

## Frequency of carrier screening and preventive orientation among first degree relatives of Thalassaemia patients

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### Abstract

**Objective:** To get preliminary data regarding the prevention of thalassaemia major in future generations.

**Methods:** This Knowledge Attitude Practices study was conducted at Pakistan Institute of Medical Sciences, Islamabad, Pakistan, from January to June 2016, using non-probability purposive sampling. Parents of children undergoing transfusion were interviewed. Questionnaires were used to collect demographics and data about awareness, attitude and frequency of screening among the first degree relatives of a thalassaemia major patient. SPSS 20 was used for data analysis.

**Results:** Of the 270 respondents 240(88.9%) had utilised screening services for their asymptomatic children and had a positive attitude towards prevention, but 30(11.1%) families did not screen asymptomatic children for thalassaemia minor. Besides, 49(18.1%) families had more than one thalassaemia major child in their nuclear family, while, 3(1.1%) were unwilling to let their children undergo tests. Nine (3.3%) respondents said they will not ask a prospective daughter/son-in-law to get tested for thalassaemia minor, while 194(71.9%) respondents had had cousin marriages.

**Conclusion:** There were significant gaps in awareness among affected families.

**Keywords:** Thalassaemia, Awareness, Attitude, Carrier screening, Genetic disease, Prevention. (JPMA 68: 50; 2018)

### Introduction

Thalassaemia is a hereditary haemoglobinopathy that is common in Pakistan. Carrier rate in Pakistan is estimated to be 5-8% with 5,000 new patients diagnosed with thalassaemia major every year.<sup>1</sup> Many factors are responsible for high incidence of thalassaemia, especially inter-family marriages, which affect people of all ethnicity. According to a local study,  $\beta$ -thalassaemia affects Punjabis (60.7%) and Saraikees (25.5%), followed by Rajputs, Jatts, Arain, Sheikhs and Pathans.<sup>2</sup>

Thalassaemia causes significant social and financial burden especially on poor families. Iron overload toxicity causes organ damage; cardiac failure is the main cause of death in transfused patients not receiving effective chelation therapy.<sup>3</sup> It also poses a risk for blood borne infections due to regular transfusion. Moreover, 49% of the  $\beta$ -thalassaemia patients were Hepatitis C Virus (HCV) positive.<sup>4</sup> If safe blood transfusion is not ensured, these patients are at risk for infections like Hepatitis B Virus (HBV), HCV and Human Immunodeficiency Virus (HIV).<sup>5</sup> Thalassaemia

major patients face poor quality of life due to financial and social stress. A significant portion of their time is spent in transfusion centres, which is also distressing for their families.

The estimated carrier rate is 5-7% in Pakistan.<sup>6</sup> Cyprus has been a pioneer nation in reducing disease burden of thalassaemia. A government policy was introduced in Cyprus about 30 years ago which included an education campaign for informing and screening the population for thalassaemia trait and the need for prenatal and antenatal diagnosis, as well as improved treatment for all the patients.<sup>7</sup> After deoxyribonucleic acid (DNA) methods were established in 1991, only five affected babies were born due to different reasons, in a 10-year period. No affected baby has been born since 2002.<sup>8</sup> Awareness and availability of relevant screening services is the key for this model to work.

In Pakistan there is not enough awareness for people to consider screening prior to marriage. Most people first learn about thalassaemia when their own child or one of a close relative is diagnosed. Patients including carriers and thalassaemia major patients are responsible for making decisions to prevent thalassaemia major in future generations. Healthcare professionals can only offer education and services. It is up to the population to make timely and good use of

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it to decrease the chances of thalassaemia major in future generations and not feed the stigma of genetic diseases on affected families. It is important to evaluate the data on awareness, attitudes and utilisation of existing screening services in the prevention of thalassaemia in future family generations. Literature search found only one local Knowledge, Attitude, Practice (KAP) study done on thalassaemia which focused on Khyber Pakhtunkhwa population. It focused on the effect of having a thalassaemia major child on the decision to have more children by couples.<sup>9</sup>

The current study was planned to fill the critical information gap in this key area. The primary objective was to determine the frequency of carrier screening among asymptomatic first degree relatives of a thalassaemia major patient. Secondary objective was to assess the awareness and attitudes of parents of thalassaemia major patients towards preventing thalassaemia in future generations.

### Patients and Methods

This KAP study was conducted at Thalassaemia Centre of Pakistan Institute of Medical Sciences, Islamabad, Pakistan, from January to June 2016, using non-probability purposive sampling.

A sample size of 266 was calculated at 95% confidence level, 6% absolute precision and 50% hypothesised frequency of awareness and utilisation of screening. After permission from the institutional ethics committee, on visits to the centre, parents accompanying —  $\beta$ -thalassaemia major patients for transfusion were interviewed after first getting informed consent.

Parents of more than one child were selected as it was pertinent to question whether the siblings of a patient had been screened for thalassaemia minor or not and if the parents planned to ask their children-in-law to get screened before marriage. Questionnaires were used to

collect data about awareness, attitude and frequency of screening among the first degree relatives of a thalassaemia major patient. Awareness included seven parameters; genetic transmission of thalassaemia, major and minor types of thalassaemia, diagnostic test (haemoglobin [Hb] electrophoresis), ability of diagnostic test to identify thalassaemia minors, antenatal testing, risk in future pregnancies, knowledge of their own minor status before birth of affected child and now.

Attitude covered their desire to get asymptomatic children tested for thalassaemia minor, reason if they had not been tested so far, and whether they would ask a prospective fiancé to be tested if a child has thalassaemia major or minor.

Frequency of screening was checked by asking had their asymptomatic children been tested and if any were found to have thalassaemia minor. Number of children with thalassaemia major was also recorded.

Demographic data was also collected regarding frequency of cousin marriages, number of children, addresses, desire for more children and age of patient at diagnosis. SPSS 20 was used for data analysis and descriptive statistics calculated for both qualitative and quantitative variables.

### Results

Of the 270 parents interviewed, 223(82.6%) were found to be in the 'aware' category (Table-1).

Besides, 240(88.9%) families had their asymptomatic children screened for thalassaemia minor, while 121(44.8%) parents reported they had some children diagnosed with thalassaemia minors. The number of children with thalassaemia minor and major in each family was also recorded (Table-2).

Attitude of parents towards thalassaemia prevention in their family was also assessed. Particular attention was paid to the 30(11.1%) parents who had not had their

**Table-1:** Awareness of parents regarding thalassaemia.

Parameter	Aware	Unaware
Transmission of thalassaemia - genetic	82.6%(223)	17.4%(47)
Types of Thalassaemia - major and carrier (minor)	68.9%(186)	31.1% (84)
Diagnostic test for thalassaemia - Hb electrophoresis	87.4% (236)	12.6% (34)
Ability of diagnostic test to identify thalassaemia minors	72.2% (195)	27.8% (75)
Risk of thalassaemia major if both parents are carrier.	42.2% (114)	57.8% (156)
Antenatal testing for thalassaemia (CVS) is available in Pakistan	72.6% (196)	27.4% (74)
Parent's knowledge of their own carrier status before thalassaemia major child	7% (19)	93% (251)
Parent's knowledge of their own carrier status after thalassaemia major child	65.9% (178)	34.1% (92)

**Table-2:** Families; number of major and minor children?

Number of families	Children with Thalassaemia major
32	2
15	3
2	4
Number of families	Children with Thalassaemia minor
119	0
70	1
33	2
13	3
1	4
3	5
0	6
1	7

**Table-3:** Family size.

Number of families	Size of family
84	Small (1-2 children)
117	Medium (3-4 children)
69	Large (> 5 children)

family tested.

These 30(11.1%) parents were further questioned; of whom 2(6.67%) said because it was expensive, 9(30%) didn't know, 18(60%) had a casual attitude despite being advised by the doctors, while 1(3.3%) chose not to disclose the reason.

Only 3(1.1%) person refused outright to have asymptomatic children tested. All except 3(10%) of the 30 parents were receptive to counselling and agreed for screening.

Besides, 261(96.7%) parents said they would discuss thalassaemia before marriage of their children with prospective fiancés and ask for a screening test.

The mean age at diagnosis of patient was  $1.27 \pm 1.86$  years.

Moreover, 194(71.9%) parents had consanguineous marriage. Family size was divided into three categories depending on the number of children; small (1-2), medium (3-4) and large >5 (Table-3).

Overall, 182(67.4%) of the affected families did not want more children.

## Discussion

This study evaluated the level of awareness among thalassaemia families about their disease. It also examined their attitude towards voluntary prevention

including premarital testing, getting asymptomatic children tested and reasons if not screened. As treatment requires regular time in hospital and away from school for children and work for parents as well as being expensive in Pakistan, voluntary prevention is the most feasible option for thalassaemia.

Awareness is crucial for people to take timely actions to have thalassaemia free healthy families.

Besides, 82.6% of the respondents were aware that thalassaemia is a hereditary disease, 68.9% had knowledge of types of  $\beta$ -thalassaemia i.e. major and minor and the symptoms and 87.4% knew that the diagnostic test is Hb electrophoresis. Only 72.2% were aware that Hb electrophoresis could also detect thalassaemia trait as well. Even in families of a thalassaemia major patient the overall knowledge was incomplete and not up to the mark.

Another study done on awareness in Karachi showed that 40% of the interviewed families had insufficient awareness.<sup>10</sup>

Awareness does not always necessarily lead to preventive practices among the carriers who might underestimate risk, as 18 out of 30 families had neglected doctor's advice for screening of asymptomatic children. Also, 49 families had more than one child with thalassaemia major, even though antenatal diagnosis is available at PIMS. In the KAP study from Cell, 18% respondents said they would go for cousin marriages even after knowing the risks.<sup>9</sup>

Thalassaemia is a genetically transmitted disease so directly linked to inter-family marriages which increase the risk of having a child with major symptomatic disease.<sup>11</sup> The result of this study shows that it is also common in non-consanguineous marriages. Therefore counselling and awareness should be targeted at all the levels.

$\beta$ -thalassaemia carrier rate in Cyprus was estimated around 15-18% initially.<sup>12</sup> Cyprus introduced a successful nation-wide prevention programme for  $\beta$ -thalassaemia, with premarital screening and counselling. Consequentially, annual birth rate dropped from expected 30-50 cases to less than 5 cases.<sup>12,13</sup>

This study focussed on first degree relatives. However, awareness among extended families is desirable because as an autosomal recessive disease, appearance of disease may skip generations. As carriers are asymptomatic and live a normal life they may be unaware of being thalassaemia minor and get married

to another carrier. Besides, 76(28%) parents in this study had out of family marriages. Awareness of general population should also be studied. Mass awareness campaigns are needed to address this major public health concern.<sup>14</sup>

Symptoms of thalassaemia appear at 6 months of age when majority of foetal haemoglobin is replaced by adult haemoglobin.<sup>15</sup> In this study the mean age at which patients were diagnosed was 1.2 years. This could be due to delay in seeking medical attention by families or an oversight on the part of health professionals.

In diagnosing and treating genetic diseases family history is particularly important with regards to diagnostic testing and severity. But if family history of thalassaemia is not shared in extended family, patients may delay in seeking treatment or doctors may delay in making a diagnosis. While immediate family members are mostly aware of thalassaemia, education of extended families is also needed to improve screening for thalassaemia minors and premarital counselling for prevention.

It is also important that families should take initiative and seek information by researching on the internet. Patients can be the ambassador and advocate to their extended families and communities to spread education on thalassaemia prevention, if they are encouraged, supported and provided necessary information.

The patient-doctor relationship is a complex partnership in treating a chronic condition like thalassaemia that also affects generations of the family. With detailed counselling by doctors, awareness of every aspect of thalassaemia could be improved. Patient education is an important part of a doctor's duties.

In this study 88.9% respondents had had their other asymptomatic children tested. Majority of the families with thalassaemia major had a positive attitude towards voluntary prevention and had screened siblings of the patient and planned to discuss thalassaemia before arranging marriages. However, a small percentage were reluctant to get screening (3 families) while 9 families were averse to discussing it at marriage proposals. To address the stigma associated with genetic diseases, national awareness campaigns need to be undertaken. Voluntary prevention by screening for carrier status, and frank dialogue and counselling with families before marriage can decrease the incidence of disease.<sup>16</sup>

Thalassaemia is a major concern in Pakistan, yet it is very poorly addressed. There are not enough thalassaemia centres and those present are concentrated in big cities. Patients interviewed came from faraway places including Hazara and Kashmir. Families with patients need to access antenatal care and transfusion services regularly. The distance and difficulty may discourage some patients. For the time being more thalassaemia centres should be opened and peripheral hospitals should also improve their services, with emphasis on thalassaemia awareness, screening and eradication. Currently there are 750 patients registered in PIMS alone. Multi-disciplinary teams including haematologists, gynaecologists and paediatricians need to engage in meaningful efforts to manage huge disease burden.

Doctors may improve prevention by adding Hb electrophoresis of pregnant women at prenatal and antenatal visits. Women who are carriers can then be counselled and their husbands and children should be tested.

Thalassaemia causes great economic and logistical burden on a family as regular transfusions mean ongoing healthcare costs, travel and time off from work and school. Bone marrow transplant is a costly procedure, needs matched donor and not available in public sector hospitals.

## Conclusion

There are significant gaps in knowledge even among affected families. Some families are averse to screening and practical action. Both doctors and patients need to gather to counsel the reluctant families whose actions contribute to stigma and high invisible carrier rate among their children. This results in increased risk of disease in future generations. The awareness can be improved by periodic mass campaigns. Hopefully, this will lead to better health seeking behaviour.

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