Original Article

Reducing the Burden of Beta Thalassemia Major Through Sibling Screening: A Cross-Sectional Study in Karachi

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ABSTRACT

Objective: To screen β-Thalassemia trait in siblings of β-Thalassemia major patients in Karachi

Study Design: An observational cross sectional research.

Place and Duration of Study: This study was conducted at the Muhammadi Institute of Hematology, Baqai Medical University Karachi from July 2022 to December 2022.

Methods: Siblings of β-thalassemia major patients were included after informed consent from the siblings or their guardian. Data included was complete history, general physical examination and laboratory testing in terms of blood samples and high-performance liquid chromatography. For data analysis, SPSS v23.0 was used to compere variables between carrier and non-carriers using independent t-test keeping $p<0.05$ statistically significant.

Results: 400 siblings were screened, out of which 168 (42%) were carriers of β-thalassemia trait. 243 (60.75 %) siblings were male while 157 (39.25 %) males. On CBC, carriers showed a significant reduction in MCV and MCH, while RBC count was higher. HbA, HbF, and Hb A2 levels showed significant difference in-between the two groups. Ethnicity and various RBC morphology variables were found to have statistical difference between carriers and non-carriers of β-thalassemia siblings.

Conclusion: Among the screened siblings of β-thalassemia major patients, a high incidence of β-thalassemia trait was reported. Therefore, proper screening for siblings of β-thalassemia major patients should be recommended and made compulsory for better outcomes.

Key Words: β-thalassemia, Chromatography, Screening

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INTRODUCTION

β-thalassemia a hereditary autosomal recessive disease occurring due to chronic anemia of hemolytic variety, featuring complete or partial deficiency in synthesizing β-globin chains that are composed of major adult hemoglobin[1]. The characteristic feature of β-thalassemia includes inherited hematological disorder having low hemoglobin and fewer than normal red blood cells[2].

B-thalassemia major encircles mutation in both Beta-chain gene synthesis because of which one of the two things occur, either production of Beta-chain is reduced or production is normal but with mutations[3].

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The signs and symptoms of β-thalassemia are poor growth, severe anemia and skeletal deformities in infancy[4]. If left untreated, usually mortality occurs in β-thalassemia major, mostly because of heart failure[5].

In Pakistan, thalassemia is a major genetic issue that affects children of the local population[6]. World over it is estimated that per annum, more than 50,000 new cases are reported with severe form of thalassemia with almost 80 % of births taking place in the under-developed populations[7]. The World Health Organization (WHO) has prioritized the control of hemoglobinopathies, especially β-thalassemia throughout the world [8].

Prevalence of genetic disorders is increasing day by day among South Asians, especially Pakistan, despite advancing developments in the field of health[9]. B-thalassemia carrier rate in Pakistan is estimated around 5-8 % with annually 5000 children newly diagnosed with β-thalassemia[10]. The lack of awareness, coupled with consanguineous marriage have main the stay reason behind such high rates of genetic disorders in the country[11].

Thalassemia major is a challenge for both affected and family. The only treatment of β-thalassemia is bone marrow transplant, which is a financial and economical constraint for majority of the local families[12]. In a research from Africa, 85.2 % of respondents were of the view that bone marrow transplant are expensive and a burden for the family[13].

Major contribution towards occurrence of β-thalassemia is consanguineous marriage. In a local study, 133 (74 %) out of 180 parents of β-thalassemia affected children were cousins[14]. Even though rates of β-thalassemia remain high, yet the populations' level of awareness is minimal in the general public. In another research, 60 % parents were unaware of β-thalassemia while only 15 % knew about β-thalassemia and 25 % had minimal knowledge[15].

METHODS

An observational cross sectional research was carried out at Muhammadi Institute of Hematology, Baqai Medical University Karachi for a period of 6 months (July 2022 to December 2022). Siblings of β-thalassemia major patients were included after informed consent from the siblings or their guardian. A total of 157 females and 243 males were included in the study. Sibling of β-thalassemia major above 6 months of age and without history blood transfusion or history of transfusion for more than 3 months was included in the study.

After ethical approval from the Ethical Review Committee of Baqai Medical University, Karachi, data collection started. Any child before the age of 6 months or with a history of transfusion within last three months was excluded from the research.

Data included was complete history, general physical examination and laboratory testing in terms of blood samples and high-performance liquid chromatography. For blood sample, 5 ml of venous blood was collected using aseptic measures and collected in commercially available EDTA tube. Complete Blood Count (CBC), high-performance liquid chromatography (HPLC) and peripheral smear morphology were tested using the blood sample. The test reported were also discussed and shared with the parents/guardian followed up by genetic counseling in order to create awareness of prevention of β-thalassemia.

Data Analysis: For data analysis, SPSS v23.0 was used to analyze the data. For categorical variables, frequency and percentages were reported and for continuous variables, mean and standard deviation were reported. To compare variables between carrier and non-carriers, independent t-test was applied keeping $p<0.05$ statistically significant.

RESULTS

A total of 400 siblings of beta thalassemia major patients were screened in this study. Among them, 168 (42%) were identified as carriers, while 232 (58%) were non-carriers [Figure 1].

Demographic Characteristics: Among the screened population, 104 (61.9%) carriers and 139 (59.9%) non-carriers were male, while 64 (38.1%) carriers and 93 (40.1%) non-carriers were female. The difference in gender distribution between carriers and non-carriers was not statistically significant ($p = 0.687$). Ethnicity distribution showed a significant association with carrier status ($p = 0.004$). The Sindhi ethnic group comprised 29.8% (50) of carriers and 23.7% (55) of non-carriers. The Balochi ethnic group had a higher proportion of carriers (36.3%, n = 61) compared to non-carriers (24.1%, n = 56). The Pathan and Punjabi ethnic groups showed no significant difference in distribution, while the Urdu-speaking population had a higher percentage of non-carriers (14.2%, n = 33) compared to carriers (6.0%, n = 10).

Age distribution among study participants did not show a significant difference between carriers and non-carriers ($p = 0.749$). The majority of participants were in the 6-10 years age group, with 39.3% (66) of carriers and 37.9% (88) of non-carriers. The 1-5 years and 11-15 years groups had nearly equal distributions between carriers and non-carriers. The 16-20 years age group had the lowest representation, with only 3.0% (5) carriers and 5.2% (12) non-carriers [Table 1].

Red Blood Cell Morphology: RBC morphology analysis showed significant differences between the two groups ($p < 0.005$). Among carriers, 97.0% (163) exhibited hypochromia and microcytosis, whereas only 3.9% (9) of non-carriers had similar findings. Anisocytosis with normochromia was observed in 19.8% (46) of carriers. Additionally, hypochromia with microcytosis and target cells was noted in 3.0% (5) of carriers, whereas normocytic normochromic RBCs were predominant in 63.8% (148) of non-carriers.

Hematological Parameters

The mean age of carriers was 8.23 ± 3.99 years, while that of non-carriers was 8.51 ± 4.14 years, with no significant difference ($p = 0.501$). Hematological parameters showed statistically significant differences ($p < 0.005$) in several indices. The mean RBC count was significantly higher in carriers (5.08 ± 0.14 million/µL) compared to non-carriers (4.37 ± 0.27 million/µL). Mean hemoglobin (Hb) levels were lower in carriers (9.0 ± 1.0 g/dL) compared to non-carriers (12.0 ± 0.00 g/dL). Similarly, MCV was significantly reduced in carriers (67.0 ± 2.0 fL) compared to non-carriers (81.0 ± 8.0 fL), and MCH was also lower in carriers (20.51 ± 1.13 pg) than in non-carriers (26.03 ± 3.05 pg).

Other significant findings included MCHC, which was lower in carriers (31.57 ± 0.5 g/dL) compared to non-carriers (31.94 ± 1.05 g/dL). RDW-SD was also lower in carriers (36.38 ± 2.61 fL) compared to non-carriers (37.72 ± 2.61 fL). The WBC count was slightly lower

in carriers (8.4 ± 1.18 × 10⁹/L) than in non-carriers (8.52 ± 2.37 × 10⁹/L), but still showed a significant difference ($p < 0.005$). Platelet counts did not show any statistically significant difference between groups ($p = 0.988$).

Hemoglobin Variants: Significant differences were observed in hemoglobin electrophoresis values ($p < 0.005$). Carriers had higher Hb A2 levels (5.6 ± 0.22%) compared to non-carriers (2.68 ± 0.27%), which is a diagnostic indicator of beta thalassemia trait. In contrast, Hb A levels were lower in carriers (94.57 ± 0.23%) than in non-carriers (96.56 ± 0.45%). The Hb F levels were also significantly lower in carriers (0.16 ± 0.08%) compared to non-carriers (0.89 ± 0.47%) [Table 2].

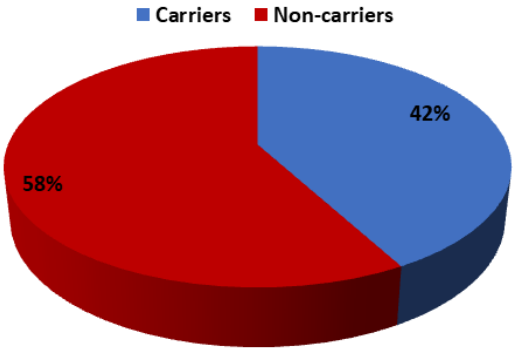

Figure No. 1: Graphical representation of frequency of carriers and non-carriers of β-thalassemia

Table No. 1: Comparison of various variables between carrier and non-carrier groups

Demographical variables		Carrier	Non-Carrier	P-value
		Frequency (%)		
Gender	Male	61.9% (104)	59.9% (139)	0.687
	Female	38.1% (64)	40.1% (93)	
Ethnicity	Sindhi	29.8% (50)	23.7% (55)	0.004
	Balochi	36.3% (61)	24.1% (56)	
	Pathan	13.7% (23)	16.8% (39)	
	Punjabi	14.3% (24)	21.1% (49)	
	Urdu Speaking	6.0% (10)	14.2% (33)	
Age Groups	1-5	29.8% (50)	28.4% (66)	0.749
	6-10	39.3% (66)	37.9% (88)	
	11-15	28.0% (47)	28.4% (66)	
	16-20	3.0% (5)	5.2% (12)	
RBC Morphology	Anisocytosis Hypochromia/		4.7% (11)	<0.005
	Anisocytosis Hypochromia /Rouleaux		3.4% (8)	
	Anisocytosis Mild hypochromia/		3.9% (9)	
	Anisocytosis Normochromic/		19.8% (46)	
	Hypochromia/Microcytosis	97.0% (163)	3.9% (9)	
	Hypochromia Microcytosis/ Basophillic stippling	3.0% (5)		
	Normocytic Normochromic		63.8% (148)	
	Normocytic Normochromic/Rouleaux		0.4% (1)	

Table No. 2: Comparison of hematological variables between the carrier and non-carrier groups

Hematological Variables	Carrier	Non-Carrier	P-value
	Mean ± SD		
Age (Years)	8.23 ± 3.99	8.51 ± 4.14	0.501
RBC	5.08 ± 0.14	4.37 ± 0.27	<0.005
Hb	9.0 ± 1.0	12.0 ± 0.00	<0.005
HCT	36.36± 1.67	36.31± 1.64	0.995
MCV	67.0 ± 2.0	81.0 ± 8.0	<0.005
MCH	20.51± 1.13	26.03± 3.05	<0.005
MCHC	31.57± 0.5	31.94± 1.05	<0.005
RDW-SD	36.38± 2.61	37.72±2.61	<0.005
WBC	8.4 ± 1.18	8.52 ± 2.37	<0.005
PLT	287.6± 108.6	287.4± 109.9	0.988
Hb A2	5.6 ± 0.22	2.68 ± 0.27	<0.005
Hb F	0.16 ± 0.08	0.89 ± 0.47	<0.005
Hb A	94.57± 0.23	96.56± 0.45	<0.005

DISCUSSION

Thalassemia is widely known to be the most common hemoglobin associated disorder round the globe. However due to improvements in safety and precautions used during blood transfusion, iron chelation regimens, supportive care and managing of complications, abetting in diseased children to have a near to normal life[16,17]. At present, the only treatment for β-thalassemia is stem cell transplantation[18].

The results of our study showed that the prevalence of β-thalassemia major carrier was reported in 168 (42 %) of siblings out of the 400 included in the study. This demonstrated a high rate of β-thalassemia major among siblings of β-thalassemia major patients. Consanguineous marriage and lack of awareness are thought to be the major factor of β-thalassemia's high incidence and complications due to lack of awareness in terms of prevention and treatment. Studies have reported the annual rate of β-thalassemia globally to range from 7000 to 9000 children[19].

In Pakistan, frequency of β-thalassemia is reported between 5 to 7 %[20]. Screening of carriers and their siblings is recommended to be preventive in nature and has already caused reduced rates of β-thalassemia in many developing countries. Likewise, a research reported reduction in β-thalassemia from 1:4000 after 2 decades to 1:250[21]. Another research has estimated around 16 % reduction in frequency of β-thalassemia among homozygous thalassemia affected patients[22].

In our research, RBC count and its indices which aid in diagnosing beta thalassemia trait were performed. HbA2 levels in carriers of beta thalassemia trait were 5.59 ± 0.22 %, while hallmark of detecting carrier state of beta thalassemia is > 3.5%. Similarly two studies reported HbA2 levels of 5.8 % and 5.56 % respectively[23]. Our research showed significant differences in CBC and hemoglobin parameters between carrier groups and non-carrier groups. RBC, Hb, HbA, HbF, HbA2, MCV and MCH all reported significant difference between groups. Similar results were observed in other research as well[24]. Screening of siblings ought to be recommended and compulsion should be made for improving the outcomes of siblings and overall family.

CONCLUSION

Among the screened siblings of β-thalassemia major patients, a high incidence of β-thalassemia trait was reported. Therefore, proper screening for siblings of β-thalassemia major patients should be recommended and made compulsory for better outcomes.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Ghazal Irfan, Maeesa Wadood
Drafting or Revising Critically:	Munazza Rashid, Muhammad Khan, Sarah Azhar, Tooba Khan
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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