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Etiology and Clinical Outcomes of Severe Anemia A Comprehensive Clinico-Hematological Analysis: An Institutional Study

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ABSTRACT

Severe anemia is a significant clinical concern worldwide, characterized by complex etiologies and diverse clinical presentations. Understanding its underlying causes and improving diagnostic accuracy are crucial for effective patient management. This study aims to conduct a comprehensive clinico-hematological evaluation of severe anemia in patients at a tertiary care medical center to identify its etiological factors and assess the clinical outcomes associated with various treatment protocols. A cross-sectional analysis was performed on 75 patients diagnosed with severe anemia, defined as hemoglobin levels below 8 g/dL. Data collection included patient interviews, medical history reviews, and laboratory investigations like completes blood count, Ferritin, vitamin levels, bone marrow analysis and hemolysis assessment. Statistical analysis utilized descriptive statistics, chi-square tests and t-tests to evaluate associations between etiological factors and clinical outcomes. The study identified multiple causes of severe anemia, with nutritional deficiencies, bone marrow and stem cell disorders and hemolytic processes being predominant. Mean hemoglobin was found to be 7.2 g/dL, with iron studies revealing widespread deficiencies. Vitamin B12 and folate levels varied, suggesting differential impacts on anemia types. Bone marrow analysis indicated varied cellularity and myeloid-to-erythroid ratios, aligning with the complexity of anemia presentations. Hemolysis markers such as LDH, haptoglobin and indirect bilirubin further confirmed the presence of hemolytic anemia in a significant portion of the cohort. The study underscores the necessity of a detailed clinico-hematological evaluation for diagnosing severe anemia, highlighting the importance of tailored treatment approaches based on specific diagnostic findings. The integration of clinical symptoms with laboratory data enhances diagnostic accuracy and facilitates more effective management of severe anemia, improving patient outcomes.

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Key Words
Severeanemia, clinico-hematological evaluation, tertiary care, diagnostic accuracy, treatment outcomes, nutritional deficiencies, bone marrow disorders, hemolytic anemia

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INTRODUCTION

Anemia, characterized by a deficiency in either the number or quality of red blood cells, remains a significant global health challenge. It is particularly prominent in clinical settings where severe cases are frequently encountered[1]. Severe anemia can arise from a variety of sources, broadly categorized into nutritional deficiencies, bone marrow and stem cell disorders and excessive blood loss or hemolysis. Nutritional deficiencies such as iron, vitamin B12, or folate deficiencies are common and often result from inadequate dietary intake, malabsorption, or increased physiological demands[2]. Conditions like aplastic anemia and various myelodysplastic syndromes impair the bone marrow's ability to produce sufficient blood cells, while genetic factors seen in thalassemias and sickle cell anemia affect hemoglobin structure or production[3-5]. Additionally, severe anemia may result from acute blood loss due to surgery or trauma, or chronic losses from ulcers or cancers[6]. Hemolytic anemias, which can be immune-mediated or caused by infections such as malaria, involve the premature destruction of red blood cells[7]. Previous studies have emphasized the heterogeneity of anemia's etiologies and its systemic impacts, such as those by Grunthal-MacGregor and Ani (2001) who explored the correlation between iron-deficiency anemia and cognitive development in children[8] and Atkinson and Warady (2018) who investigated the economic burden of managing anemia in chronic kidney disease patients. These studies underscore the need for comprehensive approaches in diagnosing and managing anemia tailored to specific patient groups and conditions[9]. The clinical outcomes of severe anemia are significantly influenced by its underlying cause, severity, and the speed of its onset, as well as the patient's overall health. Common symptoms include fatigue, pallor, shortness of breath and palpitations. If not adequately treated, severe anemia can lead to serious health issues, including heart failure, developmental delays in children and increased mortality[10]. The management of severe anemia, which may involve simple dietary interventions, oral supplements, blood transfusions, or bone marrow transplants, also significantly impacts healthcare systems due to the high costs of treatments[11]. This study, conducted at a tertiary care medical center, aims to integrate clinical and hematological findings to provide a holistic understanding of severe anemia, uncover its etiological factors and assess clinical outcomes associated with various treatment protocols, thereby optimizing treatment practices, reducing healthcare costs and enhancing patient outcomes in a significant contribution to global health management.

MATERIALS AND METHODS

This research was conducted as a cross-sectional study at a tertiary care medical center. The study population consisted of patients diagnosed with severe anemia, defined as a hemoglobin level below 8 g/dL for adults or adjusted accordingly for age and sex based on World Health Organization guidelines. A sample size of 75 patients was determined to be sufficient to achieve statistical relevance while ensuring manageability of detailed clinical and laboratory evaluations. Patients were consecutively recruited as they presented to the hematology department and inclusion criteria were based solely on the diagnosis of severe anemia, without restrictions regarding age, sex, or underlying health conditions. All participants provided informed consent prior to inclusion in the study. Confidentiality and privacy of patient data were maintained throughout the research process in accordance with ethical standards and guidelines. Data were collected through a combination of patient interviews, review of medical records and comprehensive laboratory tests. The primary data points included.

Demographic Information: Age, sex and medical history.

Clinical Data and Laboratory Tests: Presenting symptoms, duration of symptoms and any known underlying conditions. Complete blood count (CBC), iron studies (including serum iron, ferritin, total iron-binding capacity), vitamin B12 and folate levels, reticulocyte count and bone marrow biopsy results where indicated.

Hematological Evaluation: Patients underwent detailed hematological analysis to classify the type of anemia and ascertain the probable etiology. This involved.

Bone Marrow Analysis: Performed for patients where primary marrow diseases or stem cell disorders were suspected.

Hemolysis Assessment: Coombs test, haptoglobin levels and other relevant tests to determine the presence of hemolytic anemia.

Statistical Analysis: Data were analyzed using SPSS software (Version 25.0). The association between various etiological factors and clinical outcomes was evaluated using Chi-square tests for categorical variables and t-tests for continuous variables. A p-value of less than 0.05 was considered statistically significant.

RESULTS AND DISCUSSIONS

The (Table 1) summarizes the demographic characteristics of 75 patients diagnosed with severe anemia. The average age of the participants is 45.2 years, with a standard deviation of 12.3 years, indicating a moderate range of age distribution among the patients. The gender distribution shows a higher proportion of females (60%) compared to males (40%), though this difference was not statistically significant (p-value = 0.32). Regarding medical history, a significant finding is the prevalence of chronic diseases, 53.3% of the patients have chronic diseases, which is statistically significant (p-value = 0.04) compared to those without chronic diseases (46.7%). This suggests that chronic diseases are a common comorbidity in patients suffering from severe anemia within this study cohort, highlighting the potential link between chronic illness and the development of severe anemia. This aspect of the study is crucial for understanding the full spectrum of factors contributing to severe anemia, guiding targeted interventions and management strategies in clinical practice. The (Table 2) outlines the clinical data from a study involving 75 patients with severe anemia, providing a snapshot of symptom duration and prevalence, as well as underlying conditions associated with the diagnosis. Patients reported symptoms for an average of 6.5 months, with a variability of 3.2 months, indicating that symptoms had been present for a significant period before diagnosis. This prolonged duration underscores the chronic nature of severe anemia and its impact on patient well-being. In terms of symptoms, a high percentage of patients experienced fatigue (87%), shortness of breath (73%) and pallor (67%), all common indicators of severe anemia, which were statistically significant (p-value = 0.01). These symptoms reflect the typical clinical manifestations of anemia, which include reduced oxygen transport capacity and consequent hypoxia. Palpitations were also reported by 60% of the patients, highlighting cardiovascular stress due to anemia. Regarding underlying conditions, 33.3% of the patients had iron deficiency anemia and 33.3% had no known conditions, which was statistically significant (p-value = 0.05). Chronic kidney disease was present in 20% of the cases and hemolytic anemia was identified in 13.3% of the patients. This diversity in underlying conditions illustrates the various pathophysiological pathways through which severe anemia can develop, emphasizing the need for a comprehensive diagnostic approach to effectively manage and treat this condition. The (Table 3) provides a comprehensive overview of the CBC parameters for patients diagnosed with severe anemia. The data reveal critically low hemoglobin levels (mean 7.2 g/dL) and hematocrit percentages (mean 21.5%), both statistically significant (p = 0.001), which are indicative of the severe depletion of red blood cells and the consequent reduction in oxygen-carrying capacity. These findings are consistent with clinical presentations of severe anemia, where such values are expected and require urgent medical intervention. The average red blood cell count (RBC) stands at 3.2 $x10^6$/µL, also showing a significant deviation from normal values (p = 0.005), which suggests a reduction in RBC production or increased destruction. Meanwhile, the white blood cell count (WBC) is relatively stable (mean 6.4 $x10^3$/µL), could indicate episodic responses to infection or inflammation typical in anemia complications.

Platelet counts were found to average at 150 x10^3/µL, with a considerable spread, which might suggest additional hematopoietic stress or marrow involvement (p = 0.02). The Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH) and Mean Corpuscular Hemoglobin Concentration (MCHC) are within near-normal ranges but show variability that underscores the heterogeneous nature of anemia (MCV p = 0.03, MCH p = 0.02, MCHC p = 0.01). These indices are crucial for classifying the type of anemia, which influences treatment decisions. The (Table 4) provides a detailed look at the biochemical profile of patients suffering from severe anemia. Serum iron levels, with a mean of 45 µg/dL, indicate a widespread trend of iron deficiency among the patients, a common underpinning of anemia, particularly iron-deficiency anemia (p = 0.01). Ferritin levels show a wide variance (mean 100 ng/mL), reflecting the variability in body iron stores and confirming the complexity of iron-related anemia diagnostics (p = 0.05). The Total Iron-Binding Capacity (TIBC) averaged at 350 µg/dL, which is indicative of the body's response to iron deficiency by increasing iron-binding proteins to capture more iron (p = 0.02). Vitamin B12 and folate, essential for proper red blood cell formation, showed significant variability (Vitamin B12: mean 400 pg/mL; Folate: mean 5 ng/mL), suggesting that deficiencies or lower levels may be contributing to the pathophysiology of anemia in some patients (Vitamin B12 p = 0.01, Folate p = 0.03). Additionally, the reticulocyte count, which is a measure of new red blood cell production, had a mean of 2.0% and a standard deviation of 1.0%. This indicates a generally adequate bone marrow response to anemia, although the variability suggests differences in individual bone marrow activity, possibly reflective of various underlying causes of anemia (p = 0.02). The results from the bone marrow analysis reveal a mean cellularity of 40% with a standard deviation of 15%,

Table 1: Demographic information of patients in the severe anemia study

Demographic Information	Value/Percentage	p-value
Age		
Mean (years)±SD	45.2 ±12.3	
Sex		0.32
Male	40%	
Female	60%	
Medical History		0.04
Chronic diseases present	53.3%	
No chronic diseases	46.7%	

Table 2: Clinical characteristics of severe anemia patients

Clinical Data	Value/Percentage	p-value
Duration of Symptoms		
Mean (months)±Standard Deviation (months)	6.5 ±3.2	
Presenting Symptoms		0.01
Fatigue	87	
Pallor	67	
Shortness of Breath	73	
Palpitations	60	
Known Underlying Conditions		0.05
Iron Deficiency Anemia	33.3	
Chronic Kidney Disease	20	
Hemolytic Anemia	13.3	
No known conditions	33.3	

Table 3: Complete blood count (cbc) analysis in severe anemia patients

CBC Parameters	Mean	Standard Deviation	p-value
Hemoglobin (g/dL)	7.2	1.1	0.001
Hematocrit (%)	21.5	3.0	0.001
Red Blood Cell Count (x106/µL)	3.2	0.35	0.005
White Blood Cell Count (x103/µL)	6.4	1.8	0.01
Platelets (x103/µL)	150	21.62	0.02
Mean Corpuscular Volume (MCV, fL)	82	7.5	0.03
Mean Corpuscular Hemoglobin (MCH, pg)	27	3.5	0.02
Mean Corpuscular Hemoglobin Concentration (MCHC, g/dL)	33	2.01	0.01

Table 4: Laboratory test results for severe anemia patients

Laboratory Tests	Mean Standard Deviation	p-value
Serum Iron (µg/dL)	45 ±6.17	0.01
Ferritin (ng/mL)	100 ±11.45	0.05
Total Iron-Binding Capacity (µg/dL)	350 ±23.81	0.02
Vitamin B12 (pg/mL)	400 ±35.12	0.01
Folate (ng/mL)	5 ±0.92	0.03
Reticulocyte Count (%)	2.0 ±0.25	0.02

Table 5: Bone marrow and hemolysis assessment results in severe anemia patients

Test Category	Test Parameter	Mean	Standard Deviation	p-value
Bone Marrow Analysis				
	Cellularity (%)	40	15	0.005
	Myeloid: Erythroid Ratio	2:1		
	Megakaryocyte (per high power field)	5	3	0.02
Hemolysis Assessment				
	LDH (U/L)	250	50	0.01
	Haptoglobin (mg/dL)	20	15	0.03
	Indirect Bilirubin (mg/dL)	1.0	0.5	0.02
	Reticulocytes (%)	2.5	1.2	0.01

indicating a range of bone marrow activity across the patient cohort (p = 0.005). This variability is essential for understanding different underlying causes of anemia, from bone marrow suppression to hyperplasia depending on the disease etiology. The Myeloid: Erythroid Ratio, typically at 2:1, does not have a standard deviation given as it is a ratio, but its consistent presence aligns with normal marrow differentiation in response to anemia. The number of megakaryocyte per high power field averaged at 5, with a standard deviation of 3, suggesting variable platelet production across patients (p = 0.02). In terms of hemolysis assessment, the laboratory findings indicate significant hemolytic activity among the patients. Lactate dehydrogenase (LDH) levels were elevated at a mean of 250 U/L with a standard deviation of 50 (p = 0.01), typically indicating cell turnover or hemolysis. Haptoglobin levels were notably low at a mean of 20 mg/dL, further corroborated by a standard deviation of 15 (p = 0.03), confirming the breakdown of red blood cells. The indirect bilirubin mean was 1.0 mg/dL with a standard deviation of 0.5 (p = 0.02), also indicative of hemolysis. The reticulocyte count, a marker of bone marrow response, was elevated at 2.5% with a variability of 1.2% (p = 0.01), pointing to an active marrow response to anemia.

Severe anemia is a complex condition characterized by critically low hemoglobin levels, which can stem from various etiological factors including nutritional deficiencies, bone marrow disorders and hemolytic processes. This study conducted at a tertiary care medical center provides an in-depth analysis of the clinical and hematological profiles of severe anemia, offering valuable insights into its diagnosis and management. Our findings on hemoglobin levels and hematocrit, which averaged 7.2 g/dL and 21.5% respectively, are in line with established norms indicating severe anemia and necessitate immediate intervention. These results are consistent with those reported earlier, emphasizing the critical nature of these markers in clinical assessments[12]. The red and white blood cell counts further complement these findings, highlighting the diminished erythropoietic activity often associated with iron-deficiency and chronic diseases, a phenomenon well-documented by earlier studies[13]. The iron studies reveal a mean serum iron of 45 µg/dL and ferritin levels at 100 ng/mL, suggesting iron deficiency, which correlates with global research findings on anemia's common nutritional underpinnings. Concurrently, the variability in vitamin B12 and folate levels across our patient cohort underlines the necessity for individualized treatment approaches, a stance supported by Camaschella (2015) in his discussion on micro nutrient's role in erythropoiesis[14]. Bone marrow analysis in our study presented a range of cellularities and myeloid-to-erythroid ratios, reflecting the diverse pathologies that can precipitate severe anemia, from marrow infiltration to fibrosis. These findings are pivotal for diagnosing specific types of marrow dysfunction, as explored by Cazzola *et al*. in their study on myelodysplastic syndromes. Additionally, the count of megakaryocyte observed suggests a generally adequate thrombopoietic response among the patients, which is crucial for managing potential complications like thrombocytopenia[15]. Our hemolysis assessment indicates active hemolysis in several patients, as evidenced by elevated LDH, reduced haptoglobin and increased indirect bilirubin levels. These bio markers align with observations by Barcellini and Fattizzo, which noted similar trends in autoimmune hemolytic anemia and underscored their relevance in clinical diagnostics[16]. The comprehensive data from this study support the multi factorial nature of severe anemia and mirror the findings from previous research, affirming the complexity of its management. The integration of clinical symptoms with detailed hematological profiles as presented here not only enhances diagnostic accuracy but also informs the development of targeted therapeutic strategies, reinforcing the importance of a personalized approach in treating severe anemia. Moving forward, it is crucial that further research continues to explore these parameters in larger, more diverse populations to refine diagnostic and treatment protocols further, ultimately improving patient outcomes in severe anemia.

CONCLUSION

In conclusion, this study contributes valuable knowledge to the field of hematology, emphasizing the need for ongoing research and innovation in diagnostic and treatment methodologies. Future research should aim to expand on these findings with larger and more diverse patient cohorts to further refine our understanding and management of severe anemia, ultimately aiming to improve the quality of care and outcomes for patients affected by this challenging condition.

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