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PREVALENCE OF THALASSEMIA TRAIT AMONG INDIVIDUALS AT RISK IN NAWABSHAH: A CROSS-SECTIONAL STUDY

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ABSTRACT

Background: Thalassemia is a genetic condition characterized by an inability to properly produce alpha and beta hemoglobin components.

Aim of study: To determine how often the thalassemia trait occurs among healthy people in Nawabshah.

Methods: This study was conducted at the People's University of Medical and Health Sciences, Nawabshah, between Aug 2024 and Dec 2024. Individuals referred by physicians for thalassemia screening were directed to the Outpatient Department (OPD) for testing. A total of 2315 individuals underwent screening, out of which 216 individuals who tested positive for the thalassemia trait and were confirmed by physicians were included in the final analysis.

Results: Thalassemia screening included 2315 participants. Of the total, 7.2% (n = 166) tested positive for thalassemia traits during screening. In our study population, beta-thalassemia was the most common (84.60%, n=141), followed by HbE thalassemia (11.50%, n=48), whereas alpha-thalassemia was the least prevalent, accounting for 3.90% (n=16) of the cases. Of the thalassemia cases, 81.9% were associated with consanguineous marriages, indicating a significant prevalence of intrafamilial unions among affected individuals. Conversely, 18.1% of the cases were linked to exogamous marriages, demonstrating a smaller proportion of cases arising from marriages outside the family.

Conclusion: This study demonstrated that β-thalassemia was the predominant subtype among patients with thalassemia in the screened population. A significantly elevated prevalence of consanguineous marriages has been identified as the primary etiological factor contributing to thalassemia in Nawabshah.

Keywords: Thalassemia, Nawabshah, anemia, MCH, prevalence

INTRODUCTION

A genetic condition characterized by an abnormality in the production of hemoglobin alpha and beta subunits is known as thalassemia (1). Over 200 separate point mutations and, very rarely, deletion events on chromosome 11 cause β-thalassemia (1,2). There are two clinically important variants of beta-thalassemia: beta thalassemia major and beta thalassemia intermedia, which are characterized by diminished or absent production of the hemoglobin subunit beta chain and result in microcytic hypochromic anemia. People with β-thalassemia major often have numerous blood transfusions within the first six to twenty-four months of life, whereas those with β-thalassemia intermedia typically experience transfusions later in life and do not need them as frequently (3).

More than 60 nations in the Near East, Southeast Asia, the Indian subcontinent, North and West Africa, the Middle East, and the Mediterranean have a high incidence and prevalence of thalassemias. Together, these areas form what is known as the "Thalassemia Belt." Only those of ancestry from these regions with a greater frequency of thalassemia will develop the disease in Western nations (4,5).

In India, the carrier frequency of the b-thal characteristic is 3.0-4.0%, according to the World Health Organization. This translates to 35–48 million people throughout the country, with 10,000 babies born per year (6,7). There is a 3.0% average carrier rate of b-thals in Iran, which is similar to India's 4.0% rate, with frequencies ranging from 1.0% to 17.0% (8) (9). With a frequency of 4.5%, b-thal is comparable to that of Malaysia (10). Most people in Southeast Asian nations have one of the three hemoglobinopathies: a-thal, b-thal, or HbE (HBB: c.79G>A). Northern Thailand and Laos had an a-thal gene frequency of 30–40%, Malaysia 4.5–5%, and distant islands of the Philippines 5.0–5%. Furthermore, on the border between Cambodia, Laos, and Thailand, the frequency of Hb E may reach as high as 50-60% (11).

With a population of nearly 170 million, Pakistan has long had knowledge about the prevalence of hemoglobin problems (12). According to reports from 20 years ago, large cities such as Rawalpindi, Karachi, and Lahore had b-thal trait frequencies of 6.0%–13.0% based on Hb electrophoresis (13).Pakistan has an extremely high incidence of b-thal carriers (9.8 million), and every year an additional 9,000 babies are born with b-thal-major (b-TM) (14,15). Due to migration and intermarriage, the clear ethnic link to the b-thal characteristic has been lost, and most people are unaware of this high frequency (15). Pakistan is home to many-thal gene mutations (16,17).

Clinically symptomatic thalassemia is a major health concern in nations in which the thalassemia gene is common. The implementation of control programs, including screening for carriers, prenatal diagnosis, premarital screening, and extended family screening as well as widespread public education and counseling, has helped alleviate this burden in many nations. The benefits of carrier screening include genetic counseling and separation from microcytic hypochromic iron-deficiency anemia. We aimed to quantify the prevalence of thalassemia in healthy individuals who did not exhibit any symptoms. One important aspect of this study is the potential for genetic counseling and family screening recommendations to be extended to the carrier population.

MATERIALS AND METHODS

This study was conducted at the People's University of Medical and Health Sciences, Nawabshah, between Aug 2024 and Dec 2024. Individuals referred by physicians for thalassemia screening were directed to the Outpatient Department (OPD) for testing. A total of 2315 individuals underwent screening, of which 7.2% (n=166) tested positive for thalassemia trait and were confirmed by physicians and were included in the final analysis. Ethical approval for the study was obtained from the Institutional Ethical Review Committee of the hospital before the commencement of the study, ensuring compliance with ethical standards. Verbal informed consent was obtained from all participants after the purpose and procedures of the study were explained. This descriptive cross-sectional study used non-probability convenience sampling. The inclusion criteria were healthy individuals with no apparent clinical symptoms and a normal general physical examination.

Candidates with a history of chronic illness, anemia due to other causes (e.g., iron deficiency), or incomplete data were excluded from the study to minimize confounding factors.

In all, 2315 people who were eligible participants were included in the study. Venous blood samples containing EDTA were collected using disposable syringes and placed in a tube. After blood collection, the tubes were labelled appropriately. An analysis of their Whole blood was analyzed using a Sysmex KX 21 hematology analyzer. These included measuring the total red blood cell (RBC) count, hemoglobin concentration (MCHC), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and hemoglobin (Hb). Participants were tested for beta thalassemia trait if they had microcytic hypochromic indices and normal hemoglobin levels or moderate anemia (defined as hemoglobin levels of ≥8.0 g/dl for females and ≥9.0 g/dl for men). Hemoglobin electrophoresis was performed as described by Dacie and Lewis7, using cellulose acetate paper strips with a pH of 8.5. The absorbance of the eluate was measured using a spectrophotometer to estimate Hb A2. Patients with Hb A2 levels > 3.5% were considered to have β-thalassemia.

The Statistical Package for the Social Sciences (SPSS) version 26.0 or equivalent software was used to input and analyze the data obtained from the research. Descriptive statistics were used to summarize individuals' demographics and hematological data. We used the mean ± standard deviation (SD) to represent continuous variables, including age, hemoglobin concentration, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and other blood parameters. Categorical variables, including sex, marital status, geographic distribution (rural vs. urban), and socioeconomic status, were presented as frequencies and percentages.

RESULTS

Thalassemia screening included 2315 participants. We discovered 166 participants with thalassemia traits throughout the screening, which means that approximately 7.17% of the volunteers were identified as having a disease. With a standard deviation of 1.34 years and a mean age of 24.7 years, the participants' age distribution seems to be rather uniform. The sex distribution was predominantly male, with (81.3%) (135 individuals) being male and only 18.7% (31 individuals) being female (P = 0.0001). In terms of marital status, the married group was significantly higher than single, with 31.3% (52 participants) being single and 68.7% (114 participants) married (0.0001). A significant majority of the participants 83.1% (n=138) resided in rural areas compared to 16.9% (n=28) in urban areas (P = 0.0001). Socioeconomic status was distributed across three categories: the majority of the participants 65.1% (n=108) belonged to the lower class, 24.7% (n=41) were categorized as middle class, and 10.2% (n=17) as upper class (Table 1).

Table 1 Demographic characteristics of thalassemia patients

Variables	**Total 166 n(%)**	**P value**
Mean (SD) age	24.7 ± 1.34	
Gender		
Male	135 (81.3%)	0.0001
Female	31 (18.7%)	
Marital status		
Single	52 (31.3%)	0.0001
Married	114 (68.7%)	
Resident		
Rural	138 (83.1%)	0.0001
Urban	28 (16.9%)	
Socio-economic status		
Upper class	17 (10.2%)	0.0001
Middle class	41 (24.7%)	
Lower class	108 (65.1%)	

Figure 1 illustrates the prevalence of different types of thalassemia in our study population, showing that beta-thalassemia was the most common at 84.9% (n=141), followed by HbE thalassemia at 10.2% (n=17), while Alpha Thalassemia was the least prevalent, accounting for 4.8% (n=8) of the cases.

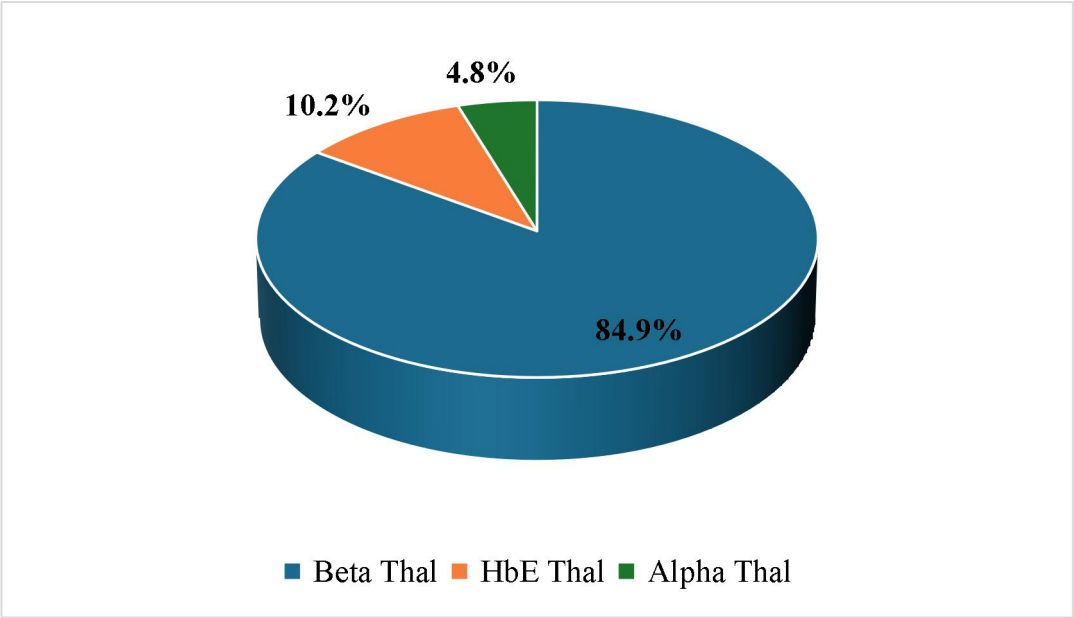

Figure 1 Prevalence of different thalassemia types in the study population.

Of the thalassemia cases, 81.9% were associated with consanguineous marriages, indicating a significant prevalence of intrafamilial unions among affected individuals. Conversely, 18.1% of cases were linked to exogamous marriages, demonstrating a smaller proportion of cases arising from marriages outside the family (Figure 2).

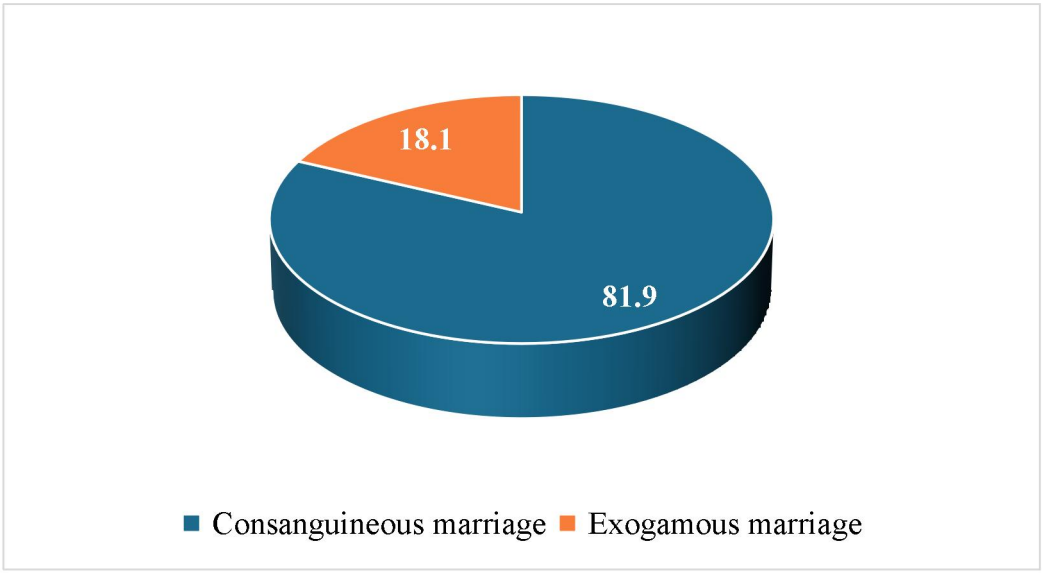

Figure 2 Distribution of Consanguineous and Exogamous Marriages Among Thalassemia Cases

The hematological profile of individuals with the thalassemia trait (n=11) revealed characteristic alterations in red blood cell indices and other blood parameters. The mean red blood cell (RBC) count was elevated at 6.1 ± 1.0 million cells/µL, reflecting the body's compensatory response to produce more red blood cells due to impaired hemoglobin synthesis. However, despite this increased RBC production, the mean hemoglobin concentration was reduced at 11.7 ± 2.4 g/dL, indicative of mild anemia commonly observed in thalassemia trait. The mean corpuscular volume

(MCV), which measures the average size of red blood cells, was significantly low at 60.4 ± 5.2 fL, demonstrating microcytosis—a key diagnostic feature of this condition. Additionally, the mean corpuscular hemoglobin (MCH), which quantifies the average amount of hemoglobin per red blood cell, was markedly reduced at 18.3 ± 0.2 pg/dL, further emphasizing the hypochromic nature of the red blood cells. The mean corpuscular hemoglobin concentration (MCHC), representing the concentration of hemoglobin in a given volume of packed red blood cells, was slightly decreased at 32.5 ± 2.3 g/dL, consistent with the abnormal hemoglobinization of cells. White blood cell (WBC) count and platelet counts remained within normal ranges, with values of 7.92 ± 1.47 × 10^9/L and 287.1 ± 82.33 × 10^9/L, respectively Table 2.

Table 2 Hematological parameters of thalassemia patients

Hematological variables	Thalassemia patients (n=166) (Mean ± SD)
RBC count (g/dl)	6.1 ± 1.0
Hemoglobin (g/dl)	11.7 ± 2.4
MCV (fl)	60.4 ± 5.2
MCH (pg/dl)	18.3 ± 0.2
MCHC (g/dl)	32.5 ± 2.3
WBC (10^9/l)	7.92 ± 1.47
Platelets (10^9/l)	287.1 ± 82.33

DISCUSSION

Our 7.17% (n=166) prevalence rate is in line with previous research in the area, although it varies somewhat from others, highlighting the fact that thalassemia carrier rates vary across communities. Ahmed et al. (2018) found that 3.5% of the general population in Hyderabad, Pakistan had beta-thalassemia trait, which is higher than the national average (18). Discrepancies in genetic susceptibility, consanguinity rates, or ethnic makeup of the sampled population could explain the greater occurrence in Hyderabad. Similar results are in line with the 0.9% prevalence rate reported in a study conducted in Karachi by Khan et al. (2016) (19).

Our study revealed that beta-thalassemia was the predominant hemoglobinopathy in the screened population, accounting for 84.9% (n=141) of the cases. HbE thalassemia was the second most common at 10.2% (n=17), whereas alpha-thalassemia was the least prevalent, representing 4.8% (n=8) of the cases. Similarly, a study across six cities in India found an overall β-thalassemia trait prevalence of 2.78%, with variations across different regions; the HbE trait was highly prevalent in specific areas such as Dibrugarh (23.9%) and Kolkata (3.92%) (20). Promil Jain et. Al also documented β-thalassemia trait as the predominant abnormality in their respective studies (21).

However, the relatively low prevalence of alpha-thalassemia 4.8% (n=8) in our study contrasts with the data from Southeast Asia, where alpha-thalassemia is more frequently observed. A meta-analysis by Fucharoen et al. reported an overall alpha-thalassemia prevalence of 22.6% in Southeast Asia, with the highest rates in Vietnam (51.5%) and Cambodia (39.5%) (22). In Thailand, the prevalence of α-thalassemia has been reported to be as high as 19.51% in some ethnic groups (23). In mainland China, the overall prevalence of α-thalassemia is 7.88% (24). These differences could be attributed to variations in the ethnic composition, geographic location, and genetic factors within the studied populations. Hemoglobin E/beta-thalassemia is also highly prevalent in Southeast Asia, representing approximately 50% of those affected with severe beta thalassemia (25).

A number of variables, such as socioeconomic position, healthcare access, and thalassemia knowledge, may have contributed to the low prevalence rate that we found in our research. Another cultural factor that might greatly affect the prevalence of thalassemia and other autosomal recessive diseases is the practice of blood-related marriages, which is common in several regions of Pakistan (26).

With 81.3% (n=135) males and 18.7% (n=31) females, our study's sex distribution clearly shows a marked male preponderance. Gender disparities and cultural norms in healthcare-seeking behaviors are two possible explanations for this gender ratio imbalance. As a result of cultural expectations,

males in certain parts of Pakistan may be better able to afford medical treatment or are more inclined to participate in community-based screening initiatives (26). However, this result contradicts previous research that discovered a more even split between the sexes among thalassemia carriers (27).

The findings of this study revealed that 81.9% of thalassemia cases in Nawabshah are associated with consanguineous marriages, while only 18.1% are linked to exogamous marriages. These results align with existing literature, which consistently highlights the significant role of consanguinity in increasing the prevalence of thalassemia.

Consanguineous marriages, particularly first-cousin unions, are culturally prevalent in many regions, including Pakistan, and are a well-documented risk factor for autosomal recessive disorders, such as thalassemia.A study by Aslam et al. (2023) reported a 96% prevalence of consanguinity among parents of β-thalassemia patients, with first-cousin marriages being the most common form of union (28). Nadeem et al. (2023) observed a similar trend, in that the rate of β-thalassemia was significantly higher (76.7%) in first cousin marriage than in second cousin marriage (23.3%) (29).

The genetic implications of consanguinity have been well-documented. Consanguineous marriages increase the probability of homozygosity for deleterious alleles, thereby elevating the risk of autosomal recessive disorders, such as β-thalassemia. Studies have shown that children born to consanguineous parents have a 2.5 times higher risk of inheriting β-thalassemia than those born to non-consanguineous parents (30). This underscores the need for targeted intervention to address this public health challenge.

Our study's hematological profile 7.17% (n=166) of people with the thalassemia phenotype closely matched the traits previously described in the literature for this illness. The changes in hemoglobin levels and red blood cell indices that have been observed provide important information on the causes and symptoms of thalassemia traits and their diagnostic indicators.

The average number of RBCs was 6.1 ± 1.0 million cells/μL, which is much greater than what is considered normal. This indicates that the body is trying to compensate for the reduced ability to transport oxygen due to poor hemoglobin production. Previous studies have repeatedly shown that thalassemia is associated with elevated RBC production, which is referred to as erythrocytosis (31). Nonetheless, the fact that the total hemoglobin content is low despite this compensatory reaction highlights how inefficiently red blood cells are produced in individuals with this illness.

Mild anemia, often seen in the beta thalassemia trait, is indicated by an average hemoglobin concentration of 11.7 ± 2.4 g/dL. An imbalance in the proportion of α- and β-globin chains, caused by faulty β-globin chain production, is the main cause of the decrease in hemoglobin levels. Subsequently, an overabundance of α-globin chains forms within RBCs, leading to an inefficient erythropoiesis process and reduced lifespan of fully developed RBCs in the bloodstream (32). Our study's findings of a moderate case of anemia are in line with the usual manifestations of the thalassemia trait, which may be identified by regular blood tests but never leads to serious symptoms.

Two important characteristics of thalassemia trait, microcytosis and hypochromia, are shown by the MCV of 60.4 ± 5.2 fL and the MCH of 18.3 ± 0.2 pg/dL. Microcytosis indicates that the red blood cells are smaller than normal, but hypochromia indicates that the hemoglobin content of the red blood cells is lower. These findings have been widely reported in the literature as key indicators for determining who has the thalassemia trait, which is characterized by reduced hemoglobin production (27). A screening test that combines low MCV with MCH may help to detect microcytic anemia early and differentiate it from other causes, such as iron deficiency, in places where thalassemia is prevalent.

Additional evidence that the red blood cells are hypochromic is provided by the slightly reduced MCHC of 32.5 ± 2.3 g/dL. Although MCHC is not used as often as MCV and MCH as diagnostic indicators, the abnormal hemoglobinization of red blood cells observed in the β-thalassemia trait is consistent with the lower levels of MCHC in our study group (32). The importance of an absolute hematological assessment in determining carrier status is further highlighted by this parameter.

The platelet count was 287.1 ± 82.33 × 10^9/L and the WBC count was 7.92 ± 1.47 × 10^9/L, both of which were within the normal range. The fact that this result does not affect leukocyte or platelet production is in line with the fact that the thalassemia trait is not progressive. Unlike other blood disorders, such as myelodysplastic syndromes or problems involving bone marrow failure, β-thalassemia does not result in abnormalities in platelet and white blood cell counts (26).

CONCLUSION

This study demonstrated that β-thalassemia was the predominant subtype among thalassemia patients in the screened population. A significantly elevated prevalence of consanguineous marriages has been identified as the primary etiological factor contributing to thalassemia in Nawabshah.

DECLARATIONS

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Disclosure statement

No conflicts of interest have been disclosed by the writers. This article's content and writing are the responsibility of the writers.

Ethical Approval

This study was approved by the institutional board of the PUMHS University, Nawabshah.

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None

Patient consent

Written informed consent was obtained from all the participants.

Authors' Contributions

Rizwan Channa was the study's principal investigators, Ahmed Ali Kanhar wrote and edited the manuscript, Sobia Khan Baqai performed statistical analysis, Hira Saeed Khan was collected the data for study, Mehwish Chandio prepared the final draft of manuscript, Dr Hajira Naila and Yasir Akbar Jamali were collected the data for study.

All authors have read and approved the final manuscript.

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