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RESEARCH ARTICLE
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FREQUENCY AND COMPLICATION OF SERUM IRON OVERLOAD IN TRANSFUSION DEPENDENT PATIENT

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Abstract

Introduction: The aim of the current study was to determine the frequency and complications of serum iron overload in transfusion-dependent patients with an aim to assess the prevalence of iron overload and identify associated complications.

Methods: The current study adopted cross-sectional and observational research design. The data was collected the transfusion-dependent patients who were receiving regular treatment at the Hayatabad Medical Complex (HMC), Peshawar. A sample of 151 patients who were dependent on transfusion was collected through convenient sampling technique. Information on the duration and frequency of blood transfusions, the frequency of serum ferritin level monitoring, and recent ferritin levels, and complications experienced by the patient due to iron overload were collected through structured questionnaire. Statistical analysis, including demographic, descriptive, chi-square and cross-tabulation was conducted through SPSS.

Results: The analysis of 151 transfusion-dependent patients revealed that liver enlargement (29.8%) and fatigue (23.2%) are the most common complications of iron overload. Results also shows that majority of patients (43.0%) have moderate serum iron overload while iron Chelation Therapy is the most commonly administered treatment, particularly for patients with severe iron overload (75%). Patients generally start experiencing complications between 10 and 30 years of age. The demographic data indicate a predominance of thalassemia and a fairly balanced gender distribution among the study participants.

Conclusion: Regular monitoring of serum ferritin levels and related issues is crucial for early diagnosis and treatment. Patients need to be educated about the risks of iron overload and the need of sticking to their treatment plans.

Keywords: serum iron overload, transfusion, hemoglobin, thalassemia

Introduction

Among illnesses affecting just one gene, those involving the haemoglobin (Hb) gene are the most common. More than 330,000 babies are born with these illnesses every year, with 17% of those babies having thalassemia [1]. These are major health concerns globally. Recessive abnormalities of haemoglobin synthesis, known as thalassemias, cause a reduction in the production of the ß-globin chain. Extreme anaemia necessitating frequent blood transfusions is a symptom of the homozygous condition [2]. Untreated or improperly transfused beta thalassemia major can cause a variety of symptoms, including growth retardation, anaemia, jaundice, weak muscles, knock-knee, enlarged liver and spleen, leg ulceration, extramedullary hemopoeisis, the development of masses, and skeletal changes caused by bone marrow expansion. Without treatment, patients in this group often don't make it beyond their first year of life. Patients' lives are extended and treated mostly by the use of blood transfusions administered at regular intervals. Transfusions save lives, but they also put patients at risk for iron overload and a host of other issues, including hypersplenism, hypercoagulation, hypertension, venous thrombosis, and osteoporosis [3].

Topical lotion, the most common cause of mortality in patients who rely on blood transfusions is iron overload and its consequences. Growth retardation and erectile dysfunction were symptoms of iron excess in these kids. Iron excess may lead to heart difficulties, liver malfunction, and endocrine disorders as complications [4, 5]. The exact process by which glandular damage caused by serum iron excess manifests has been the subject of several suggested mechanisms. Theoretically, iron chelation is required since daily iron needs are around 1 mg, which is the same as the amount of iron absorbed and excreted.1 Erythrocytes synthesise heme with the help of iron, and other cells in the body utilise it for metabolic purposes. Hepatocytes and macrophages store excess iron as part of a dynamic cycle that also recycles iron. Iron recycling relies on macrophages, which consume old red blood cells and release iron from their heme into the blood plasma. On the other hand, there is no way for the body to get rid of the extra iron that comes from transfusions, which may amount to 0.3-0.6 mg/kg/day in total daily transfusions (TDT) (based on a transfusion rate of 2-4 units per month and 200-250 mg of iron per unit) [6, 7].

In cases of iron excess, the endocrine system, liver, heart, and spleen experience heightened activity. Iron excess is the primary cause of mortality and morbidity in thalassemia. Patients with continuous transfusion have been reported to have hypogonadism, hypothyroidism, hypoparathyroidism, cardiomyopathy, arrhythmia, progressive liver failure, and impaired renal function, as shown in several investigations. The Centres for Disease Control and Prevention (CDC) documented complications in adult patients with a median age of 31.3 years, an average age of 4.5 ± 8.2 years when transfusions began, and a median duration of 18.5 ± 12.3 years of transfusions [8, 9].

Transfusion-dependent patients, particularly those with chronic conditions like thalassemia and sickle cell anemia, are at significant risk of developing serum iron overload due to frequent blood transfusions [10]. Iron overload can lead to severe complications, including liver disease, heart problems, and endocrine disorders. Despite the critical nature of this issue, there is limited data on the prevalence and complications of serum iron overload in such patients, particularly within the context of healthcare facilities in Peshawar. This study seeks to address this gap by investigating the frequency and associated complications of serum iron overload in transfusion-dependent patients at Hayatabad Medical Complex.

Research Objective

The objective of the current study is to determine the frequency and complications of serum iron overload in transfusion-dependent patients with an aim to assess the prevalence of iron overload and identify associated complications.

Materials and Methods

The current study adopted cross-sectional and observational research design, involving collection and analysis of the data at single point in the time to access the frequency and complications of serum iron overload in transfusion-dependent patients. The data was collected the transfusion-dependent patients who were receiving regular treatment at the Hayatabad Medical Complex (HMC), Peshawar. In this study, those patients were included, having conditions like thalassemia, sickle cell anemia, and similar chronic anemias which necessitate regular blood transfusions.

A sample of 151 patients who were dependent on transfusion was collected through convenient sampling technique. While the sample size was calculated as given below;

$n_0=Z^2p(1-p)/e^2$

n_0 stands for Sample size

Z stands for Z-value i.e., 1.96

p value is 0.5 for maximum variability

e is margin error i.e., 0.05

$n_0 = (1.96)^2 x\ 0.5\ x\ (1-0.5)/\ (0.05)^2$

$n_0 = 384.16$

Given the limited population, the formula for finite population adjustment was used as below;

$n = n_0/1+ n_{0/N}$

where the anticipated population is 250 and N is the size of the population;

$n = 384.16/1+ 384.16/250 = 151$

$n = 151$

The data was collected through a structured questionnaire having below measurement tools.

Table1: Measurement

Data Collection Tool	Description
Demographic Information	Collects basic patient data such as age, gender, weight, height, underlying condition (e.g., Thalassemia, Sickle Cell Anemia), and duration of the condition.
Transfusion History	Gathers information on the duration and frequency of blood transfusions, the total number of transfusions received in the past year, and awareness of iron overload risks.
Monitoring and Treatment of Iron Overload	Assesses whether patients are undergoing treatment for iron overload (e.g., Iron Chelation Therapy, Phlebotomy), the frequency of serum ferritin level monitoring, and recent ferritin levels.
Complications Related to Iron Overload	Identifies any complications experienced by the patient due to iron overload (e.g., liver enlargement, heart problems, diabetes).

Statistical analysis, including demographic, descriptive, chi-square and cross-tabulation was conducted through SPSS, as presented below.

Results

Table2, as shown below, shows the results of the demographic analysis of the patients.

Table 2: Demographic Analysis

Demographic Characteristic	Category	Number of Patients (n)	Percentage (%)
Age Distribution			
<10 years		5	3.3%
10-20 years		25	16.6%
21-30 years		40	26.5%
31-40 years		50	33.1%
>40 years		31	20.5%
Gender Distribution			
Male		85	56.3%
Female		66	43.7%
Underlying Condition			
Thalassemia		60	39.7%
Sickle Cell Anemia		45	29.8%
Aplastic Anemia		20	13.2%
Myelodysplastic Syndrom s (MDS)		16	10.6%
Other		10	6.6%
Duration of Condition			
<1 year		10	6.6%
1-5 years		60	39.7%
6-10 years		40	26.5%
>10 years		41	27.2%

Table2, shows that;

- The majority of patients are between 31-40 years old, followed by those in the 21-30 year age range. There are more male patients than female patients.
- Thalassemia is the most common underlying condition among the patients, followed by Sickle Cell Anemia. Most patients have had their condition for 1-5 years, indicating that iron overload is a significant concern for those who have been managing their condition for a moderate period.

Similarly, Table3 shows the results of the descriptive analysis

Table3: Descriptive Statistics

Variable	Mean	Standard Deviation (SD)
Duration of Blood Transfusions	5.8	3.1
Frequency of Blood Transfusions (per year)	45	12.5
Serum Ferritin Level (µg/L)	3200	2200

Table3 shows that;

- On average, patients have been receiving transfusions for about 5.8 years, with a standard deviation of 3.1 years.
- Patients receive an average of 45 transfusions per year, reflecting frequent transfusion therapy for managing their conditions.
- The mean serum ferritin level is 3200 µg/L with a significant standard deviation, suggesting a wide range of iron overload levels among patients.

Table4 presents the percentage and frequency of serum iron overload

Table 4: Serum Iron Overload

Serum Iron Overload Level	Number of Patients (n)	Percentage (%)
Mild	50	33.1%
Moderate	65	43.0%
Severe	36	23.8%

Table4 shows that;

- Majority of patients (43.0%) have moderate serum iron overload. A smaller percentage of patients exhibit severe iron overload (23.8%).
- While Mild iron overload is present in 33.1% of the patients, suggesting that early detection and treatment could prevent progression to more severe levels.

Table5 shows the treatment distribution of the serum iron overload

Table5: Treatment

Treatment Type	**Mild (%)**	**Moderate (%)**	**Severe (%)**
Iron Chelation Therapy	28%	55%	75%
Phlebotomy	12%	20%	45%

Table 5 shows that;

- Iron Chelation Therapy is the most commonly administered treatment, particularly for patients with severe iron overload (75%), indicating its primary role in managing high serum iron levels.
- Phlebotomy is less commonly used, but still more frequent in severe cases (45%), suggesting its role as an adjunct or alternative treatment.

Table6 writes the Frequency Distribution of Complications Related to Iron Overload

Table6: Complications Related to Iron Overload

Complication	Number of Patients (n)	Percentage (%)
Liver Enlargement (Hepatomegaly)	45	29.8%
Liver Fibrosis or Cirrhosis	30	19.9%
Heart Problems (Cardiomyopathy)	25	16.6%
Diabetes	20	13.2%
Joint Pain or Arthritis	22	14.6%
Delayed Growth or Puberty	8	5.3%
Skin Darkening	12	7.9%
Fatigue	35	23.2%
None	26	17.2%

Table6 shows that;

- Liver Enlargement (Hepatomegaly) is the most frequently reported complication, affecting 29.8% of patients. Fatigue is also common, affecting 23.2% of patients, suggesting that it is a prevalent and likely impactful symptom.
- Liver Fibrosis or Cirrhosis (19.9%) and Joint Pain or Arthritis (14.6%) are notable complications. Heart Problems (Cardiomyopathy) and Skin Darkening are less common but still relevant, affecting 16.6% and 7.9% of patients, respectively.
- Delayed Growth or Puberty is the least reported complication (5.3%). None reported by 17.2% of patients suggests that some may not experience complications or may have well-managed conditions.

Table7 presents the result of the Chi-Square

Table7: Chi-Square Test of Independence Results

Association	Variable 1	Variable 2	Chi-Square Value	p-Value
Gender and Complications	Gender	Presence of Complications	2.15	0.14
Duration of Transfusions and Complications	Duration of Transfusions	Presence of Complications	0.35	0.95
Frequency of Transfusions and Monitoring Frequency	Frequency of Transfusions	Monitoring Frequency	2.78	0.43

Table7 shows that;

- No significant association was found between gender and the presence of complications (p=0.14)..
- There is no significant association between the duration of transfusions and the presence of complications (p=0.95), indicating that the length of time a patient has been receiving transfusions does not significantly impact the likelihood of complications.
- No significant association was found between the frequency of transfusions and monitoring frequency (p=0.43), suggesting that how often transfusions are administered does not affect how frequently patients monitor their iron levels.

Discussion

The analysis of 151 transfusion-dependent patients revealed that liver enlargement (29.8%) and fatigue (23.2%) are the most common complications of iron overload. Patients generally start experiencing complications between 10 and 30 years of age. The demographic data indicate a predominance of thalassemia and a fairly balanced gender distribution among the study participants. These results are consistent with the previous studies [10, 11]. Life expectancy for thalassemic patients has been greatly increased with the advent of transfusion therapy with adjuvant chelation. However, this treatment is not without its risks, including serum iron overload, which can cause growth retardation, hypoparathyroidism, hypothyroidism, diabetes mellitus, and cardiac complications [12]. The most common side effect in our research was short height, which might be because other variables than iron excess, such as chronic anaemia, chelation toxicity, zinc insufficiency, and social stress, can also cause growth retardation [13]. Roughly 89% of the people in our research had small stature [14]. Its occurrence was much higher than that of previous studies conducted in other locations. Serum ferritin and bodily iron reserves may not necessarily have a linear connection, and it might alter daily. An acute-phase reactant, serum ferritin levels may rise in response to inflammation and tissue injury. Both the kind and length of chelation treatment have a role in this. [15] When evaluating bodily iron, liver iron content is preferable to serum ferritin. We all know that iron builds up in the body, first in the liver and then in the cardiovascular and hormonal systems [16].

Patients undergoing chelation treatment with serum ferritin monitoring and unclear results may be examined for LIC. When serum ferritin levels are over 4000 mcg/L, the research found that the association with LIC is not linear, and individuals may see a decrease in LIC without a discernible trend in serum ferritin levels within 6 to 12 months.1,8 Iron chelation treatment efficacy evaluation requires LIC iron burden monitoring. The overarching objective is to detect iron overload at an early stage and improve chelation treatment to forestall these consequences [17]. Although there are limitations, serum ferritin is a useful tool for tracking therapy success. Unfortunately, not everyone in the research group has access to LIC, despite its reliability. Research has shown that compared to Europeans, Asians with TDT are more likely to have low height. Hypogonadism, hypothyroidism, malnutrition, inherited short stature, desferrioxamine-induced bone dysplasia, iron overload, growth hormone insufficiency, and chronic anaemia are among the potential causes of low stature in

thalassaemia [18]. It is important to look into the possibility of growth hormone deficit in individuals who have had iron overload after receiving an optimal blood transfusion. The prevalence of hypogonadism is higher in individuals with TDT, particularly those with beta-thalassemia major, and is more frequent in the elderly, according to a comprehensive review.19 More individuals with gonadal disorders are likely to be seen as the average age of TDT patients increases. We must therefore keep a careful eye on them to detect any problems early and start iron chelation and hormone replacement treatment as soon as possible [17, 18].

Conclusion

The current study revealed that both tiredness (26.5%) and liver enlargement (29.8%) were found to be the most prevalent effects of iron overload, according to the findings of an investigation that was conducted on 151 patients who were reliant on transfusions. Patients often begin to have difficulties between the ages of 10 and 30. According to the demographic data, the majority of the people who participated in the research had thalassemia, and the gender distribution at the time of the study was reasonably even**.**

Recommendations

The monitoring of serum ferritin levels and the problems that are associated with them on a regular basis is essential for early diagnosis and therapy. Instruction should be given to patients on the dangers of iron excess as well as the significance of following treatment regimens. Customise treatment strategies to meet the specific requirements of each patient in order to successfully manage and reduce problems.

Significance of the Study

This research reveals the high occurrence of problems linked to iron overload in patients who are reliant on transfusions, highlighting the need for enhanced monitoring and treatment of the condition. This not only offers essential data for the development of targeted therapies, but it also improves our knowledge of the effect on the quality of life of patients.

Limitations of the study

The design of the research, which was cross-sectional, makes it difficult to determine whether or not there is a causal connection between the frequency of transfusions and difficulties. Furthermore, the dependence on self-reported data and medical records may result in the introduction of bias in the reporting process. Due to the fact that the sample originated from a single medical centre, the results may not be able to be generalised to other medical facilities.

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