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ORIGINAL ARTICLE

Hemostatic assay in iron overloaded frequently transfused thalassemia patients.

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ABSTRACT… Objective: To determine the hemostatic abnormalities in iron overloaded frequently transfused thalassemia patients. **Study Design:** Cross Sectional study. **Setting:** Departments of Pathology and Paediatrics, Sheikh Zayed Medical College/Hospital, Rahim Yar Khan, Pakistan. **Period:** October 2022 to April 2023. **Material & Methods:** Was conducted on 112 patients using convenient sampling technique. The collected data was analyzed using SPSS version 23. **Results:** Total 112 thalassemia patients were included in the study, 62 were males and 50 of them were females. A normal PT value was recorded in 107 (95.5%), while 5 (4.5%) had prolonged PT, a normal APTT value was recorded in 98 (87.5%), while 14 (12.5%) patients had prolonged APTT, a normal BT value was recorded in 89 (79.5%), while 23 (20.5%) patients had prolonged BT, and a normal platelet count was recorded in 86 (76.7%), while 26 (23.2%) patients had thrombocytopenia. The mean level of serum ferritin was (4169.08±2193.49) and the mean age of total study subjects was (11.7 ± 3.39). **Conclusion:** It was concluded that high serum ferritin levels resulted in disturbance of hemostatic profile in thalassemia patients.

Key words: Hemostatic Assay, Iron Overload, Serum Ferritin, Thalassemia.

INTRODUCTION

Hemoglobinopathies are the genetic blood disorders affecting more than 300,000 newborns globally each year. Thalassemia, one of these hemoglobinopathies, is prevalent in more than 60 countries.[1] Molecular defect in α-globin gene cluster on chromosome 16 or the β-globin gene cluster on chromosome 11 results in defective hemoglobin synthesis.[2] β-thalassemia disease is one of the most prevalent congenital hemolytic anemias, frequently found in malarial belt regions including the Mediterranean, Middle East, Transcaucasia, South and Southeast Asia, Africa and China. More than 40,000 babies are born annually with beta-thalassemia disease[3], and carriers of β-thalassemia are estimated to be 80 million. Silent carriers, β-thalassemia trait, intermedia thalassemia and beta thalassemia major are the four subtypes of β-thalassemia categorized on the basis of genotype-phenotype correlations.[4] Epidemiological data from North Pakistan reported that prevalence of beta-thalassemia in pathan population is 7.96% and in Punjabis 3.26%. It is because of the social and cultural system and the first choice is marriages within the ethnic group.[5]

Splenomegaly, thalassemia facies, jaundice, anemia, decreased activity and retarded growth are manifestations of β-thalassemia. Blood transfusion is a necessary component of the ongoing treatment of this illness, however these patients can be cured with bone marrow transplant.[6] The causes of iron overload in thalassemia patients include multiple blood transfusions, ineffective erythropoiesis, increased iron absorption through the gastrointestinal tract, inhibition of hepcidin synthesis by proteins (GDF-15 & TWSG-1 released from erythroblasts, and hereditary haemochromatosis associated with mutation in the HFE gene.[7] A unit of transfused blood usually contains 200-250 milligrams of iron. Therefore, individuals who get an average of 2-4 units of blood per month will consume

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5000 to 10,000 milligrams of iron annually. The endocrinopathies especially diabetes mellitus, hypothyroidism, and hypoparathyroidism as well as hepatitis, liver cirrhosis, and even hepatocellular carcinoma are all brought on by the distribution and deposition of non-transferrin bound iron in heart, endocrine organs, and liver cells.[8]

Patients with beta-thalassemia major experience abnormalities in extrinsic and intrinsic coagulation pathways resulting in prolonged prothrombin time (PT) and activated partial thromboplastin time (APTT). The effects of iron overload on the liver and other organs disturb the platelet functioning as well. Regular blood transfusions are required to treat the severe thalassemia condition; nevertheless, these transfusions can also cause abnormalities in the hemostatic profile and liver function. In order to keep the patient's liver function and hemostatic profile under control, early diagnosis is crucial. Considering the available resources and limited facilities this study was planned to determine the hemostatic assay of iron overloaded frequently transfused thalassemia patients.

OBJECTIVE

To determine the hemostatic assay in iron overloaded frequently transfused thalassemia Patients.

MATERIAL & METHODS

This cross sectional study was conducted in Pathology and Pediatric Departments of Sheikh Zayed Medical College/Hospital, Rahim Yar Khan, Pakistan in 6 months from October 2022 to April 2023. Convenient sampling technique was used to collect samples from 112 patients of known beta thalassemia major and intermedia bearing serum ferritin more than 1000 ng/ml and the patients who had more than 10 blood transfusions. Venous blood samples were drawn in citrate coated vial and EDTA containing vacutainer after observing complete aseptic measures. Hemostatic assay was assessed performing prothrombin time (PT) test, partial thrombin time (APTT) test and platelet count. Bleeding time was done by Duke Method at bed side. Informed verbal consent from participants was sought out. Ethical authorization was taken from Institutional Review Board (IRB) of Sheikh Zayed Medical College/Hospital Rahim Yar Khan (244/IRB/SZMC/SZH). All the collected data was recorded and analyzed using SPSS version 25. After analysis the quantitative data was presented as mean and standard deviation, while the qualitative data was presented as frequencies and percentages.

RESULTS

Total 112 thalassemia patients were enrolled in the current study, 62(55.4%) study subjects were males followed by 50(44.6%) females. Study subjects from rural area were 74(66.1%), whereas from urban area were 38(33.9%). 74(66.1%) male patients received 2 transfusions per month, followed by females 50(44.6%) Table-I. The mean age of the study subjects was 11.7 years with mean ferritin level 4169 ng/ml, mean platelet count was 237892/cmm, mean PT found 16 seconds, mean APTT 36.7 seconds, mean BT 6 minutes and mean number of transfusions per month was 2 in number, data expressed in descriptive statistics in Table-II. Platelet count of 26(23.2%) patients was decreased i.e. thrombocytopenia state, 23(20.5%) had abnormal (prolonged) BT, 14(12.5%) had abnormal (Prolonged) APTT, 5(4.5%) had abnormal (prolonged) PT, Figure-2.

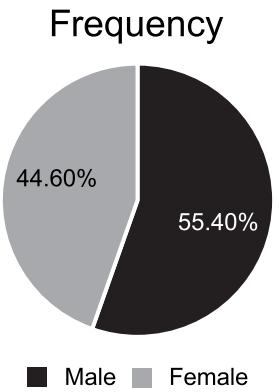

Figure-1. Gender wise distribution of study subjects

Number of Transfusions Per Month	Frequency (n)	Percentage (%)
1	28	25
2	74	66.1
3	10	8.9

Table-I. Number of transfusions per month in patients

Variables	Mean±SD
Age (years)	11.7±3.39
Serum Ferritin (ng/ml)	4169.08±2193.49
Platelet count (Per cmm)	237892.85±149670.28
PT (Seconds)	15.9±1.94
APTT (Seconds)	36.7±4.24
BT (Minutes)	5.85±2.80
Per month transfusions	1.83±0.5

Table-II. Descriptive statistics of Age, Ferritin, PT, APTT, BT and transfusions

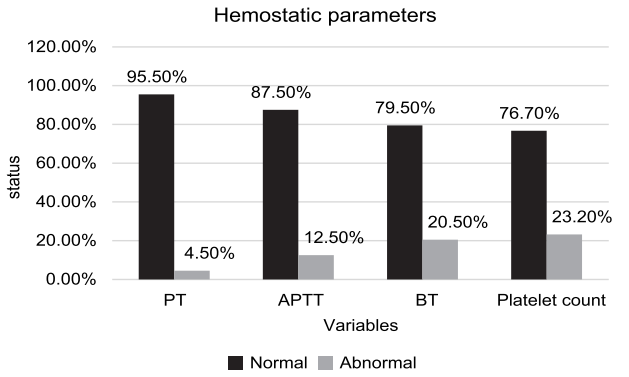

Figure-2. Hemostatic parameters among study subjects

DISCUSSION

A related study conducted in India in 2021 showing the prolonged PT and APTT recorded in 5.55% and 37.03% of patients, while 13.2% of patients face thrombocytopenia (platelet count < 150 x 10^9/L).[9] A similar study was done in Iraq in 2016, reported prolonged PT and APTT in 54% and 56% patients respectively while thrombocytopenia in 43.5% of study subjects.[10] Another study from India showed prolongation of PT and APTT in 12% and 6% cases respectively and thrombocytopenia in 40% cases.[11] Another study reported prolonged PT and APTT in 40.7% and 46.3% cases while thrombocytopenia in 33.3% cases. PT denotes extrinsic lane activity (network factors) and shared lanes, while APTT denotes intrinsic track and joint lane activity. Patients with thalassemia who frequently receive blood transfusions may experience PT and APTT prolongation due to liver damage brought on by circulating hemolysis and/or iron overload. Hemolysis, transfusion, and hyper coagulation status are all related. Proteases that act like kallikreins are released from tissues as a result of iron overload. In younger thalassemia patients, APTT was more disturbed than PT. Repeated transfusions had a more detrimental effect on the intrinsic pathways.[12,13]

CONCLUSION

High serum ferritin level in thalassemia patients play a role in the disturbance of hemostatic assay. Complete coagulation profile should be evaluated routinely in these patients for early diagnosis and prompt management. Regular iron chelation therapy must be given to prevent iron overload which lead to subsequent irreversible liver damage that disturb the hemostatic status in thalassemia patients.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

No.	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Muhammad Bilal Ghafoor	Concept of study, Designing, Literature, Review and supervision of study.	
2	Faiza Sarwar	Manuscript writing, Analysis and interpretation.	
3	Hafiz Muhammad Tayyab	Colelction of data, literature review.	
4	Sana Khan	Critical review, Statistical analysis.	
5	Farhan Ali Khanzada	Interpretation of results, Discussion.	
6	Muhammad Saleem Leghari	Facilitated for reagents, Material analysis.	
7	Saba Aftab	Data collection, Experimentation.	