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Demographics, Clinical, Hematological, Blood Group Distribution and Transfusion profile of patients with β- Thalassemia Major in District Karak, Pakistan

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Abstract

β-globin, Defective synthesis of the chain is the hallmark of β-thalassemia major, is a severe hemoglobin condition that causes chronic decrease in RBCs and a lifelong reliance on blood transfusions. To evaluate the blood group distribution, transfusion patterns, clinical aspects, hematological parameters, and demographics of patients with β-thalassemia major in District Karak, Pakistan was the major goal of this study. In cooperation with DHQ Hospital Karak, 250 diagnosed patients from distract Karak participated in a cross-sectional study design. A standardized questionnaire and patient medical records, including reports from hemoglobin electrophoresis and complete blood counts (CBCs), were used to gather required information. For statistical analysis SPSS was used. The outcomes indicated a male predominance, with 57.5% of patients being both male 42.8% and female 76.8% of patients were between the ages of 1 and 10. In 56.8% of instances, a good family history was noted. Parental consanguinity was very common with 78.8% of first-cousin weddings and 14.8% of second-cousin weddings. Hepatomegaly (14.8%), splenomegaly (24.8%), and weakness (22.4%) were the most prevalent clinical characteristics. Hematological study showed decreased MCV and MCH values consistent with microcytic hypochromic anemia, as well as a mean hemoglobin level of 6.7 ± 0.94 g/dL, indicating severe anemia. According to analysis of blood group, the most common

was O+ (24%), then B+ (23.2%) with AB+ (19.22%). In terms of transfusion patterns, 31.2% of patients needed a blood transfusion every three weeks, compared to 56.8% who needed one every four weeks. The results show that District Karak has a high β-thalassemia major disease burden, which is closely linked to consanguineous marriages and inadequate healthcare resources. Early diagnosis, routine monitoring, better transfusion procedures, the application of preventive measures including genetic counseling and premarital screening are the important highlighters of the study.

Keywords: β-thalassemia, Blood Group, Anemia, CBC, MCV, MCH

Introduction

β-Thalassemia major (β-TM), also referred to as transfusion-dependent β-thalassemia (TDT), is a severe inherited disorder of hemoglobin synthesis caused by pathogenic variants in the β-globin gene, resulting in reduced or absent production of β-globin chains. The resulting imbalance between globin chains leads to ineffective erythropoiesis, chronic hemolytic anemia and, in severe cases, lifelong dependence on regular red blood cell transfusions (1,2). Thalassemia is among the most important inherited hematological disorders worldwide, and its burden remains particularly significant in South Asia and the Middle East. Recent global burden estimates have demonstrated that thalassemia continues to contribute substantially to morbidity, mortality and disability worldwide (3). Pakistan has a particularly important burden of β-thalassemia. The frequency of β-thalassemia carriers in Pakistan has been estimated at approximately 5–8%, with millions of individuals carrying β-thalassemia mutations and thousands of children being born with β-thalassemia major each year (4,5). The high carrier frequency, together with consanguineous marriages and inadequate population-level screening, contributes to continued transmission of the disease. A recent review of thalassemia prevention in Pakistan emphasized that premarital screening, genetic counseling, carrier detection and prenatal diagnosis are important strategies for reducing the birth of children affected by β-thalassemia major (6). These preventive measures are particularly relevant in communities where consanguinity is common and access to specialized genetic services is limited. The clinical presentation of β-thalassemia major is generally associated with severe anemia beginning during infancy or early childhood. Untreated patients may develop pallor, weakness, fatigue, growth retardation, hepatosplenomegaly, skeletal abnormalities and other consequences of chronic ineffective erythropoiesis and anemia. Modern management has considerably improved survival; however, patients require lifelong monitoring for complications associated with the disease and its treatment (7,8). Regular transfusion therapy is the principal supportive treatment for patients with transfusion-dependent β-thalassemia.

Current international recommendations emphasize maintaining appropriate pre-transfusion hemoglobin levels and providing Leuk depleted red blood cells at regular intervals, generally every 2–4 weeks depending on the individual patient's requirements (9). The 2025 Thalassemia International Federation guidelines further emphasize individualized transfusion programs, monitoring of transfusion requirements and prevention of transfusion-related complications (10). Hematological assessment is an important component of the diagnosis and long-term management of β-thalassemia major. Complete blood count parameters, including hemoglobin concentration, red blood cell count, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) and red cell distribution width (RDW), provide useful information regarding the hematological status of affected patients. Molecular and hematological investigations are also important for differentiating β-thalassemia from other causes of microcytic anemia and for confirming the underlying genetic disorder (11). The clinical and hematological profile of patients may vary according to age at diagnosis, genotype, transfusion history, treatment adherence, nutritional status and the presence of complications. Blood group distribution is another important aspect of patients with β-thalassemia major because these individuals receive repeated blood transfusions throughout their lives. The ABO and Rh blood group systems are essential for selecting compatible blood and maintaining transfusion safety. Studies conducted in Pakistan have demonstrated variations in ABO blood group frequencies among β-thalassemia patients. In a study from Lahore, the distribution of ABO blood groups among β-thalassemia patients was reported in the order O>B>A>AB, with β-thalassemia major representing the largest clinical group (12). Another Pakistani study conducted in 2023 reported blood group B as the most frequent group, followed by O, A and AB, while Rh-positive individuals constituted the large majority of patients.

The study also found a significant association of consanguinity and family history with β-thalassemia major, although no significant relationship was observed between ABO/Rh blood groups and thalassemia subtype (13). Such regional blood-group information may be useful for blood-bank planning and maintaining an adequate supply of compatible blood. Repeated transfusion is essential for survival in β-thalassemia major, but it also creates several clinical challenges. Patients receiving chronic transfusion therapy are exposed to risks including transfusion reactions, red-cell alloimmunization and transfusion-transmitted infections. Alloimmunization occurs when patients develop antibodies against red-cell antigens that are absent from their own erythrocytes. Contemporary transfusion literature recommends appropriate antigen

matching and antibody screening to minimize this complication, particularly in patients receiving lifelong transfusion therapy (14–16). Leukoreduction and careful compatibility testing are also important components of safe transfusion practice (9). Another major complication of chronic transfusion therapy is iron overload. Because each unit of transfused blood introduces additional iron into the body and humans have no effective physiological mechanism for excreting excess iron, iron gradually accumulates in tissues. Excess iron may damage the liver, heart and endocrine organs and can contribute substantially to morbidity and mortality in transfusion-dependent patients (17). Iron overload therefore requires regular monitoring and appropriate iron-chelation therapy. Serum ferritin, liver iron concentration and cardiac iron assessment by magnetic resonance imaging are among the approaches used to evaluate iron burden and guide treatment (18). Despite the availability of effective chelating agents, adherence, adverse effects, cost and inadequate monitoring can limit successful control of iron overload (19). Transfusion-transmitted infections also remain an important concern in patients receiving repeated blood transfusions, particularly in developing countries. A systematic review of transfusion-dependent thalassemia patients in Asia highlighted the continued risk of infections such as hepatitis B virus, hepatitis C virus and HIV among multiply transfused patients (20). In Pakistan, the availability and safety of blood products, donor screening, voluntary blood donation and appropriate transfusion practices are therefore important components of long-term thalassemia care. District Karak, Khyber Pakhtunkhwa, represents a population in which local information regarding β-thalassemia major may be limited. Demographic characteristics, clinical manifestations, hematological findings, ABO/Rh blood group distribution and transfusion practices may vary between geographical regions because of differences in genetic background, consanguinity, socioeconomic conditions, healthcare accessibility and availability of blood-transfusion services.

Therefore, documenting these characteristics among β-thalassemia major patients in District Karak is important for understanding the local disease burden and identifying areas requiring improvement. The present study is therefore designed to assess the demographic, clinical, hematological, blood group distribution and transfusion profile of patients with β-thalassemia major in District Karak, Pakistan. The findings may provide useful baseline information regarding the characteristics of affected patients, their hematological status, ABO and Rh blood-group distribution, and patterns of transfusion dependence. The study may also contribute to improved local transfusion planning, patient monitoring, clinical management, blood-bank services and

future preventive strategies, including carrier screening, genetic counseling and premarital screening.

Material and Methods

A cross-sectional study was conducted to determine the clinical profile, transfusion patterns, complications, and risk factors among patients with β thalassemia major in District Karak, Khyber Pakhtunkhwa. The study was conducted in health facilities, thalassemia treatment centers, and community gatherings from November 1, 2025, to March 1, 2026. A total of ninety patients met the inclusion criteria. The participants were between 1 and 30 years old, of either gender, or had been diagnosed with β thalassemia major. The diagnosis was based on the presence of regular blood transfusions or those receiving follow-up treatment. Patients with thalassemia minor or intermedia, those older than 25 years, those who did not provide complete information, and those who declined to participate in the study were excluded. Convenience sampling was used due to time constraints and the lack of a sampling frame. The data were collected using a structured questionnaire. The questions were about socio-demographic data, clinical profile, and the frequency of blood transfusions, family history of the disease, splenectomy, blood group, complete blood count, and hemoglobin electrophoresis. The questionnaires were administered during face-to-face interviews or over the phone, and patient's records were examined. The questionnaires were translated for the participants who spoke Pashto. Informed consents were obtained from the participants or their guardians, and their confidentiality was maintained. The study was approved by the Lawaghar Institute of Medical Sciences, Chokara, Karak. The data were analyzed using SPSS. The descriptive statistics, including the frequencies, percentages, mean, and standard deviation, were generated to summarize the data. The chi-square test, independent sample t-test, and one-way ANOVA were conducted to determine the associations and differences between the variables. A p-value of <0.05 was considered statistically significant.

Results

Demographic Data of Participants

This current study comprised 250 patients diagnosed with Beta Thalassemia Major and was conducted at Lawaghar Institute of Medical Sciences (LIMS) in collaboration with DHQ Hospital in District Karak. The beta thalassemia major disease was diagnosed in patients using HB electrophoresis. Furthermore, demographic data from 250 patients were obtained using various criteria such as age, gender, domicile, and family history.

Based on Gender

Based on gender distribution, male patients (57.5%) were more common than female patients (42.8%), as indicated in the figure below.

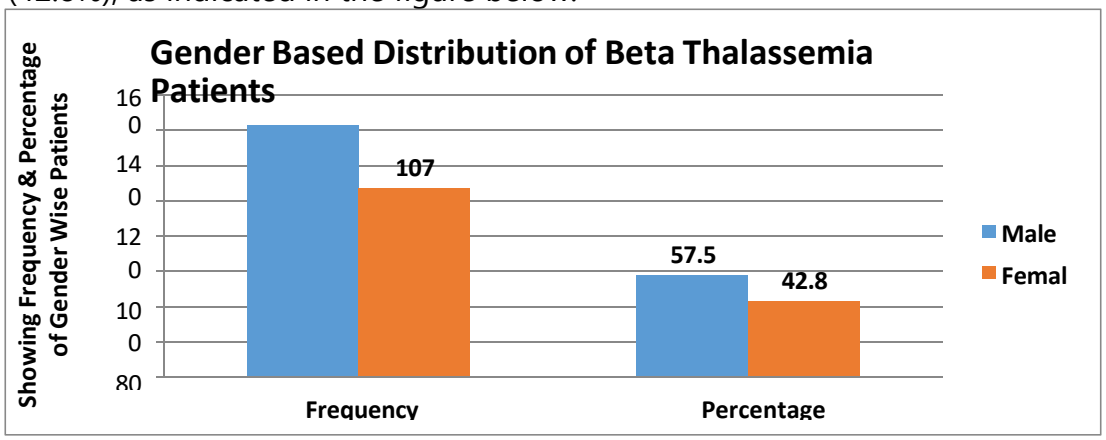

Figure-1: Illustrate Gender Based Distribution of Patients

Based on Age

The age of patients was arranged in several age groups such as 1-10, 11-20, and 21-30 years, with most patients (76.8%) falling into the 1-10 years age group as represented in the table below.

Table 1: *Showing Age Based Categorization of patients*

Age group	Frequency	Percentage (%)
1-10	192	76.8
11-20	43	17.2
21-30	15	6

Based on Residence

In this study, most beta thalassemia major diagnosed patients (62.8%) were from urban regions while 38.8% were from rural areas of Karak district.

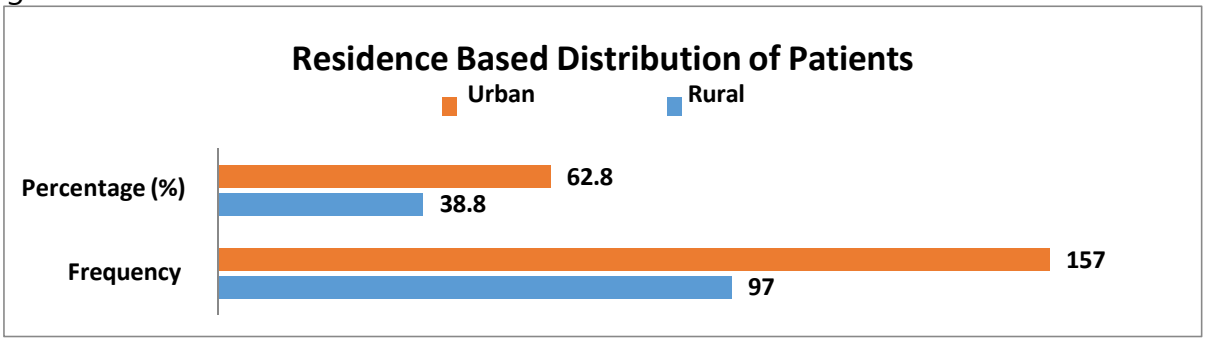

Figure-2: Illustrate Patients Residence

Parental Consanguinity of Patients

Out of 250 patients with Beta Thalassemia Major, parental consanguinity was assigned to first cousins (78.8%) and second cousins (14.8%), with 10.4% born to non-consanguineous parents. The findings indicate that parental consanguinity is common in families with Beta Thalassemia Major patients. This shows that consanguineous marriages provide a significant risk for disease transmission in the current study area. Parental consanguinity is far more common among patients than non-consanguineous marriages. This research indicates a substantial link between consanguineous marriages and the development of Beta Thalassemia Major, which is inherited in an autosomal recessive fashion.

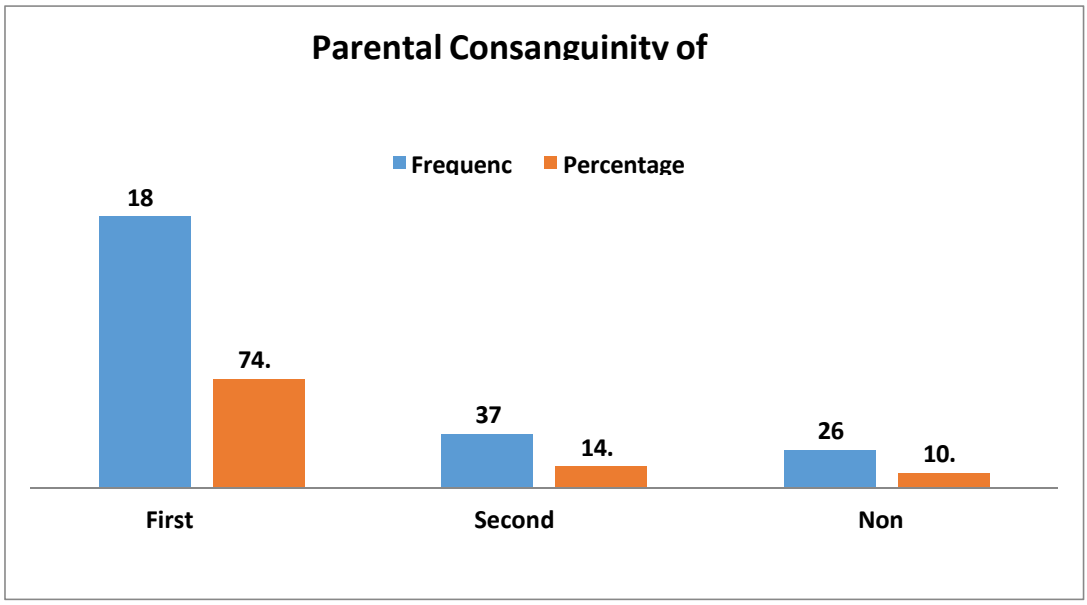

Figure-4: Illustrate Parental Consanguinity

Based on Family History

The current study also found that 56.8% of patients had a positive family history of thalassemia, compared to 43.2% who had a negative family history.

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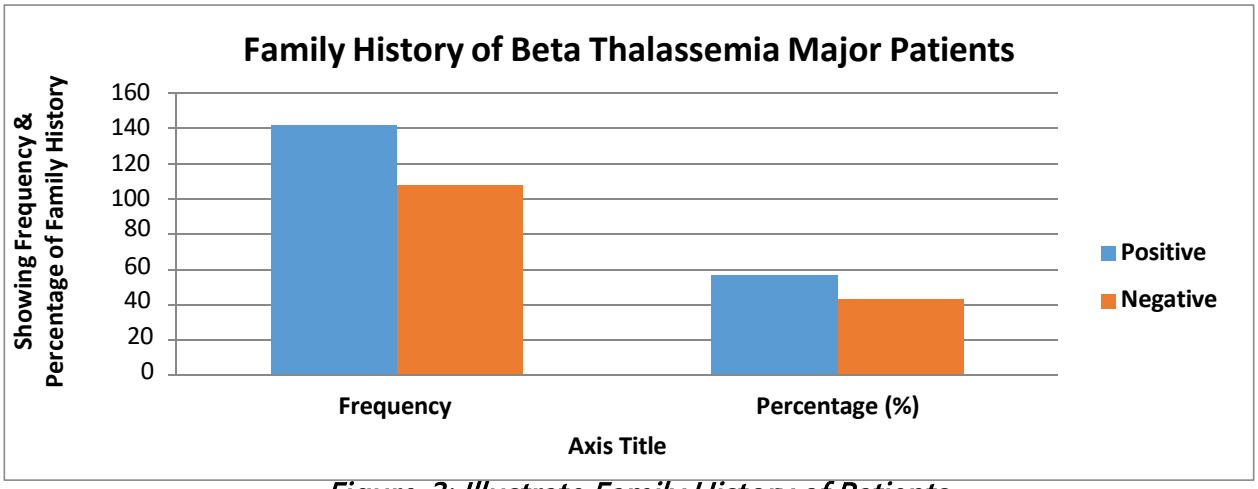

Figure-3: Illustrate Family History of Patients

Clinical Features of Patients Associated with Beta Thalassemia Major

The most prevalent clinical characteristics found in patients in this study were splenomegaly, hepatomegaly, weakness, growth retardation, and fever. Splenomegaly was the most common clinical sign seen in 24.8% of patients, followed by weakness (22.4%) and hepatomegaly (14.8%), as illustrated in figure 5.

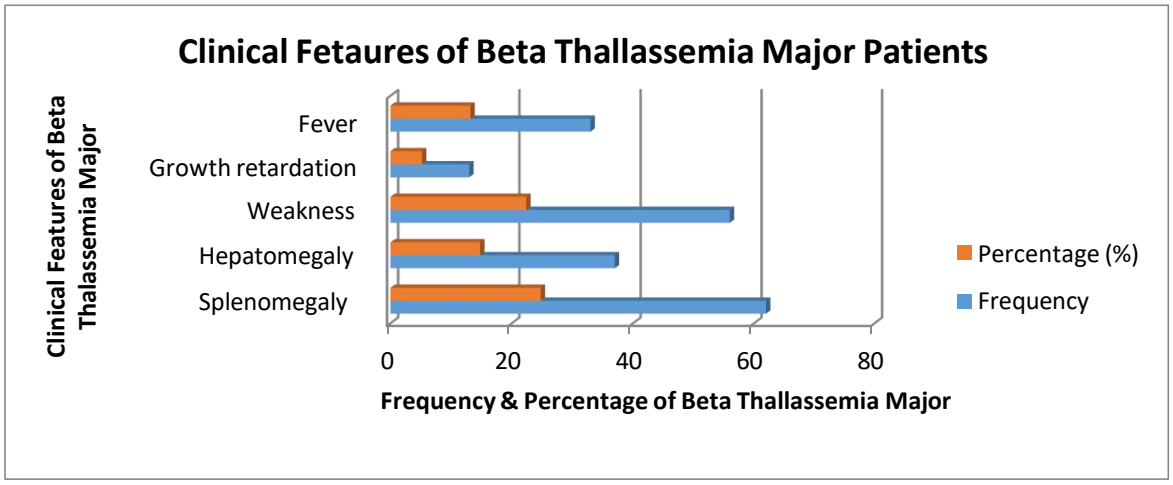

Figure-5: Illustrate Clinical Presentation of Beta Thalassemia Patients

Hematological Profile of Patients

The patients' hematological profile revealed a mean hemoglobin level of 6.7 g/dL, indicating severe anemia. Low MCV and MCH readings indicated microcytic hypochromic anemia, a typical finding in Beta Thalassemia Major patients, as seen in table 2.

Table 2: *Showing Hematological Parameters of Patients*

Hematological Parameters	Means ± SD
Hemoglobin (Hb)	6.7±0.94
RBC	3.15±0.58
HCT	21.44±3.59
MCV	62.95±8.77
MCH	20.22±4.77
MCHC	30.26±2.92
WBC Count	1928.60±6964.70

Blood Group of Patients

The most prevalent blood group found among patients was O+ (24%), followed by B+ (23.2%) and AB+ (19.22%). Negative blood types were less prevalent among all patients. The distribution of blood groups is important for blood transfusion management in patients with Beta Thalassemia Major, as these patients require regular blood transfusions at appropriate intervals.

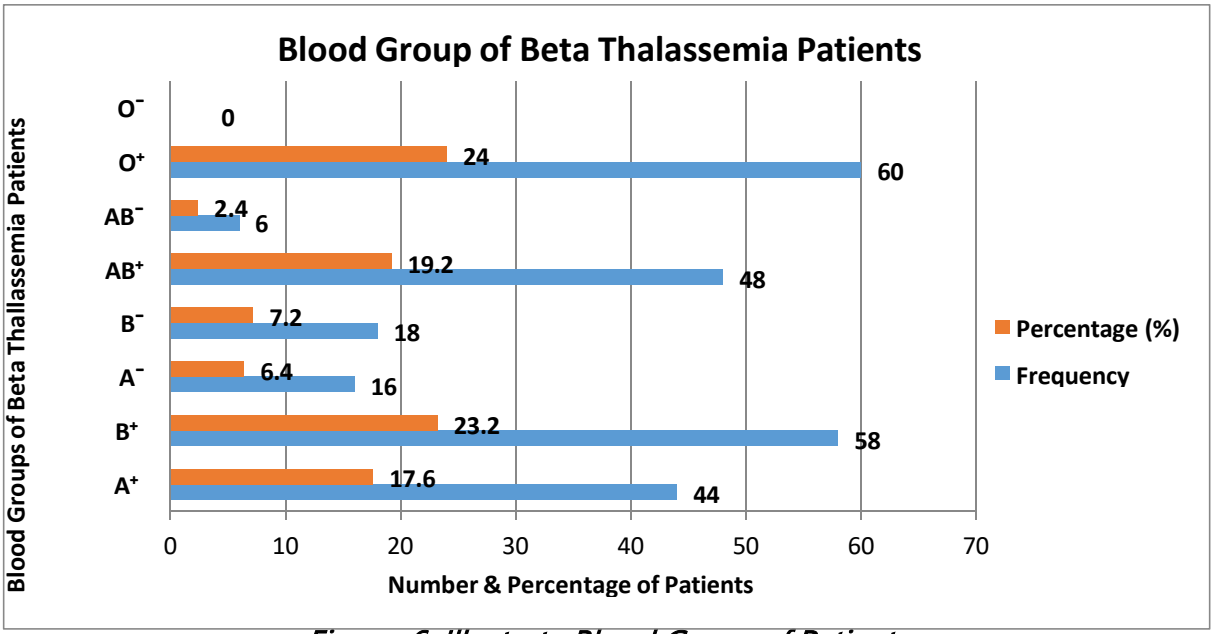

Figure-6: Illustrate Blood Group of Patient

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Blood Transfusion Frequency of Patients Associated with Beta Thalassemia Patients

In this current research study, the majority of patients (56.8%) had blood transfusions every four weeks, while 31.2% required transfusions every three weeks, as illustrated in Figure 7.

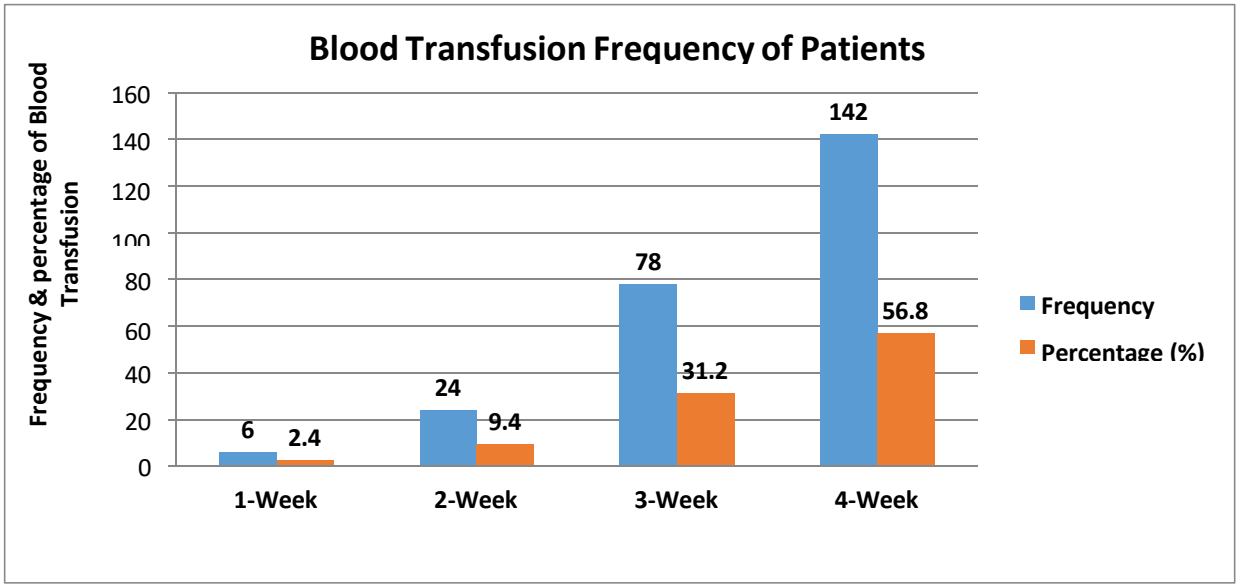

Figure-7: Illustrate Blood Transfusion Frequency

Inferential Statistics

Inferential statistics were used to determine the relationship between the various study variables. The chi-square test was used for categorical variables, the independent sample t-test for two-group comparisons, and one-way ANOVA for comparisons of more than two groups. A p-value of <0.05 indicated statistical significance.

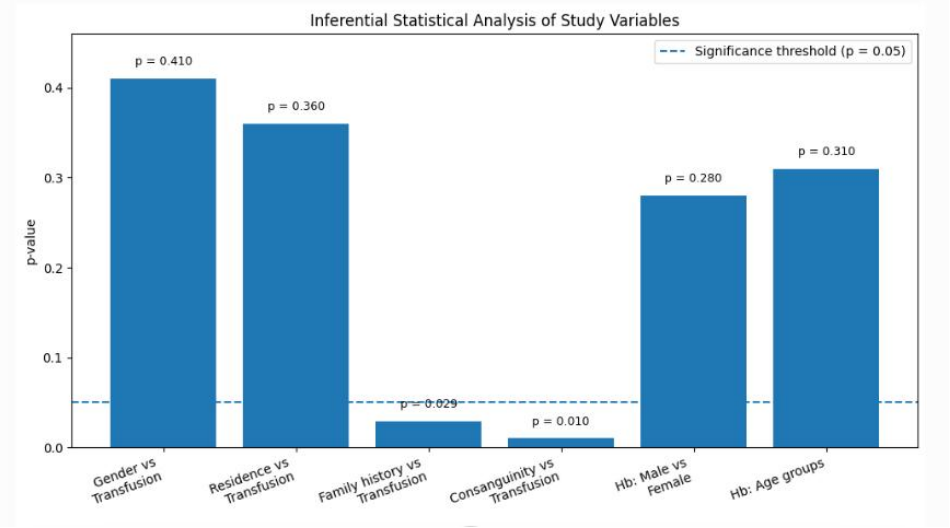

Figure-8 Shows The figure presents the results of inferential statistical analyses performed to assess the associations and differences among the study variables. The findings showed that gender and residence were not significantly associated with blood transfusion frequency (p = 0.41 and p = 0.36, respectively). In contrast, family history of thalassemia and parental consanguinity showed statistically significant associations with transfusion frequency (p = 0.029 and p = 0.010, respectively). No statistically significant difference was observed in mean hemoglobin levels between male and female patients (p = 0.28) or among different age groups (p = 0.31). Overall, family history and parental consanguinity were the only variables demonstrating statistically significant associations, as their p-values were below the significance level of 0.05.

Discussion

In this study, a total of 250 patients with β-thalassemia major were analyzed. Gender-wise Discussion. The present study evaluated the demographic, clinical, hematological, blood-group, and transfusion characteristics of 250 patients with β-thalassemia major in District Karak. The findings demonstrate a considerable burden of β-thalassemia among children and young individuals in the study population. Male patients were more frequent than females (57.5% vs. 42.8%), which is comparable with observations from other Pakistani studies reporting a higher proportion of male β-thalassemia patients. However, β-thalassemia is an autosomal recessive disorder and therefore does not have a biological sex preference; the observed difference may reflect differences in healthcare access, registration, or attendance at treatment centers rather than a true sex-related predisposition (21,22). A particularly important finding was the predominance of children aged 1–10 years (76.8%). This may be explained by the severe clinical nature of β-thalassemia major, which usually becomes apparent during early childhood and

requires regular transfusion therapy. Similar emphasis has been placed on early diagnosis and initiation of appropriate treatment to improve growth, development, and long-term outcomes in transfusion-dependent thalassemia (23). The high proportion of young patients also highlights the importance of early screening and preventive programs in the local population. Parental consanguinity was very common in the present study, with 78.8% of patients born to first-cousin parents and 14.8% to second-cousin parents. This finding is particularly important in the Pakistani context because consanguineous marriage increases the probability that both parents carry the same autosomal-recessive β-thalassemia variant. Recent Pakistani research has also reported a strong relationship between consanguinity, family history, and β-thalassemia major (21). Therefore, the high proportion of consanguineous marriages observed in District Karak supports the need for premarital carrier screening, genetic counseling, and family-based testing. More than half of the patients (56.8%) had a positive family history of thalassemia. This finding further supports the familial nature of β-thalassemia and suggests that families with an affected child may represent an important target group for cascade screening.

Identification of carriers within affected families can facilitate genetic counseling and help reduce the risk of subsequent affected births (22,24). The most common clinical manifestations in this study were splenomegaly (24.8%), weakness (22.4%), and hepatomegaly (14.8%). These findings are consistent with the pathophysiology of β-thalassemia major, in which ineffective erythropoiesis, chronic anemia, increased red-cell destruction, and extramedullary hematopoiesis can contribute to enlargement of the spleen and liver. Current recommendations emphasize regular clinical monitoring for complications associated with chronic anemia and transfusion-dependent disease (23,25). The hematological findings demonstrated severe anemia, with a mean hemoglobin level of 6.7 ± 0.94 g/dL. The reduced MCV (62.95 ± 8.77 fL) and MCH (20.22 ± 4.77 pg) indicate a marked microcytic and hypochromic pattern, which is characteristic of β-thalassemia. The low mean hematocrit of 21.44% further supports the presence of significant anemia. These findings emphasize the dependence of the study population on regular transfusion therapy to maintain adequate hemoglobin levels and suppress ineffective erythropoiesis (23,25). Regarding blood groups, O+ was the most frequent blood group (24%), followed by B+ (23.2%) and AB+ (19.22%), while Rh-negative groups were less common. These findings are broadly consistent with Pakistani studies demonstrating a predominance of Rh-positive blood groups among β-thalassemia patients, although the relative frequency of individual ABO groups varies between populations. Mushtaq et al. reported B as the most frequent ABO group followed by O,

whereas Waheed et al. reported an O>B>A>AB pattern among β-thalassemia patients in Lahore (21,26). Such differences may reflect regional variation in the underlying population rather than an association between ABO blood group and β-thalassemia itself. The transfusion profile showed that 56.8% of patients required transfusion every four weeks, whereas 31.2% required transfusion every three weeks. This pattern is consistent with the recommended individualized transfusion approach for transfusion-dependent β-thalassemia, in which transfusion intervals are adjusted according to pre-transfusion hemoglobin, growth, clinical condition, and individual transfusion requirements (23). More frequent transfusion requirements may reflect greater disease severity or increased transfusion needs. The inferential analysis showed that gender and residence were not significantly associated with transfusion frequency. In contrast, family history ($p=0.029$) and parental consanguinity ($p=0.010$) were significantly associated with transfusion frequency. These findings suggest that genetic and familial factors may contribute to differences in disease severity and transfusion requirements, although the cross-sectional design does not establish causation. No significant difference was observed in mean hemoglobin between males and females or among different age groups, indicating that sex and age alone did not significantly influence hemoglobin levels in this cohort. Overall, the findings emphasize that β-thalassemia major remains an important health problem in District Karak. The high frequency of consanguinity and positive family history indicates a need for stronger preventive measures, while severe anemia and regular transfusion requirements demonstrate the continuing need for reliable transfusion services. Extended blood-group and antigen matching is also important because chronically transfused thalassemia patients are at risk of red-cell alloimmunization; recent evidence supports more comprehensive antigen matching to reduce transfusion-related complications (27,28). Therefore, integrating early diagnosis, family screening, genetic counseling, safe transfusion practices, and regular hematological monitoring could substantially improve the management and prevention of β-thalassemia in the study population.

Conclusion

β-thalassemia major is a significant health burden in District Karak, characterized by severe anemia and lifelong transfusion dependence. Most patients were young, male, had a positive family history, and were born to consanguineous parents. O+ and B+ were the most common blood groups, while most patients required transfusions every four weeks. Improved screening, genetic counseling, regular monitoring, and safe transfusion services are essential to improve patient outcomes.

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