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Family-Based Screening of Thalassemia: A Study of Relatives of Diagnosed Children

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ABSTRACT

Thalassemia is a dangerous inherited blood disorder that poses a significant health risk, particularly in regions where the gene is prevalent. This study screened 320 members of families of children diagnosed with thalassemia to identify carriers. Findings revealed that 25.6% of participants were carriers, indicating a substantial genetic risk. This highlights the importance of cascade screening and structured genetic counseling to prevent transmission in future generations. Disseminating knowledge and supporting families can reduce new cases and empower informed reproductive decisions.

Introduction

Thalassemia is one of the most common inherited hemoglobin diseases in the world, and it is a serious public health issue, particularly in low- and middle-income nations [1,2]. Thalassemia is a hereditary disease with a prevalence of 3-4 percent. of population, while 8,000-10,000 children are born with severe forms of the disease every year [3,4]. Carrier rates differ by geography and ethnicity; for example, tribal populations in India have rates of 1.5 percent-37.9 percent [5].

Mutations in the α- and β-globin genes lead to the development of thalassemia, which is characterized by impaired hemoglobin production, chronic anemia, and, in severe instances, the inability to live without transfusion [6,7]. Carriers are mostly asymptomatic but are exposed to reproductive risks; two carriers that marry each other can produce offspring with thalassemia major [7]. Therefore, prevention is necessary at an early stage. Worldwide experience indicates that systematic screening and genetic counseling are effective. In Sardinia, the frequency of thalassemia major frequency decreased as a result of extensive screening and prenatal diagnosis initiatives to 1:250 to 1:4,000 births [8,9].

Some strategies include premarital, antenatal, and cascade (family) screening [10,11]. Cascade screening targets the families of affected patients and is cost-effective, especially in settings where resources are limited.

Laboratory procedures include complete blood count, red cell indices, hemoglobin electrophoresis, high-performance liquid chromatography, and molecular testing [6]. In low-resource environments, low-cost testing, including NESTROFT, can be helpful but can give false results because of technical variations [12,13]. Extended family screening is fruitful because there is a greater likelihood of relatives possessing pathogenic mutations [11].

Formal family based screening is uncommon in Pakistan, particularly in rural regions. The Southern Punjab District of Layyah has a low level of genetic screening facilities, although the prevalence of diseases is high in the region. The paper seeks to establish the common occurrence of carriers of thalassemia in the extended family members of the affected children and prove the practicability of cascade screening as a specific and valid preventive measure

Literature Review

Screening for inherited blood disorders (thalassemia) is of paramount importance in controlling them and must be performed through family based screening [14] (Kattamis et al., 2023). Diagnostic testing helps identify carriers early and make informed choices regarding reproductive and healthcare [15]. The attendance of community-based education and culturally sensitive screening programs enhances participation and minimizes disease burden [16, 17]

In India, 35% of the family members of an affected child are asymptomatic carriers, which proves the possibility and high productivity of focused family based screening with limited resources [5]. Cascade screening has proven to be cost-effective since extended family screening in Indonesia showed that 42.7% of affected families were carriers, as opposed to 10.6% of control families [18].

The WHO advises prolonged screening of family members in high-prevalence areas to avoid the possibility of intergenerational spread. Socioculturally sensitive screening promotes acceptance and attendance [14]

Methodology

Study Design and Population

This cross-sectional study was conducted in Muzaffargarh District. The population under study was the biological family members (uncles, aunts, and first cousins) of children with thalassemia major who receive regular transfusions. Couples intending to marry who were relatives of an affected family were also invited.

Sampling 3.2: Snowball sampling was used to recruit 320 participants for this study. Eligibility criteria: age 6 months to 30 years. Individuals older than 30 years who had already undergone childbearing or could not have a child were excluded.

Data Collection Consent was obtained, and thereafter, 10 mL venous blood samples were collected. The tests conducted included CBC, red cell indices, hemoglobin estimation, reticulocyte count, serum iron tests, and morphology of the peripheral smear

Screening and Diagnosis:

- **Initial Screening:** NESTROFT
- **Confirmatory Testing:** HPLC ($HbA_2 \geq 3.5\%$ classified as carrier)
- Serum iron analyzed using automated biochemical analyzers [19]

Statistical Analysis

Carrier distribution, gender differences, and predictors were evaluated using descriptive statistics (frequencies, percentages, means, SDs), chi-square tests, and logistic regression. Significance: $p < 0.05$. Analyses were performed using R 4.3.2.

Ethical Considerations

Approved by the institutional review board. Written consent from adults and guardians of minors. Confidentiality strictly maintained. Participants received individualized counseling and follow-up recommendations.

Study Flowchart

Study Design

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Target Population (Extended Family Members)

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Data Collection (Questionnaire + Blood Sampling)

↓

Laboratory Analysis (CBC, NESTROFT, HPLC, Iron Profile)

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Statistical Analysis (Descriptive + Inferential)

↓

Ethical Compliance (Consent, Confidentiality, Counseling)

↓

Reporting & Recommendations

↓

Limitations (Sample Size, Self-Reported Data, Cultural Barriers)

Results

Table 1. Carrier Status Distribution

Status	Count	Percentage (%)
Carrier	82	25.6
Non-Carrier	233	72.8
Other	5	1.6
Total	320	100

Table-2. Carrier Status by Gender

Gender	Carrier	Non-Carrier	Other	Total	Carrier Prevalence (%)
Male	40	136	4	180	22.2

Female	42	97	1	140	30.0
Total	82	233	5	320	25.6

Table 3. Age-Wise Distribution of Thalassemia Findings

Age Group (Years)	Total Individuals	Non-Carrier	Carrier	Other	Carrier Prevalence (%)
0–5	52	42	8	2	15.4
6–10	66	46	18	2	27.3
11–15	85	60	23	2	27.1
16–20	53	37	16	0	30.2
21–25	48	38	10	0	20.8
26–30	16	8	8	0	50.0
Total	320	233	82	5	25.6

Table 4. Chi-Square Analysis of Gender and Carrier Status

Gender/Finding	Observed (O)	Expected (E)	$(O-E)^2/E$
Male Carrier	40	46.125	0.813
Male Non-Carrier	136	131.0625	0.186
Male Other	4	2.8125	0.501
Female Carrier	42	35.875	1.046
Female Non-Carrier	97	101.9375	0.239
Female Other	1	2.1875	0.645
Total χ^2			**3.430**

Table 5. Logistic Regression for Female Gender

Predictor	Coefficient	Std. Error	z-value	p-value	OR (95% CI)
Intercept	-1.224	0.165	-7.415	<0.001	-
Female Gender	0.387	0.239	1.617	0.106	1.47 (0.92–2.35)

Discussion of Main Results

Overall Carrier Status (Table 1)

Table 1 reveals that among the 320 members of the extended family screened, 82 subjects (25.6) were carriers, 233 (72.8) were non-carriers, and five (1.6) were inconclusive. This means that the risk of thalassemia among relatives of children with this condition is high; thus, cascade screening should be performed through family based screening. • The prevalence rate is consistent with the results of comparable studies in high-prevalence areas, indicating that family screening is more cost-efficient than population-wide strategies.

Gender Differences (Table 2, Table 4, Table 5)

There were 22.2 percent carriers and 30 percent carriers among males and females, respectively. The chi-square test (Table 4) did not indicate any statistically significant association between sex and carrier status (2 = 3.43, p = 0.180). There was

a significant difference between women and men in the likelihood of being a carrier, as logistic regression revealed that women were 1.47 times more likely to be carriers than men, but this was not statistically significant (p = 0.106). Interpretation: Sex had no significant effect on carrier status, which is in agreement with autosomal recessive inheritance, where both males and females are equally likely to carry the gene. The differences observed were probably due to sampling variability.

Age-Wise Distribution (Table 3)

- The prevalence of carriers was most very high within the group of young adults, age 2630 years (50%), age 1620 years (30.2%).
- The prevalence was lowest among children age 05 years and below (15.4%).

It is important to screen older adolescents and young adults since early diagnosis before reaching reproductive age enables the family to make well-informed reproductive choices, so a newborn will not transmit thalassemia to its generation.

Key Observations Across Tables

- **Substantial carrier prevalence:** Approximately 1 in 4 relatives carry the thalassemia gene.
- **Gender effect minimal:** No statistically significant difference between males and females.
- **Age pattern:** Higher prevalence in reproductive-age individuals emphasizes timely screening**.**
- **Other/inconclusive results:** Minimal (1.6%), highlighting the effectiveness of the applied screening methods.

Conclusion

This study filtered 320 extended family members of children with thalassemia and identified that 25.6% were carriers; therefore, the genetic risk is high in these families. The prevalence of carriers peaked in young adults (16–30 years), indicating that early screening before an individual reaches reproductive age is important for proper family planning. Although the carrier rate in females was slightly higher than that in males, this was not significant, which is also in line with the autosomal recessive model of thalassemia inheritance. The results highlight the importance of family based cascade screening as a specialized, cost-effective approach for the detection of silent carriers. By identifying carriers early and offering genetic counseling, healthcare systems can lower the number of cases, reduce the long-term healthcare burden, and enable families to make informed choices regarding reproduction. Since the prevalence of carriers is very high in at-risk families, the main point of the study is the strong need to increase the number of cascade screening programs, especially in resource-constrained environments, as a crucial intervention in the public health context to avert intergenerational thalassemia transmission.

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