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The Prevalence and Distribution of Beta Thalassemia Trait among Outpatient Individuals in A Tertiary Care Hospital of Lodhran, Pakistan

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ABSTRACT

Thalassemia is an autosomal recessive genetic disorder characterized by impaired synthesis of hemoglobin due to mutations affecting the production of alpha (α) or beta (β) globin chains. This imbalance causes ineffective erythropoiesis, microcytic anemia, and hematological abnormalities. **Objectives:** To assess the prevalence and distribution of β-thalassemia carriers for implementing targeted screening and preventive strategies. **Methods:** This retrospective observational study analyzed 108 samples from patients who were suspected of a complete blood count parameter; which included Mean Corpuscular Volume, Mean Corpuscular Hemoglobin, and total red blood cell count. After that analysis of the suspected patients' blood for Hb A2 through Hb Electrophoresis for the screening of the thalassemia trait was carried out. The data were sourced from Shahida Islam Medical College Hospital, reflecting the carrier status of the participants. **Results:** The findings of the study are distributed between 62 male and 46 female and demonstrated the presence of β-thalassemia trait across various age groups (mean age 25) and found typically higher (52.8%) in the age of 21 to 30 years. Specifically, 68 out of the 108 patients tested positive for the β-thalassemia trait having raised Hb A2 level on the Hb electrophoresis. **Conclusions:** It was concluded that the β-thalassemia trait is widespread across diverse ethnic groups. It highlights the necessity for standardized blood testing protocols for β-thalassemia screening. Implementing comprehensive screening programs, coupled with enhanced public awareness and educational campaigns, is crucial to mitigate the incidence of thalassemia major. These measures are essential for populations to prevent the transmission of this genetic abnormality.

INTRODUCTION

Thalassemia represents a spectrum of inherited hematologic disorders due to defective hemoglobin (Hb) chain synthesis [1]. Beta-thalassemia arises from impaired or absent beta-globin chain production, similar to alpha-thalassemia, which affects alpha-globin chain synthesis. Imbalances in globin chains disrupt erythropoiesis and induce hemolysis [2]. Thalassemia is derived from Greek terms meaning "sea" and "blood," thalassemia encompasses three main types: Thalassemia Minor (beta-thalassemia carrier or trait) and Thalassemia Major (also called Cooley's Anemia or Mediterranean Anemia) and Thalassemia Intermedia [3]. Thalassemia is characterized by inadequate Hb production, leading to the generation of unstable, unpaired globin chains that damage red cell membranes, reducing erythropoiesis and contributing to the clinical symptoms of the disease [4]. Thalassemia is among the illnesses that result in Hb that is not produced properly [5]. The formation of beta chains is faulty in β-thalassemia, resulting in the production of unpaired chains. These structures are unstable, which leads to

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membrane damage, poor erythropoiesis, and other disease-related clinical characteristics [6]. The majority of people with thalassemia traits are discovered by chance irrespective of age, some people are diagnosed with older age above 50 years and some with an early age, when a slight microcytic anemia is detected on a complete blood count [7]. In severe cases, infants under two years old may present with profound microcytic anemia, mild jaundice, and hepatosplenomegaly, suggestive of thalassemia major. Thalassemia intermedia, while presenting with similar symptoms, manifests later and is often milder [8]. Carriers typically remain asymptomatic but may occasionally exhibit minor hematologic findings. Over 200 mutations affecting the beta-globin gene have been documented, mostly point mutations in functionally critical regions, with deletions being rare [9]. The beta-thalassemia trait, like other inherited characteristics such as hair or eye colour, is passed from parent to child [10]. Generally asymptomatic and often referred to as beta-thalassemia minor, this trait does not typically affect health [11]. If one parent carries the trait, each child has a 50% chance of inheriting it. 50% (1 in 2) of parents who have beta thalassemia trait have a kid who has it. 50% (1 in 2) of parents do not have a characteristic in their child. In thalassemia minor, Hb A levels are significantly reduced, while Hb F and Hb A2 levels are markedly elevated [12]. Beta-thalassemia minor, also referred to as the carrier trait, typically presents as mild anemia, and carriers are generally asymptomatic. When both parents carry the beta-thalassemia trait, there is a 25% risk in each pregnancy of having a child affected by beta-thalassemia major. The moderate anemia-like symptoms of beta thalassemia are minor like fatigue, weakness or dizziness, frequent migraines and yellowish skin [11]. Evaluation of Thalassemia trait key important parameters of complete blood count (CBC) are important like mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) red cell count along with a patient's medical history can help exclude certain etiologies. In cases of thalassemia minor, the MCV typically falls below 80 fL, whereas in iron deficiency, it rarely drops below 80 fL unless the hematocrit level is under 30%, same as MCH is also low or borderline normal and the red blood cells (RBC) count is slightly higher (5.5 x106/dL) and this is accompanied by elevated Hb A2 levels [13]. On peripheral blood smear examination, red blood cells (RBCs) in carriers exhibit minimal morphological abnormalities compared to those seen in affected individuals, and erythroblasts are generally absent [14]. The prevention of beta-thalassemia heavily depends on prenatal diagnostic techniques, carrier screening, and genetic counselling. Genetic counselling aims to educate individuals and couples at risk (e.g., carrier-carrier pairs) about inheritance patterns, genetic risks, disease progression, and available or emerging treatment options.

This study aims to assess the occurrence rate of the β-thalassemia trait as indicated by suspected abnormalities in complete blood count (CBC) parameters among patients in a tertiary care hospital.

METHODS

This retrospective study was conducted at Shahida Islam Medical College Hospital, a Tertiary Care Centre in Lodhran, Pakistan. The duration of the study was July to September 2024, 3 months of records of hematological reports. The sample size of 108 was determined using a formula based on a 95% confidence level (Z=1.96) and a predefined margin of error [15]. A non-probability convenience sampling method was employed after obtaining approval from the Institutional Review Board (Letter No: SIMC/ET.C./00010/24). Patient selection was based on complete blood count (CBC) parameters indicative of suspected β-thalassemia trait, including low mean corpuscular volume (MCV) less than 80 (normal values 80 – 105 fL), low or borderline-normal mean corpuscular Hb (MCH) less than 29 (normal values 27–30 pg), and slightly elevated red blood cell (RBC) counts specifically ≥5.5x106 / dL (normal values 4.5–6.0 x106/dL). These criteria were used to identify potential carriers of β-thalassemia. Hb A2 levels were measured to confirm the diagnosis, utilizing the high-performance liquid chromatography (HPLC) technique commonly used in Hb electrophoresis test [16]. Hb electrophoresis is a laboratory technique used to separate and identify different types of Hb based on their electrical charge and structure. This technique is especially useful in diagnosing hemoglobinopathies, such as thalassemia, and other Hb variants. In the case of beta-thalassemia, electrophoresis helps identify abnormal Hb patterns, including elevated levels of HbA2 and sometimes Hb F, which are characteristic of the disease. HPLC provided precise separation and quantification of Hb variants, enabling the identification of β-thalassemia carriers [17]. Data were collected using a structured self-designed performance. Categorical variables were summarized as frequencies in the form of percentages. Categorical variables were summarized as frequencies and percentages. Mean and standard deviation (SD) were calculated for continuous variables. Statistical analysis was performed using SPSS version 28.0, and significance was also assessed at a 5% level. The prevalence of the β-thalassemia trait which was measured through the HPLC technique also present in the tabular as well as graphical chart form.

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RESULTS

This study included 108 outdoor patients. Among them 62 (57.4%) were male and 46 (42.6%) were female (Table 1).

Table 1: Gender Distribution Table (n=108)

Gender of Patients	Frequency (%)
Male	62 (57.4%)
Female	46 (42.6%)
Total	108 (100%)

According to the data, the age of patients is divided into 6 groups and the mean age of 25 years. 1-10 years, 11-20 years, 21-30 years, 31-40 years, 41-50 years and 51-60 years. There were 8 (7.4%) patients with age 1-10 years, 17 (15.7%) patients with age 11-20 years, 57 (52.8%) patients with age 21-30 years, 18 (16.8%) patients with age 31-40 years, 5 (4.6%) patients with age 41-50 years and 3 (2.7%) patients with age 51-60 years (Table 2).

Table 2: Distribution of Patients by Age (n=108)

Age of Patients	Frequency (%)
1-10	8 (7.4%)
11-20	17 (15.7%)
21-30	57 (52.8%)
31-40	18 (16.8%)
41-50	5 (4.6%)
51-60	3 (2.7%)
Total	108 (100%)

Table 3 categorizes patients based on their Mean Corpuscular Volume (MCV) values, reflecting the average size of red blood cells. Among the 108 patients, the largest group (45, 41.7%) had MCV values between 65–75 fL. This was followed by 33 patients (30.6%) with MCV values in the 75–80 fL range, representing borderline low levels. The smallest group (30, 27.8%) had MCV values below 65 fL, consistent with suggestive of severe microcytosis with combined iron deficiency. These findings highlight the predominance of low MCV values in the study population, aligning with the inclusion criteria focused on identifying the β-thalassemia trait. Results present the distribution of patients based on their Mean Corpuscular Hemoglobin (MCH) levels, which indicate the average Hb content per red blood cell. The majority (50, 46.3%) exhibited MCH values in the borderline low values range of 25–27 pg, while 40 patients (37.0%) had MCH levels below 25 pg which suggested the combined iron deficiency or any microcytic cause. A smaller proportion (18, 16.7%) had MCH values between 27–29 pg which is borderline normal. The predominance of low and borderline-normal MCH levels (less than 29 pg) supports the focus on diagnosing conditions like β-thalassemia trait. Results classify patients based on their red blood cell (RBC) count, an important parameter in diagnosing hematological disorders. Over half of the patients (60, 55.6%) had RBC counts between 5.5–6.5×10^6/µL, reflecting the characteristic erythrocytosis seen in β-thalassemia carriers. A significant minority (28, 25.9%) exhibited RBC counts above 6.5×10^6/µL, while 20 patients (18.5%) had RBC counts of exactly 5.5×10^6/µL. These results emphasize the diagnostic value of elevated RBC counts in identifying β-thalassemia carriers. Results summarize the distribution of patients based on their Hb A2 levels, a key diagnostic parameter for identifying β-thalassemia trait. Among the 108 patients, the majority (68, 62.9%) had Hb A2 levels greater than 3.5%, which is diagnostic of the β-thalassemia trait. Elevated Hb A2 levels are a hallmark of this condition, as they result from reduced beta-globin chain production and increased delta-globin chain compensation. A significant proportion (29, 26.9%) exhibited Hb A2 levels in the range of 2–3%. These levels are considered within the normal range. A smaller subset of patients (11, 10.2%) had HbA2 levels below 2% (Table 3).

Table 3: Biochemical characteristics of the study participants

Mean Corpuscular Volume (MCV) fL	
Unit (fL)	**Frequency (%)**
<65	30 (27.8%)
65–75	45 (41.7%)
75–80	33 (30.6%)
Total	108 (100%)
Mean Corpuscular Hemoglobin (MCH) pg	
Unit (pg)	**Frequency (%)**
<25	40 (37.0%)
25–27	50 (46.3%)
27–29	18 (16.7%)
Total	108 (100%)
Red Blood Cell Count (RBC count) 10^6/µL	
Unit (10^6/µL)	**Frequency (%)**
≤ 5.5	20 (18.5%)
5.5–6.5	60 (55.6%)
> 6.5	28 (25.9%)
Total	108 (100%)
According to the Results of Hb A2	
Hb A2 (%)	**Frequency (100%)**
>3.5%	68 (62.9%)
2-3%	29 (26.9%)
<2%	11 (10.2%)
Total	108 (100%)

Further study presents the results of the screening for β-thalassemia trait in the study population of 108 patients which are based on the HbA2 results which are measured by Hb Electrophoresis. Among the participants, 68 patients (62.9%) were screened out for the β-thalassemia trait. This group represents those who also exhibited the characteristic hematological and genetic markers for the trait, including elevated Hb A2 levels, low levels of MCV and MCH, and increased red blood cell count. These findings

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confirm the presence of the β-thalassemia trait. And 40 patients (37.1%) did not show evidence of the β-thalassemia trait due to normal levels of Hb A2 either their CBC meets the suggestive line (Table 4).

Table 4: Suggestive of Beta Thalassemia Trait (n=108)

According to the Results of Hb A2	Frequency (%)
Detected	68 (62.9%)
Not Detected	40 (37.1%)
Total	108 (100 %)

DISCUSSION

The objective of this study was to assess the occurrence rate of the β-thalassemia trait based on abnormalities in complete blood count (CBC) parameters among patients in a tertiary care hospital. The findings of this study highlight the CBC parameters also give us an idea of the suggestive carrier of Thalassemia, so according to our we see a significant association between CBC parameters, such as mean corpuscular volume (MCV), mean corpuscular Hb, red blood cell (RBC) count, and HbA2 levels, in the detection of β-thalassemia trait. In total, 108 outdoor patients were included in this study. The gender distribution revealed that 57.4% of the participants were male, while 42.6% were female. The study's age distribution showed that the majority of patients fell within the 21-30-year age range, which constituted 52.8% of the sample. This finding is consistent with previous studies, which have shown that thalassemia traits are often detected in young adults, typically between the ages of 20 and 30 years, due to routine screening or clinical symptoms appearing in this age group [18, 19]. The mean corpuscular volume (MCV) and mean corpuscular Hb are critical hematological parameters used in the initial identification of microcytic anemia, a hallmark feature of the β-thalassemia trait. The majority of patients in this study had MCV values between 65–75 fL (41.7%) and MCH values between 25–27 pg (46.3%). These findings are consistent with typical characteristics of β-thalassemia carriers, where a decrease in MCV and MCH is commonly observed due to reduced Hb production and the presence of unpaired globin chains in the red blood cells [20]. Elevated RBC counts were also observed in the majority of patients, further suggesting erythrocytosis, which is often seen in individuals with thalassemia traits as the body compensates for reduced Hb production [21]. Hb electrophoresis, particularly through high-performance liquid chromatography (HPLC), plays a vital role in the definitive diagnosis of β-thalassemia trait. In this study, 62.9% of the participants exhibited HbA2 levels greater than 3.5%, which is diagnostic of the β-thalassemia trait. Elevated HbA2 levels are a key marker for β-thalassemia, as they result from the reduced production of beta-globin chains, leading to an increase in delta-globin chains [22]. This finding aligns with existing literature, which states that a HbA2 level above 3.5% is diagnostic of the β-thalassemia trait in the presence of suggestive hematological features, such as low MCV and MCH [23]. While 37.1% of the patients did not exhibit elevated HbA2 levels, their CBC parameters still met the criteria suggestive of the β-thalassemia trait. This discrepancy could be attributed to variations in genetic factors or the possibility of other factors influencing HbA2 levels, such as coexisting iron deficiency or other hemoglobinopathies. It highlights the importance of using multiple diagnostic tools, including Hb electrophoresis, to confirm the presence of the β-thalassemia trait [24]. This study found that 62.9% of the patients screened showed evidence of the β-thalassemia trait, which is consistent with global prevalence rates of β-thalassemia in populations with high carrier rates, such as those in the Mediterranean, Middle East, and South Asia regions, including Pakistan. A similar study conducted in a neighboring region found a prevalence of approximately 60% in the general population [25]. These results emphasize the need for widespread screening programs, especially in regions with a high frequency of thalassemia, to prevent the transmission of the disorder and reduce the burden of severe thalassemia.

CONCLUSIONS

It was concluded that this study demonstrates a high prevalence of the β-thalassemia trait among patients in a tertiary care hospital in Pakistan, with 62.9% of the participants showing elevated HbA2 levels, which were indicative of the trait. The findings underline the importance of CBC parameters, such as MCV, MCH, and RBC count, in the early detection of potential β-thalassemia carriers. The study also highlights the crucial role of Hb electrophoresis in confirming the diagnosis. These results can inform future research and the development of screening programs aimed at early identification and genetic counselling for thalassemia carriers in Pakistan.

Authors Contribution

Conceptualization: FAK
Methodology: UC, SN, RA
Formal analysis: KKR, AS
Writing review and editing: FAK, SA

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Weatherall DJ. The Inherited Diseases of Hemoglobin Are an Emerging Global Health Burden. Blood, The Journal of the American Society of Hematology. 2010 Jun; 115(22): 4331-6. doi: 10.1182/blood-2010-01-251348.

[2] Sari DP, Wahidiyat PA, Setianingsih I, Timan IS, Gatot D, Kekalih A. Hematological parameters in individuals with beta thalassemia trait in south sumatra, Indonesia. Anemia. 2022;2022(1):3572986. https://doi.org/10.1155/2022/3572986

[3] Tabassum S, Khakwani M, Fayyaz A, Taj N. Role of Mentzer index for differentiating iron deficiency anemia and beta thalassemia trait in pregnant women. Pakistan Journal of Medical Sciences. 2022 Mar;38(4Part-II):878.. https://doi.org/ 10.12669/pjms.38.4.4635

[4] Das R, Saleh S, Nielsen I, Kaviraj A, Sharma P, Dey K, Saha S. Performance analysis of machine learning algorithms and screening formulae for β-thalassemia trait screening of Indian antenatal women. International Journal of Medical Informatics. 2022 Nov 1;167:104866. https://doi.org/10.1016/j.ijmedinf.2022.104866

[5] Anastasiadi AT, Paronis EC, Arvaniti VZ, Velentzas AD, Apostolidou AC, Balafas EG, Dzieciatkowska M, Kostomitsopoulos NG, Stamoulis K, Papassideri IS, D'Alessandro A. The post-storage performance of RBCs from beta-thalassemia trait donors is related to their storability profile. International Journal of Molecular Sciences. 2021 Nov 13;22(22):12281. https://doi.org/10.3390/ijms222212281

[6] Rao P, Raj EA, Natesan S, Gudi N. Prevalence of Sickle cell disease, Sickle cell Trait and HBS-beta-thalassemia in India: a systematic review and Meta-analysis. Clinical Epidemiology and Global Health. 2024 Jun 19:101678. https://doi.org/10.1016/j.cegh.2024.101678

[7] Jain AK, Sharma P, Saleh S, Dolai TK, Saha SC, Bagga R, Khadwal AR, Trehan A, Nielsen I, Kaviraj A, Das R. Multi-criteria decision making to validate performance of RBC-based formulae to screen β-thalassemia trait in heterogeneous haemoglobinopathies. BMC Medical Informatics and Decision Making. 2024 Jan 2;24(1):5. https://doi.org/10.1186/s12911-023-02388-w

[8] Taher AT, Musallam KM, Cappellini MD. β-Thalassemias. New England Journal of Medicine. 2021 Feb; 384(8): 727-43. doi: 10.1056/NEJMra2021838.

[9] Saleh KK and Kakey ES. Thalassemia Major Is a Severe Anemia That Requires Blood Transfusions. In This Study, We Searched into the Hematological and Biochemical Status of Beta-Thalassemia Major Patients in Koya. Hematological Analysis Revealed Severe Anemia in Beta-Thalassemia P. Zanco Journal of Pure and Applied Sciences. 2021 Oct; 33(5): 76-84. doi: 10.21271/ZJPAS.33.5.9.

[10] Yalçıntepe S. Beta Globin Mutations in Beta Thalassemia Minor Patients in Genetics Diagnosis Center of Trakya University Faculty of Medicine. Ege Journal of Medicine. 2019 Dec; 58(4): 330-5. doi: 10.19161/etd.660966.

[11] Jahan A, Singh G, Gupta R, Sarin N, Singh S. Role of red cell indices in screening for beta thalassemia trait: an assessment of the individual indices and application of machine learning algorithm. Indian Journal of Hematology and Blood Transfusion. 2021 Jul;37:453-7. https://doi.org/10.1007/978-981-99-8933-1_4

[12] Khan MI, Khan HN, Usman M. Beta thalassemia Trait: Diagnostic Importance of Haematological Indices in Detecting Beta Thalassemia Trait Patients. The Professional Medical Journal. 2018 Apr; 25(04): 545-50. doi: 10.29309/TPMJ/2018.25.04.343.

[13] Mosca A, Paleari R, Ivaldi G, Galanello R, Giordano PC. The role of haemoglobin A2 testing in the diagnosis of thalassaemias and related haemoglobinopathies. J Clin Pathol. 2009;62:13–7 https://doi.org/10.1136/jcp.2008.056945.

[14] Yao QC, Zhai HL, Wang HC. Ratio of Hemoglobin to Mean Corpuscular Volume: A New Index for Discriminating Between Iron Deficiency Anemia and Thalassemia Trait. World Journal of Clinical Cases. 2023 Dec; 11(35): 8270. doi: 10.12998/wjcc.v11.i35.8270.

[15] Arthur WN, David GN. Pathophysiology and clinical manifestations of the β-thalassemias. Cold Spring Harb Perspect Med. 2012;2(12):a011726. https://doi.org/10.1101/cshperspect.a011726.

[16] Madan N, Sharma S, Sood SK, Colah R. Frequency of B-Thalassemia Trait and Other Hemoglobinopathies in Northern and Western India. Indian Journal of Human Genetics. 2010 Jan; 16(1): 16. doi: 10.4103/0971-6866.64941.

[17] Mutua B, Chelangat R, Mustafa B, Were T, Makani J, Sowayi G *et al.* High-Performance Liquid Chromatography Local Reference Ranges of Hemoglobin Fractions (HbA, HbA2, and HbF) in Detection of Hemoglobinopathies in Western Kenya. The Egyptian Journal of Internal Medicine. 2022 Dec; 34(1): 95. doi: 10.1186/s43162-022-00187-9.

[18] Kuntaruk S, Tatu T, Keowkarnkah T, Kasinrerk W. Sandwich ELISA for Hemoglobin A 2 Quantification and Identification of B-Thalassemia Carriers.

DOI: https://doi.org/10.54393/pjhs.v5i11.2473

International Journal of Hematology. 2010 Mar; 91: 219-28. doi: 10.1007/s12185-009-0490-3.

[19] Malakar R, Kour M, Malviya SN, Dangi CB. A Review on: Β-Thalassemia. World Journal of Pharmaceutical Research. 2016 Mar; 5(6): 432-45.

[20] Debnath M. Prevalence of Thalassemia in Indian Population-A review. North Bengal Anthropologist. 2021(9): 99-112.

[21] Brancaleoni V, Di Pierro E, Motta I, Cappellini MD. Laboratory Diagnosis of Thalassemia. International Journal of Laboratory Hematology. 2016 May; 38: 32-40. doi: 10.1111/ijlh.12527.

[22] Arthur WN, David GN. Pathophysiology and clinical manifestations of the β-thalassemias. Cold Spring Harb Perspect Med. 2012;2(12):a011726. https://doi.org/10.1101/cshperspect.a011726.

[23] Carla MG, Rafael SP, Isabel FG, Cristina GF, Teresa SM. New haematologic score to discriminate beta thalassemia trait from iron deficiency anaemia in a Spanish Mediterranean region. Clinica Chimica Acta. 2020 Aug 1;507:69-74. https://doi.org/10.1016/j.cca.2020.04.017

[24] Değermenci Ş, Aslan D. HbA2 levels in children with β-thalassemia trait associated with iron deficiency: A perspective for pediatricians. American Journal of Clinical Pathology. 2024 Dec;162(6):544-8. https://doi.org/10.1093/ajcp/aqae085

[25] Sun A, Chang JY, Jin YT, Chiang CP. Differential diagnosis between iron deficiency anemia and thalassemia trait-induced anemia. Journal of Dental Sciences. 2023 Oct;18(4):1963. https://doi.org/10.1016/j.jds.2023.07.036