ORIGINAL ARTICLE

IRON OVER LOAD AND ITS RELATION WITH HAEMOSTATIC PARAMETERS IN β-THALASSEMIA PATIENTS

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Background: Patients with β-thalassemia major have been observed to experience changes in their coagulation profile. These changes include an elongated prothrombin time and partial thromboplastin time as well as bring down levels of natural anticoagulants and coagulation factors. The mechanisms underlying the occurrence of thrombotic tendencies in some thalassemia patients remain unclear. This study aims to examine the alterations in the iron and coagulation profile among β-thalassemia patients. **Methods:** After informed consent, 50 children having β-thalassemia, and 50 healthy controls were included in this study. Blood samples were collected and serum ferritin, haematological and haemostatic parameters were measured. Data was analysed on SPSS-24. **Results:** The laboratory assessment revealed 43.5% of the patients had thrombocytopenia, 54% had prolonged prothrombin time (PT), and 56% of the patients had prolonged activated partial thromboplastin time (aPTT). All estimated coagulation factors exhibited lower activity levels in comparison to the control group. Serum ferritin exhibited a positive relationship with PT and aPTT and a substantial negative relationship with total platelet count. **Conclusion:** High serum ferritin levels are associated to abnormal haemostatic parameters in thalassemia patients. Regular monitoring of serum ferritin levels is essential to ensure that thalassemia patients receive appropriate treatment and support.

Keywords: Thalassemia, Bleeding, Haemostasis, Anticoagulants, Thrombocytopenia

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INTRODUCTION

Thalassemia is a collection of inherited blood conditions that affect the formation of haemoglobin, the protein liable for uptake of oxygen in RBCs. It is considered as abnormal formation of RBCs, causing anaemia and other problems. Numerous blood transfusions are often essential for thalassemia patients to relieve symptoms and rally their quality of life.[1]

Thalassemia patients may have low levels of some clotting factors such as factor V and factor VIII. This can cause reduced blood clotting and an enhanced chance of bleeding. Fibrinogen plays a role in blood clot formation. Thalassemia patients may have low amount of fibrinogen, which can disturb their ability to form more stable blood clots. Activated Partial Thromboplastin Time (aPTT) and Prothrombin Time (PT)[2] indicate the time it needs to form blood to clot. Thalassemia patients may have slightly extended PT and aPTT, showing lessened clotting function. Thalassemia patients may also have risks of thrombocytopenia, which is a situation deliberated by a low number of platelets. This can further enhance the peril of bleeding in these patients.

Although thalassemia patients may have various changes in their haemostatic factors that increase the chances of bleeding, they are also at high risk to thrombotic events, for instance deep vein thrombosis.[3]

The transfusion procedure implicates the infusion of healthy RBCs to patient, growing their haemoglobin amounts and refilling the oxygen carrying capability. While this offers immediate reprieve, it also familiarizes a potential hazard factor known as iron overload. Iron overload happens when the body collects undue amounts of iron due to blood transfusions. Since the body does not have a usual way to expel surplus iron, it can accumulate over time and have damaging effects on numerous organs and tissues. This is mainly concerning for thalassemia patients as they need lifelong transfusion therapy to cope with their condition.[4,5]

The influence of iron overload in thalassemia patients is noteworthy and complicated. The surplus iron can gather in vital structures and may cause serious problems such as liver cirrhosis, heart failure, and hormonal imbalances. Iron overload can also affect the endocrine system, disturbing hormone making and regulation. This can lead to growth abnormalities, diabetes, and delayed puberty. Other potential significances include increased susceptibility to infections, bone density issues, and impaired overall quality of life. Iron overload can also disturb other systems in the body.[6] Identifying and speaking iron overload is critical for the comprehensive supervision of thalassemia patients. Regular monitoring of iron levels through serum transferrin saturation and ferritin levels allows healthcare specialists to evaluate the level of iron overload and regulate proper mediations. Treatment

options for iron overload comprise iron chelation therapy; through medication excess amount of iron can be removed from the body. This therapy assists to inhibit the long-term complications linked with iron overload, maintaining the overall health and wellbeing of patients.[7]

To regulate the influence of iron overload in thalassemia patients, regular assessments are critical. These valuations typically comprise measuring serum ferritin levels. Dealing iron overload in thalassemia patients includes chelation therapy as the chief treatment which eliminates extra iron from the body. Upholding a healthy diet, skirting iron-rich foods and supplements, and closely observing iron levels are necessary for avoiding further problems.[8]

Quantifying serum ferritin level is one method to measure iron overload in thalassemia patients. Regular monitoring the serum ferritin level helps to regulate the efficacy of iron chelation therapy.[9] Raised levels of serum ferritin specify a too much build-up of iron, signifying iron overload in thalassemia patients.

Liver function tests can also be used to estimate the influence of iron overload on liver. Raised levels of liver enzymes such as ALT and AST indicate liver impairment. Regular monitoring of iron levels is critical to inhibit complications linked with iron overload and certify the overall wellbeing of thalassemia patients.[10]

For thalassemia patients, handling iron overload is a crucial feature of their treatment excursion. The undue iron build-up resulting from transfusions can have damaging effects on various structures, including the endocrine system, liver, and heart. It is necessary to explore and understand the existing treatment options for successfully managing iron overload in these patients. This study aims to examine the alterations in the iron and coagulation profiles among β-thalassemia patients.

METHODOLOGY

This cross-sectional study was carried out from Mar 2023 to Mar 2024 at Thalassemia Department, Fatima Jinnah Medical College, Lahore. The study included 50 β-thalassemia patients and 50 healthy controls after their written informed consent. All participants were part of a regular blood transfusion process and received a chelating agent deferoxamine (DFO). The protocol received approval from the Ethical Committee.

Information about age and education was collected on a standardised questionnaire. Through venipuncture, 9 mL blood was drawn; 3 mL of blood was placed in an EDTA vacutainer for complete blood count, 3 mL blood was placed in another vial to measure prothrombin time and activated thromboplastin time using Biobase kits, and 3 mL of blood was used to measure serum ferritin levels. The results were statistically analysed on SPSS-24. Descriptive statistics, including Mean±SD, and frequencies, were computed. Inferential statistical tests, including ANOVA and regression analysis, were applied to identify significant differences and relationships among the study variables taking $p \leq 0.05$ as statistically significant.

RESULTS

The mean serum ferritin in patients was 4,750±2,700 ng/dL, and 130±100 ng/dL in controls ($p<0.0001$). (Table-1). The mean haemoglobin level was 8.92±0.992 g/dL. There were no significant differences in the WBC count between patients and controls. Compared to the controls, the patients' mean platelet count was low. (Table-2).

The PT of patients was significantly prolonged ($p<0.001$) compared to controls. (Table-3). Twenty-seven (54%) patients with thalassemia had deranged PT, while 28 (56%) patients had abnormal aPTT. (Table-4).

Table-1: Iron and ferritin parameters between patients and controls

Biochemical parameter	Patient	Control	*P*
Serum ferritin (ng/mL)	4,750±2,700	130±100	<0.0001

Table-2: Haematological parameters of patients and controls

Parameters	Patient	Control	*p*
Hb (g/dL)	8.92±0.992	13.0±0.6	<0.05
WBC ($\times 10^9$/L)	8.83±9.7	8.677±8.2	0.8
Platelet ($\times 10^9$/L)	60±24	199±128	<0.05

Table-3: Coagulation parameters of control and patients

Parameters	Patient	Control	*P*
PT	16.21±2.4	12.0±0.5	<0.001
aPTT	49.9±9.7	49.8±9.6	NS

Table-4: Coagulation profile of thalassemia patients [n (%)]

Parameters	Deranged	Normal	Total
PT	27 (54)	23 (46)	50
aPTT	28 (56)	22 (44)	50

DISCUSSION

In β-thalassemia major, elevated serum ferritin levels are well-documented due to frequent blood transfusions, which is necessary to manage severe anaemia but results in iron overload.[11] Studies show that while transfusions alleviate anaemia, they also lead to the accumulation of non-transferrin-bound iron (NTBI), which is highly reactive and toxic.[12] In present study serum ferritin levels were reported as high in thalassemics versus control results. Haemoglobin levels were notably lower in patients compared to controls. The prothrombin time (PT) was significantly prolonged in patients, while the activated partial thromboplastin time (aPTT) was comparable between groups.

The main reason of thrombocytopenia is the higher level of ferritin in serum and chelating therapy. In an earlier study, normal platelet count was found as all their patients having iron chelating therapy were

excluded.[14] The levels of PT in control group and patients in our study were significantly different (p<0.001). This is similar to reported results[15]. The prolongation of the PT was reported in the patients, which is quite higher than the reported results in Darvishi-Khezri study[16] (3%), Naithani study[5] (40%), and prolongation of PT shows positive relation with serum ferritin level. This finding is comparable to Naithani study[5]. In 56% of the patients, perpetuation of aPTT level was reported, which is more than the value reported by Naithani[5] (48%) and Wadaha study[17] (6%). In thalassemia patients having transfusion of blood there is decrease in the activities of PT and aPTT which is due to the overloading of iron or haemolysates circulation leading to the parenchymal tissue damage of liver and causing the perpetuation of aPTT and PT.[18]

For activation of intravascular haemolysis and intrinsic coagulation pathway, multiple transfusions are required. There is a relationship between hyper-coagulable state and haemolysates infusion.[8] Protease activity similar to kallikrein triggered by iron overload.[19] The higher results in our study may be attributed to patient non-compliance with iron chelating therapy, resulting in iron overload and elevated serum ferritin, to alter the coagulation process.

CONCLUSION

Serum ferritin level was high in thalassemia patients, and is linked with deranged haemostatic profile in terms of prolonged PT, the aPTT remaining unchanged. Regular monitoring of serum ferritin levels is recommended to ensure that thalassemia patients receive appropriate treatment and support.

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