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ORIGINAL ARTICLE

THALASSEMIA AND PREMARITAL SCREENING: POTENTIAL FOR IMPLEMENTATION OF A SCREENING PROGRAM AMONG YOUNG PEOPLE IN PAKISTAN

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□ *Pakistan has a high prevalence of β-thalassemia (β-thal) but lacks a screening program for its prevention. This questionnaire-based cross-sectional study was conducted in six randomly chosen non medical universities to assess the students' knowledge of β-thal and premarital screening, and their attitude towards such a program. Comparison was made between the respondents' attitude towards premarital screening before and after providing them some information regarding the disease. Only 54.5% (207) of 380 students had heard of β-thal, with a mean knowledge score of 13.0± 4.4 out of 27 questions. Most respondents were aware of the concept of premarital screening. Out of 207 students, 60.4% wanted to know if they were carriers, 69.1% wanted to know their spouse's carrier status and 59.4% wanted premarital screening to be made mandatory in Pakistan. These figures increased to 72.5, 78.3 and 67.6%, respectively after provision of written information (*p *values: 0.03, 0.02, and 0.01, respectively). The positive attitude towards premarital screening with low background knowledge of the disease highlights the need of a mass awareness campaign and subsequent implementation of a premarital screening program.*

Keywords Thalassemia, Premarital screening, Pakistan, Knowledge, Attitude, Young people

INTRODUCTION

Hemoglobinopathies are the most common monogenic disorders in the world (1). Globally, nearly 1.1% couples are at risk of bearing a child with a

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hemoglobin (Hb) disorder (2). Among these disorders, β-thalassemia (β-thal) is the second most common hemoglobinapthy after sickle cell disease and it affects 0.46 per 1000 conceptions annually (2). Southeast Asia alone accounts for more than 50.0% of total β-thal-affected births every year. Out of the 20,400 Southeast Asian children born with β-thal each year, 10,000 are transfusion-dependent. Of these, only 10.0% receive blood transfusions resulting in an annual death rate of nearly 9,000 in this region (2).

β-Thalassemia is also a common inherited disorder in Pakistan (3). Although precise estimates for incidence and prevalence of the disease are not available, small scale studies suggest that the carrier rate of β-thal is close to 5.6% (4), and the total number of β-thal major (β-TM) patients born each year is estimated to be between 4,000 to 9,000 (5). High prevalence of hemoglobinopathies in a large population (181 million[6]) creates a huge burden on the health sector, and with an estimated 10 million β-thal carriers in Pakistan, is a major public health concern (7).

A severe form of β-thal is associated with considerable morbidity and mortality and requires frequent blood transfusions and effective iron chelation therapy in the absence of successful bone marrow transplantation (8). Management of affected cases demands a significant share of the health expenditure, which is a cause of concern for a low-income country such as Pakistan, whose total annual health expenditure is only 2.2% of the country's Gross Domestic Product (GDP) (9).

Therefore, the most cost-effective strategy for reducing the burden of Hb disorders is to complement disease management with awareness and prevention programs. Inexpensive and reliable blood tests can identify couples at risk for having affected children (10–12). This genetic screening is especially useful before marriage or pregnancy, allowing couples to discuss potential outcomes (11).

Premarital screening programs have been introduced worldwide in many β-thal affected countries (13). Several countries have benefitted from such programs. For example, Cyprus, which reduced the prevalence of β-thal from extremely high to almost negligible levels following the introduction of a screening program (14). Implementation of premarital screening has also been witnessed in countries such as Iran and Saudi Arabia, which share a religious commonality with Pakistan (15,16).

In order to devise a successful screening program, however, it is necessary to first look at the knowledge and attitude of Pakistan's population toward β-thal and premarital screening. Only a few studies have been conducted to determine the awareness of β-thal among the population. To date, no studies have been carried out that focus on unmarried young adults in Pakistan in this regard. Since these individuals will be the ones making future marital decisions, and hence contributing to the country's population growth, gauging their knowledge and attitude toward β-thal and premarital screening, would

play a significant role in preventing further births of β-thal affected children in this country.

Therefore, this study was carried out on young, unmarried, non medical university students to assess their knowledge and attitude regarding β-thal and premarital screening. It is hoped that the obtained information will help us devise an effective screening program in the future.

METHODOLOGY

Study Design and Setting

A questionnaire-based cross-sectional study was conducted among non medical university students, between the ages of 18 and 28, to assess the knowledge and attitude of unmarried literate young people toward β-thal and premarital screening. The study was approved by the Ethical Review Committee of Aga Khan University, Karachi, Pakistan. Written, informed consent was obtained from each study participant.

Sample Size and Sampling Methodology

There are a total of 24 Higher Education Commission (HEC) registered non medical universities in Karachi, Pakistan (17). Six of these universities were randomly selected, of which five belonged to the private sector, while one belonged to the public sector. A sample size of 385 was calculated using OpenEpi™ software, with a 95.0% confidence interval, and a 5.0% bound on error, considering 50.0% prevalence of knowledge.

A total of 420 self-administered questionnaires were equally distributed among the six universities (70 to each university). An effort was made to get an equal representation of both genders from every university. Students were approached at convenient locations within the university during their leisure time. Assistance was provided to the study participants only if a medical term in the passage was unclear (*e.g.,* anemia).

Demographic profiles were obtained from all study participants. Only those who had heard of β-thal before were asked to proceed further with the questionnaire and information was collected regarding knowledge on various aspects of β-thal (causes, transmission, prevention and treatment of the disease) and their understanding of premarital screening.

The questionnaire was adapted from a similar study carried out in the United States (18). There were 27 questions to assess knowledge regarding β-thal followed by questions that inquired about the knowledge and attitude of students toward premarital screening.

After completion of the questionnaire to this point, brief written information regarding β-thal, its inheritance pattern and medical consequences, was

provided to the students. Visual aid in the form of a simplified diagram was also provided to help the students understand the concept of inheritance in β-thal. Questions that had tested the students' attitude toward premarital screening prior to being informed about β-thal were then asked once again and any change in the students' responses was noted. Responses were graded using a Likert scale. In addition, the students' attitude was also assessed using a case scenario (vignette) in which questions were asked regarding two cousins who were known carriers and were getting married.

Statistical Analysis

Data entry was done using Epidata™ 3.1 and statistical analysis was done using SPSS v.17.0. To assess the extent of correct knowledge regarding β-thal, mean knowledge score was calculated and the percentage score was tabulated against the percentage of students achieving that score. Independent sample *t*-test was used to assess if there was a difference between the knowledge levels of the two genders. Pearson correlation coefficient was used to determine correlation between age of the participants and their knowledge levels. The two-tailed Wilcoxon Signed Ranked test was used to evaluate the difference in attitude of participants before and after being informed about the disease.

RESULTS

A total of 420 non medical university students took part in the study. Due to incomplete information, final analysis was done on 380 participants. The demographic characteristics of the sample are shown in Table 1.

Knowledge Regarding β-Thalassemia

Of 380 non medical university students, 173 (45.5%) had never heard of β-thal. The source of information of the remaining 207 (54.5%) students is displayed in Table 1. Out of the 27 questions on β-thal, the mean number of questions answered correctly was 13.0 ± 4.4. Figure 1 shows that 74.8% of these 207 students failed to answer 60.0% of the questions correctly.

No significant difference was found between the knowledge levels of the two genders ($t = -0.032$, $p = 0.98$). There was no correlation between the age of the students and their knowledge levels (Pearson coefficient = 0.04).

Knowledge Regarding Premarital Screening

The 60.9% of 207 students who had heard of β-thal had also heard of premarital screening, and nearly all of them identified the correct definition

TABLE 1 Demographic Characteristics and Source of Knowledge of Non Medical University Students in Karachi, Pakistan, Regarding β-Thalassemia

Variables		%
Age (years)	mean (standard deviation)	20.2 (1.6)
Gender (%) ($n = 380$)	males	46.2
	females	53.8
Residence (%) ($n = 380$)	Karachi	94.9
	other than Karachi	5.1
Monthly household income (%) ($n = 380$)	>50,000 Pakistani rupees	62.7
	<50,000 Pakistani rupees	37.3
Heard of β-thal (%) ($n = 380$)	never	45.5
	yes	54.5
Source of knowledge (%) ($n = 207$)[a]	print/electronic media	25.5
	family	16.8
	school/university	16.3
	friends	12.6
	β-thal subject	6.6
	others	1.3

[a] Students had the option of citing more than one source of knowledge if they had heard of β-thal before.

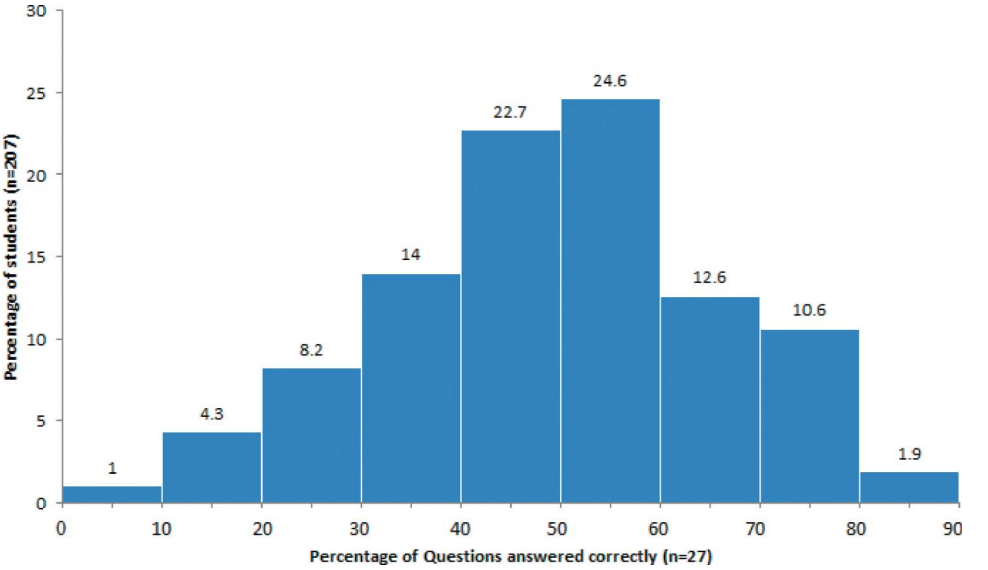

FIGURE 1 Histogram showing percentage of questions ($n = 27$) correctly answered by non medical university students in Karachi, Pakistan, who had previously heard of thalassemia ($n = 207$).

(Table 2). When asked about the purpose of premarital screening, 74.9% correctly identified that the program was used to check if someone was a carrier of the disease, while 69.6% agreed with the statement that it was used to avoid having children with genetic diseases (Table 2).

TABLE 2 Knowledge Among Non Medical University Students of Karachi, Pakistan, Regarding the Meaning and Purpose of Premarital Screening and the Various Diseases For Which the Program Can Be Used

Knowledge Regarding Premarital Screening	Percentage of Students ($n = 207$)
General:	
• heard of premarital screening	60.9
• correct definition of premarital screening	58.0
Purpose of Premarital Screening:	
• to see if someone is a carrier	74.9
• to avoid having children with genetic diseases	69.6
• to see if someone is fit for marriage	39.1
Diseases For Which Premarital Screening Can Be Used:	
• human immunodeficiency virus (HIV)	87.9
• thalassemia	76.8
• hepatitis B and C viruses (HBV and HCV)	69.1
• asthma	52.7
• epilepsy	30.0

Attitude Toward Premarital Screening For β-Thalassemia

Prior to being informed about β-thal, 60.4 and 69.1%, respectively, of the students wanted themselves and their partners to be screened before marriage, respectively. After being informed, this percentage significantly increased to 72.5 and 78.3%, respectively (Table 3). There was a significant rise in the number of students who wanted premarital screening to be made mandatory in Pakistan after being informed about β-thal (Table 3). There was

TABLE 3 Comparison of Non Medical University Students' Attitude Toward Premarital Screening and Marriage Between Carriers Before and After Being Informed About β-Thalassemia

Attitude Toward Premarital Screening	Percentage Who Agreed Before Being Informed About β-Thal ($n = 207$)	Percentage Who Agreed After Being Informed About β-Thal ($n = 207$)	p Value[a]
I would like to know if my spouse is a β-thal carrier	69.1	78.3	0.02
I would go for premarital screening to find out if I am a β-thal carrier	60.4	72.5	0.03
Premarital screening should be made mandatory for everyone in Pakistan	59.4	67.6	0.01
Two known β-thal carriers should not marry	49.2	39.6	0.03
I would not marry a β-thal carrier	21.8	24.1	0.92

[a] Wilcoxon Ranked Test p value (values of <0.05 are significant).

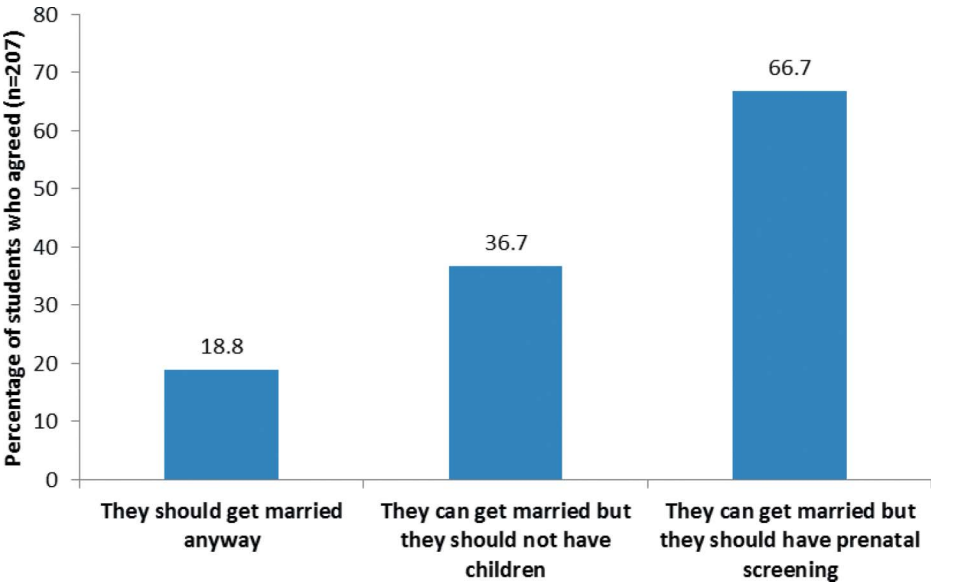

FIGURE 2 Non medical university students' response to case scenario in which two cousins, who were known carriers, were getting married ($n = 207$).

also a significant drop in the number of students who had agreed earlier that two carriers should not marry (Table 3).

Case Scenario (vignette)

The results showed that 57.5% were against two cousins, who were known carriers, be allowed to get married. If the couple did get married, 66.7% agreed that prenatal screening should be carried out (Figure 2).

DISCUSSION

Our study explored knowledge regarding β-thal and acceptance of a premarital screening program for this disorder among young people in Pakistan. Previous studies in Pakistan that targeted specific groups have shown that parents of children with β-thal generally lacked knowledge of the disease (5), whereas legal and medical communities were shown to have better knowledge of the disease (19). Another study done on a small number of Pakistani adults in the UK (20) also demonstrated a lack of awareness of β-thal among these individuals.

Our results showed that non medical university students were extremely deficient in their knowledge regarding β-thal. Nearly half the students (45.5%) had never even heard of β-thal before (Table 1), while those who

had heard of the disease also lacked adequate knowledge as shown in Figure 1. A similar study done in Malaysia, whose carrier rate is comparable to that of Pakistan, revealed that 76.4% of their population had heard of β-thal (21). It is important to note that in a country such as Pakistan, these university students represent an educated minority which has access to all the modern means of information available in the country. Although knowledge regarding β-thal in the general population still remains to be assessed, the results may be even worse, given the lack of knowledge and resources available to the majority of the uneducated population.

We also found that a majority of students had a better understanding of the meaning and purpose of premarital screening than of the disease itself (Table 2). This may be a result of the many awareness campaigns that exist for other diseases such as HIV (22). The fact that many students pointed out that premarital screening could be used to screen for HIV (Table 2) demonstrates that such campaigns may have helped students acquire knowledge regarding the program in addition to creating awareness regarding the disease.

The results also revealed that the students were receptive to the idea of screening before marriage and wanted to know if they were carriers of the disease (Table 3). Interestingly, the results of premarital screening did not affect their overall decision to marry someone. Table 3 shows how only a small number of students decided not to proceed with marriage if their partner was found to be a carrier. These findings correlate closely with the study carried out on the Saudi Arabian screening program in which a majority of the high-risk couples (89.6%) continued with the decision to marry each other, despite their good understanding of premarital screening and its value and their known high-risk status (15). This was attributed to religious and cultural constraints, lack of adequate education of the high-risk couples regarding the disease and late screening in the marriage process as concluded by this (15) and other Saudi Arabian studies (23,24).

The success of screening and antenatal diagnosis programs around the world has been based on the excellence of public education programs about the disease, followed by the development of effective screening regimens and facilities for antenatal detection. For religious, cultural, organizational and economic reasons, screening programs of an extensive nature may be much more difficult to establish in the large mainland populations of Southeast Asia. To begin with, educational programs should be established and backed up with facilities for carrier screening on a voluntary basis. This type of approach could provide the basis for further disease control strategies in future.

Since our study found no significant difference in the knowledge regarding β-thal across genders ($t = -0.032$, $p = 0.98$), it is important that these awareness programs target both the genders equally. Our study also found media and schools to be the two most commonly quoted external sources that provided knowledge to students regarding β-thal (Table 1). We therefore

suggest that schools and educational institutes be made an integral part of such programs, incorporating mass communication methods wherever possible and delivering the message in appropriate regional and local languages.

It is worth noting that many students supported the idea of undergoing prenatal screening if two known carriers were getting married (Figure 2). In cases of marriage regardless of the results of premarital screening, the identification of β-globin gene mutations (carrier-couple screening) followed by genetic counseling and prenatal diagnosis (PND) would help reduce the birth rate of affected infants, and thus alleviate the financial burden caused by this disease. Such a strategy has prevented homozygous β-thal in a number of at-risk populations worldwide (13).

However, the choice of a particular carrier screening strategy varies with social attitudes, cost and opportunity within the health system. To date, genetic counseling and PND in Pakistan have largely been restricted to metropolitan and major regional centers (4), and although acceptable to most couples and communities, the financial cost incurred may be prohibitive, especially for couples from lower socioeconomic communities and rural backgrounds (25,26). Screening during pregnancy (27) enables fewer options, requires more tests, is ethical only if PND is freely available, and often identifies risk too late for the option of PND (28). On the other hand, the offer of testing in high school (29,30) or before marriage (31,32), allows a wide range of choices and requires the least number of laboratory tests (12).

Although our results revealed that the percentage of students who wanted premarital screening to be made mandatory in Pakistan significantly rose after they were informed of the risks of having an affected child (Table 3), population screening may not be the most desirable strategy for the country as yet. Since approximately 61.0% of all marital unions in Pakistan are consanguineous (33), and the knowledge that 13 β-thal mutations are commonly reported in the Pakistani population, of which five common mutations account for 91.66% of these mutations (34,35), family studies may be more cost-effective. However, for couples who do not wish to be tested before getting married, screening after marriage and subsequent PND should be recommended.

Sustained genetic education and public awareness programs are crucial for premarital screening and genetic counseling to gain optimum acceptability. Once these educational programs have been established, a premarital screening program will stand a better chance of being successful in reducing the high prevalence of this disease in our country.

CONCLUSIONS

A lack of knowledge regarding β-thal, but a better understanding and positive attitude towards premarital screening seen in this study highlights the

need for a mass awareness campaign and subsequent implementation of a premarital screening program.

Declaration of Interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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