconomic group 25 (59.5%)

(Table 3).

Table 3. Association of Etiologies with Demographic Factors

Factors	Subgroup	Malaria n(%)	Sickle Cell Disease n(%)	Sepsis n(%)	Iron Deficiency Anemia n(%)	Thalassemia n(%)
Age (years)	≤10	5 (10.9%)	1 (2.2%)	12 (26.1%)	23 (50.0%)	1 (2.2%)
	>10	3 (9.7%)	4 (12.9%)	0 (0.0%)	5 (16.1%)	10 (32.3%)
	p-value	1.000**	0.151**	0.002**	0.003**	<0.001**
Gender	Male	5 (10.4%)	4 (8.3%)	5 (10.4%)	18 (37.5%)	10 (20.8%)
	Female	3 (10.3%)	1 (3.4%)	7 (24.1%)	10 (34.5%)	1 (3.4%)
	p-value	1.000**	0.645**	0.193**	0.790*	0.045**
Socioeconomic Status	Low	3 (7.1%)	3 (7.1%)	1 (2.4%)	25 (59.5%)	6 (14.3%)
	Middle	4 (14.8%)	1 (3.7%)	10 (37.0%)	3 (11.1%)	4 (14.8%)
	High	1 (12.5%)	1 (12.5%)	1 (12.5%)	0 (0.0%)	1 (12.5%)
	p-value	0.644**	0.674**	0.001**	<0.001**	1.000**

*Chi-square Test **Fischer Exact Test

DISCUSSION

In present study iron deficiency anaemia was found to be the most common aetiology of severe anaemia requiring red cell concentrate transfusion, accounting for 28 (36.4%) of cases. This finding was not unexpected, as iron deficiency remains the leading cause of anaemia in paediatric population worldwide, particularly in developing countries where dietary iron intake is inadequate and parasitic infestations further depletes the iron stores. Low socioeconomic status and rural residency which was present in majority of patients in present study also contributes significantly to poor nutritional status and reduced access to iron-rich diet.

Sepsis was the second leading cause, accounting for 12 cases (15.6%), and there was a marked prevalence of the condition among younger children (≤10 years) (p = 0.002). The above relationship is explained by the immaturity of the immune system in young children making them more vulnerable to infection. Various ways through which sepsis leads to anaemia include increased destruction of RBCs, inhibition of erythropoiesis, and iron retention induced by inflammation.

Iron deficiency anaemia was the most common aetiology identified in present study, accounting for 28 (36.4%) of cases. This finding is in agreement with Vijayaraghavan et al. 14 who reported iron deficiency anaemia as the predominant cause of severe anaemia requiring packed red cell transfusion in their cross-sectional study of 110 adult patients, with females being more commonly affected due to menorrhagia and nutritional deficiency. Similarly, Kambourou et al. 15 also noted nutritional and infective causes as major contributors to severe anaemia in paediatric population, though sickle cell disease was the leading aetiology in their cohort (57.6%), which differs from present findings. This difference may be explained by geographical and genetic variation, as the Congo study was conducted in sub-Saharan Africa where sickle cell disease has significantly higher prevalence due to inherited haemoglobinopathy being endemic in that region. In contrast, iron deficiency in present study was strongly associated with low socioeconomic status, where 25 (59.5%) of iron deficiency cases belongs to low income group (p<0.001), a pattern also supported by Kambourou et al. 15 who reported low socioeconomic status in 206 (68.7%) of their patients and identified it as independent predictor of mortality.

Sepsis was identified in 12 (15.6%) patients in present study and was significantly more prevalent in children aged ≤10 years (p=0.002). This is consistent with findings of Sohail et al. 16 who reported sepsis and multiorgan dysfunction as the most frequent diagnosis in 50 (34.0%) of critically ill children requiring red cell transfusion in their PICU-based study. The higher burden of sepsis-related anaemia in younger children in present study can be explained by immature host immunity and increased susceptibility to bacterial infections in early childhood. Kristof et al. 17 further supports the severity of sepsis-associated anaemia, demonstrating that patients with sepsis requiring red cell transfusion had significantly worse 90-day mortality (34.1% versus 19.6%, p=0.004), highlighting that anaemia in septic patients reflects underlying disease severity rather than being an isolated haematological finding. Song et al. 19 similarly reported that severe anaemia within 72 hours significantly increased risk of necrotising enterocolitis

in very-low-birth-weight neonates (OR 2.404), further underscoring that untreated severe anaemia in vulnerable paediatric and neonatal populations carries substantial risk of serious complications beyond the haematological system itself.

Thalassaemia was present in 11 (14.3%) patients and shows significant association with older age group >10 years, where 10 (32.3%) of affected patients were identified ($p<0.001$), and was significantly more common in males 10 (20.8%) versus females 1 (3.4%) ($p=0.045$). Kambourou et al. 15 similarly reported that children with haemoglobinopathies including sickle cell disease had previously received red cell concentrates in 138 (46%) of their cases, reflecting the chronic and recurrent transfusion dependency that characterises these conditions. The male predominance of thalassaemia in present study may reflects referral bias or under-diagnosis in females rather than a true biological difference, as thalassaemia major is an autosomal recessive condition with no established gender predilection. Margo et al.

18 also noted that chronic anaemia arising from haematological disorders constitutes a distinct category requiring repeated transfusion exposure, which is consistent with pattern observed in thalassaemic patients in present study who represents a group with long-term transfusion burden. Maheshwari et al. 20 further highlighted that repeated red cell transfusion in vulnerable paediatric patients, particularly those with chronic haematological conditions, carries risk of cumulative complications, and that the relationship between anaemia severity and transfusion requirement is complex and influenced by underlying aetiology, a finding that aligns well with the transfusion dependency pattern seen in thalassaemic patients in present study.

There are certain limitations to the current study that should be noted. First of all, it has been performed using the single-center design, which limits the possibility to generalize the results to the larger pediatric population outside the specific geographic area. Secondly, the total number of subjects in the sample is 77, which is quite a small sample size. Additionally, the cross-sectional study design does not allow making conclusions about the causality between the causes and the clinical results.

CONCLUSION

In the current study, it is evident that iron deficiency anaemia is still the commonest cause of severe anaemia requiring transfusion with packed red cells among pediatric patients, followed by sepsis and thalassemia. Poverty and rural dwelling were among some of the risk factors associated with the form and degree of anaemia.

Ethical Approval

Ethical permission for this research was taken from the Institutional Ethical Committee of the concerned hospital under Ethical Certificate Ref. No. RC-EA-2025/88.

Patients' Consent

All participant were informed about the study and written consent was taken from them before their inclusion in the research.

Competing Interests

The authors declares that there was no conflict of interest related with this research work.

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