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Unraveling of Multifactorial Etiology and Risk Factors of Severe Anemia HB ≤ 6 g/dL

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ABSTRACT

Background: Anemia is an alarming worldwide health condition affecting individuals from modernized and countries that underdeveloped, with significant implications for human health and socio-economic development.
Aims: This research aimed to find the primary risk factors linked with severe anemia (HB ≤ 6 g/dL) and assess the relative contribution of different factors, including nutritional status, chronic diseases, infections, and genetic factors.
Methodology: A cross-sectional study investigated the fundamental causes and risk factors of disease anemia (HB≤ 6 g/dL). The following study was conducted at the Abbas Institute of Medical Sciences, Muzaffarabad AJK Pakistan. The data was collected through a nonprobability purposive sampling technique. Multivariate analysis was applied using logistic regression to identify specific risk factors for severe anemia.
Results: The mean age of the patients was 34.2 years (SD 10.8), with 60% from low socioeconomic status. The mean iron level was 30.4 (SD 12.5) and the mean vitamin B12 level was 190.3 pg/mL (SD 2.3). 46.7% had a history of chronic diseases, with 20.0% having type 2 diabetes and 13.3% having renal diseases. 26.7% were suffering from infections. Chronic disease history significantly increases the risk (OR 2.50, p=0.004).
Conclusion: The study population had low hemoglobin and iron levels, with a high proportion of patients having chronic diseases. Severe anemia was significantly associated with low iron levels and Vitamin B12 deficiency, chronic diseases, and infections, increasing the risk of severe anemia.

INTRODUCTION

Anemia is an important health problem worldwide that results from many reasons. It may affect senior people and it has been associated with high rates of mortality and morbidity, especially among people over the age of 80. The number of cases can be decreased with iron supplements and therapies in endoscopy (1).

The condition known as anemia, is based on the World Health Organization is defined as a decrease in hemoglobin (HB) level lower than a particular threshold point that is determined by male and female, age, ethnic background, and physiologic status. HB levels of less than 13 grams per deciliter in males and lower than 12 grams per deciliter in females are globally approved threshold points for young individuals(2). Individuals may be without any symptoms and can be with symptoms associated with diseases such as cardiovascular diseases (CVD). Individuals may have a higher risk of falling, mental illnesses, and or impaired physical fitness (3).

Worldwide, 1.3 million people are suffering from anemia, making it a major global health concern (4). Based on the Ethiopian Demographics and Health Survey (EDHS) approximately 57 percent of children aged six months to fifty-nine months suffer from condition anemia (5)

A lack of iron is a highly prevalent reason for anemia worldwide, resulting in fewer and paler blood cells called red blood cells (RBCs) in the periphery smear. Participants commonly expressed complaints such as tiredness and difficulty breathing after physical activity. Based on the studies, participants with a lack of iron anemia stay more in the hospital and are more susceptible to experiencing negative consequences(6).

The most common deficiencies of nutrients associated with anemia are vitamin B12, folate, and iron. (7). A low level of hemoglobin (HB) often causes fatigue, pale skin, difficulty in breathing, tachycardia, and potentially leads to death. HB levels have to be extremely low. It can be lower than 6 g/dL. It leads to death (8).

Several studies have found that lack of iron was the most common cause of anemia in elderly people, particularly since the widespread administration of novel oral anticoagulants in patients with irregular heartbeats, pulmonary embolism (PE), and venous thromboembolism (VT) (9). The most frequent causes of anemia are deficiency of iron and insufficiency of dietary such as vitamin 12 and deficiencies of folate, chronic diseases-associated anemia, and hematological disorders (10). According to a study conducted by Aboubakari et al. in Togo reported a high prevalence of anemia in children in Togo. This study reported that younger children and maternal anemia were strongly associated with anemia occurring in children, while the age of children and high levels of education in mothers were negatively linked with childhood anemia (11).

National and Regional Data on the anemia prevalence and risk factors associated with it among children who are under five years are available in many regions of country Ethiopia, like Gordon Town where anemia prevalence is about 66.8 percent (12)

A study conducted by Blum et al revealed that intravenous iron supplementation elevated levels of HB and decreased the requirement for blood transfusions in aging surgical patients with a deficiency of iron in anemic individuals (13).

The research we conducted sought to determine the primary risk factors associated with severe anemia where HB level can equal to or less than 6 g/dL and evaluate the relative contribution of different factors, such as nutritional status, chronic diseases, infections, and genetic factors.

METHODOLOGY

Research Design

It was a cross-sectional study designed to evaluate the unraveling of multifactorial etiology and risk factors of anemia (HB ≤ 6 g/dl)

Study Area: This study was conducted in the Department of General Medicine, AIMS Hospital Muzaffarabad, AJK Pakistan

Sample Size: The sample size for this research was determined by using the following population formula $S= Z^2 *P* (1-P)/M^2$. By keeping a level of CI of 95%, a margin of error of 5%, and a probability of 50%. The sample size calculated was 75.

Sampling Technique: A non-probability convenient sampling technique was used to collect data.

Data Collection

Data collection includes collecting comprehensive demographic information, such as age, gender, and socioeconomic status of patients to understand the patient's background. It also includes proper medical history, such as focusing on a history of chronic diseases (diabetes, and renal diseases), infections like malaria and HIV, and genetic factors such as thalassemia and sickle cell disease. An assessment of dietary nutrients such as vitamin B12, and folate. Laboratory tests were performed, like complete blood count, HB levels, iron level in blood, ferritin, and CRP to provide a complete understanding of the patient's health status.

Statistical Analysis

The variables related to demographics have been described using statistical measures the mean, standard deviation, frequencies, and percentages. Between the groups, the t-test for continuous data variables and the chi-square test for variables with

categorical data. Ultimately, we used logistic regression to determine risk factors for severe anemia while accounting for confounding variables.

Ethical Consideration

The study followed ethical guidelines. All participants provided informed consent, and the confidentiality of participants was respected.

RESULTS

The individual's demographic details are shown in Table 1. The patient's mean age was age 34.2 years, with a SD of age 10.8 showing a moderate spread around the mean age. 53.3% were male among 75 patients. In terms of socioeconomic status, 60% belong to low socioeconomic status, 33.3% were from the middle category, and 5 out of 75 participants were from the high socioeconomic category. This distribution revealed a significant representation of patients from lower socioeconomic backgrounds in this study.

Table 1
Demographics Characteristics of Patients

Variable	Mean (SD)/ n (%)
Age (years)	34.2 (10.8)
Gender	
Male	40 (53.3%)
Female	35 (46.66%)
Socioeconomic Status	
Low Socioeconomic Status	45 (60.0%)
Middle Socioeconomic Status	25 (33.3%)
High Socioeconomic Status	5 (6.7%)

Table 2 shows the dietary and medical characteristics of the population. The mean hemoglobin (HB) level was 5.2 grams per deciliter with an SD of 0.7, indicating that individuals had low levels of HB. The mean iron level was 3.4 (Standard Deviation =12.5), while the mean vitamin B12 level was 190.3 per mol/milliliter, with an SD of 2.3. In terms of clinical history, 46.7% of patients had a history of chronic diseases, with 20.0% of patients having diabetes type 2 and 13.3% having renal diseases. 20 patients (26.7%) were suffering from infections, 13.3% had a history of genetic disorders.

Table 2
Nutritional and Clinical Characteristics

Variable	Mean (SD)/ n (%)
Hemoglobin (g/dl)	5.2 (0.7)
Iron Levels (µg/dL)	30.4 (12.5)
Vitamin B12 (pg/mL)	190.3 (45.8)
Folate (ng/mL)	4.1 (2.3)
History of Chronic Disease	35 ((46.7%)
Diabetes	15 (20.0%)
Renal Disease	10 (13.3%)
Infections	20 (26.7%)
Genetic Disorders	10 (13.3%)

A comparative investigation of severe anemia, characterized by hemoglobin levels of gram/deciliter or less than 6 g/dL, showed that the average age among individuals with severe anemia was 35.2 years, with an average SD of 11.3. There was no association found between age and severe anemia with a p-value of 0.234. 60% of males suffer from severe anemia. There was no association between gender differences p-value=0.098. The severely anemic group had significantly lower levels of iron with mean=29.4µg/dl, with a p-value of 0.045 which shows a significant association. The text covers various associations, including Vitamin B12 levels being significantly reduced, folate levels approaching significance, a history of chronic disease being significantly more common, infections being present in a significant percentage of severely anemic individuals, and genetic disorders not showing a significant correlation with severe anemia.

Table 3
Comparative Analysis of Severe Anemia (HB≤ 6g/dL)

Variable	Severe Anemia (HB ≤6g/DL)	p-value
Age (years)	35.2 (11.3)	0.234
Gender (Male)	45 (60.0%)	0.098
Iron levels	29.4 (13.5)	0.045)
Vitamin B12 (pg/mL)	185.6 (50.1)	0.032*
Folate (ng/mL)	3.9 (2.5)	0.078
History of Chronic Disease	40 (53.3%)	0.002**
Infections	25 (33.3%)	0.015*
Genetic Disorders	10 (13.3%)	0.114

The table below displays the findings of the logistical regression that evaluated the potential risk factors for severe anemia, called hemoglobin

(HB) levels of 6 grams/deciliter or less than 6 g/dL. The analysis stated that lower levels of iron are associated with a higher risk of severe anemia, with an ODD ratio (OR) of 1.35 with a CI of 95% (1.10 to 1.55) and a statistically significant probability value of 0.025. Lower vitamin levels of B12 are also a risk factor with an odds ratio of 0.95 and a p-value of 0.031, suggesting that as vitamin B12 levels decrease, the risk of severe anemia also increases. A history of chronic disease significantly increases the risk, with an OR (odds ratio) of 2.50 and a p-value of 0.004. The presence of infection is associated with a higher risk of severe anemia, with an OR of 1.75 and a probability value of 0.040.

Table 4
Logistic Regression Analysis of Risk Factors for Severe Anemia (HB ≤ 6 g/dL)

Variables	***Odds Ratio (OR) (95% CI)***	***P-value***
Iron Levels (µg/dL)	1.35 (1.10-1.55)	0.025
Vitamin B12 (pg/mL)	0.95 (0.92-0.98)	0.031
History of Chronic Disease	2.50 (1.40-4.45)	0.004
Infection	1.75 (1.05-2.90)	0.040

DISCUSSION

Anemia is a common problem in daily medical practice. While it may be relatively direct to evaluate in healthy patients, it can be more complicated in those patients who have complicated medical histories. The World Health Organization (WHO) has set hemoglobin (HB) levels of below 13 g/dl for males and less than 12 grams/deciliter for females. However, these standards were generally designed for international nutrition research and not for diagnosing anemia in every patient (14). It is crucial to emphasize that ranges should not be regarded as obsolete because standardized ranges for testing in laboratories commonly depend on a range that includes 95 percent of healthy individuals. However, some specific individuals may have normal variations that affect the definitions of what is taken as normal and what constitutes anemia. Such as in the case of African Americans, a decreased level of hemoglobin (HB) 0.5 to 1 gram/deciliter may be taken as normal (14,15). Nevertheless, is not obvious how this variation arises and whether it is the result of a hemoglobinopathy, or a higher incidence of iron deficiency anemia (16)according to research performed by Loannu et al. throughout the trial, 846 young children were admitted with anemia. The median age was 81 years old, and 44.8 percent of those with anemia were male. Logistic regression was applied to evaluate that higher levels of vitamin B12 and long-term hospital stay were independently associated with higher levels of mortality (1). Our study comprises 53.3 percent male and about 46 percent female patients. The average age of the patient was a total of 34.2 years, with an SD (standard deviation) of 10.8 years, indicating a moderate variation in the mean age. Another research study conducted in an Israeli hospital medical ward compared the anemic patient's characteristics with and without diabetes. The following study discovered that most of the anemic patients were 65 years of age (17). The substantial information from the global burden of illness study assessed a significantly greater incidence of anemia in females in all 204 countries, although these statistics don't exclusively reflect inpatient cases (18).

Patients with anemia in the study conducted by Loannu et al (1) most COVID-19 patients have CVD multiple medical conditions, with most of them having cardiac failure, CHD, and HTN.CKD was also prevalent. Additional research found comparable findings, with the majority of patients suffering from chronic cardiac disorders such as cardiac failure or coronary artery disease (CAD), as well as kidney disease (CKD). According to our study, In terms of clinical history, 46.7% of patients had a history of chronic diseases, with 20.0% of patients having diabetes type 2 and 13.3% having renal diseases. 20 patients (26.7%) were suffering from infections, 13.3% had a history of genetic disorders.

According to a study conducted by Melk et al.(19), the mean age of the children was thirty months at the time. 28.6 percent of children were anemic: seventeen percent were mildly anemic. 10.3 percent were moderately anemic, and 0.7 percent were seriously anemic. The severity of childhood anemia is linked with descriptive characteristics such as age, marital status, and also delivery methods. Contrary to this in our study, patients suffering from severe anemia had a mean age of 35.2 years and were iron deficient, and also vitamin B12 levels. In our study gender difference was not statistically significant, and genetic

disorders did not show a significant association with severe anemia.

According to a study conducted by Aliyo et al (20), anemia was significantly associated with a history of gastrointestinal protozoan infection (AOR=2.55,95% confidence interval (CI)=1,28-10.42) infection with malaria(AOR=5.01,95% CI=0.18-11.44), and helminths transmitted by soil infection (AOR=6.39, 95% Confidence interval= 1.75-29.08). Our findings showed that a history of chronic disease considerably raises the risk with an odds ratio of 2.50 and p-value of 0.004. Infection increases the chance of server anemia, with an OR of 1.75 and an adjusted p-value of 0.040.

CONCLUSION

The population studied had notably low hemoglobin (HB) and iron levels, with a significant proportion of patients having chronic diseases, particularly diabetes type 2 and chronic kidney diseases (CKD), as well as infections and genetic disorders. In the analysis of severe anemia, iron levels, and Vitamin B12 deficiency were significantly associated with severe anemia, while age, gender, and genetic disorders showed no significant association. Chronic diseases and infections were more common among severely anemic individuals. Lower levels of iron and vitamin B12, a history of chronic disease, and the presence of infection are significant risk factors for severe anemia, with increased odds ratios (ORs)and statistically significant p-values. The analysis indicates that as these factors worsen, the risk of severe anemia rises.

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