

Role of Genetic Counselling in Prenatal Diagnosis of β -Thalassaemia in Pakistan

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ABSTRACT

Objective: To compare the response towards prenatal diagnosis (PND) of β -thalassaemia, in individuals who had not received genetic counselling and a genetically counselled population.

Study Design: Cross-sectional survey.

Place and Duration of Study: Department of Haematology, Armed Forces Institute of Pathology (AFIP), Rawalpindi, from March 2009 to December 2010.

Methodology: Using non-probability consecutive sampling, a total of 176 individuals having thalassaemic children, were interviewed regarding PND of thalassaemia, by using a structured questionnaire. Forty two individuals were taken as controls as they had received genetic counselling for PND, whereas the remaining 134 were taken as cases. Responses towards PND were compared using chi-square test. Odds ratio was also calculated for subsequent PND utilization.

Results: Seventy (52.2%) cases and 42 (100%) controls were aware of the availability of PND in Pakistan. This difference in awareness was statistically significant ($p < 0.001$). In the controls, 40 (95.3%) individuals were aware of the appropriate timing of the test, in contrast to 52 (39%) cases ($p < 0.001$). PND was used in subsequent pregnancies by 50 (37.3%) cases and 32 (80%) controls ($p < 0.001$). The calculated odds ratio for subsequent PND utilization was 5.37.

Conclusion: The study reflects a very positive attitude of genetically counselled thalassaemia affected families towards PND. For better utilization of PND, genetic counselling services should be available at all health strata.

Key Words: Prenatal diagnosis. Genetic counselling. β -thalassaemia. Pakistan.

INTRODUCTION

β -Thalassaemia is one of the most common haemoglobin disorder of the Indian subcontinent.¹ It is the most common single gene disorder in Pakistan, where the reported rate of β -thalassaemia trait is 5% and every year over 5000 children are born with β -thalassaemia major.² The ideal approach towards this disorder must encompass effective prevention services which include, carrier screening for β -thalassaemia, prenatal diagnosis (PND) and genetic counselling. The domain of genetic counselling in thalassaemia includes information regarding cardio-protection,³ protection against Malaria⁴ and hypertension⁵ in β -thalassaemia carriers, as this helps curb negative feelings associated with the condition.⁶ At the same time, it also includes an integrated effort to ensure successful PND utilization.

In Pakistan, the first PND of thalassaemia was performed successfully in 1994.⁷ By 2007, more than

2000 PND for thalassaemia were performed at one of the major diagnostic centres in Pakistan.⁸ This shows the gradual acceptability of the affected families towards PND. The fact that the test can be performed after 10 weeks of gestation by chorionic villous sampling (CVS), makes termination of pregnancy (TOP) a practical possibility. Islamic religious scholars have termed TOP as permissible before 17 weeks of gestation, if it is confirmed that the fetus is suffering from a potentially severe disorder.⁹

PND still remains an underutilized facility in Pakistan due to various reasons.¹⁰ Therefore, this survey was conducted to assess the awareness, response and attitude of thalassaemia affected families towards PND, its utility, acceptability and other related issues like TOP.

The main aim of the study was to assess the role of genetic counselling towards PND and to identify practical measures for improved utility of PND.

METHODOLOGY

This survey of knowledge, attitude and future practices, was conducted at the Department of Haematology, AFIP, Rawalpindi, after requisite approval of the institutional ethical committee. The study was completed in 22 months, from March 2009 to December 2010. Candidates for the study were selected by non probability consecutive sampling. The study included 176 individuals/couples, who visited AFIP for haemoglobin studies of subsequent children born after the birth

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of a child with thalassaemia. The 134 individuals, who had not received genetic counselling regarding thalassaemia, were taken as cases, whereas the 42 individuals who had received genetic counselling in the past were taken as controls. Families undertaking haemoglobin studies of their children on suspicion of thalassaemia, with no past history of the disease in the family, were excluded from the study.

The interviews were conducted, in a non-directional manner, to assess the awareness, response and attitude of these individuals towards PND and TOP. Informed consent was obtained from the candidates after reassuring them about the confidentiality of personal views. All the interviews were conducted in Urdu, the National language, with the purpose of maintaining uniformity and eliminating any bias which might have occurred due to the difference in the education levels of the individuals. Qualified doctors documented the responses by filling in a questionnaire in English. Documented proof of religious verdict (*Fatwa*) on TOP, by two well known Islamic scholars,⁹ was presented to the interviewed individuals.

The subjects were questioned regarding their awareness of PND for thalassaemia in Pakistan and their knowledge regarding the appropriate gestational age for undergoing PND. Those who knew about the test but did not utilize it were inquired about the reasons for not using PND. Individuals were also asked about their plans on utilizing this facility in the future. The subjects were requested to offer their views on TOP and whether the religious verdict on the issue of TOP was acceptable or not. At the end, the participants were encouraged to ask relevant questions and have a general discussion on the subject, in order to have an idea about their apprehensions, ambiguities, reservations and suggestions.

All the collected data were entered in Statistical Package for Social Sciences (SPSS) version 11.0 and an analysis was made based on the results of the biostatistics software. Frequencies and percentages were calculated for qualitative variables which include PND awareness, knowledge of appropriate gestational age for PND, PND utilization in subsequent pregnancies, willingness towards future PND use, acceptability towards TOP and religious verdict on TOP. Chi-square test was applied to compare the above mentioned qualitative variables between the two groups and p-value of ≤ 0.05 was considered to be significant. Odds ratio was calculated for subsequent PND use in both groups by using 2 x 2 table.

RESULTS

Out of the 176 individuals interviewed, 134 (76%) did not receive any sort of genetic counselling and were taken as cases, while the 42 (24%) who did receive it were

taken as controls. Counselling was done at the level of diagnostic services in 30 (71%, 95% Confidence Interval [CI] = 51.6 – 90.4%) controls and at the level of health care providers including general practitioners and paediatricians in 12 (29%, 95% CI = 9.6 – 48.4%) controls. The overall average family size of the sample under study was 4.3 (± 2.73). Consanguineously married couples made-up 80.6% of the total sample.

Among the study population, 70 (52.2%, 95% CI = 40 – 63.9%) cases and 42 (100%, 95% CI = 98 – 100%) controls were aware about the availability of PND in Pakistan. The difference in awareness regarding the availability of PND in Pakistan, amongst the cases and the controls, was found to be statistically significant ($p < 0.001$). Only 52 (39%, 95% CI = 27.3 – 50.7%) cases were familiar with the appropriate gestational age of 10 weeks for undergoing prenatal diagnosis, as compared to 40 (95.3%, 95% CI = 86.2 – 100%) controls. This difference in knowledge was again calculated to be significant ($p < 0.001$). Fifty (37.3%, 95% CI = 25.7 – 48.9%) cases and 32 (76%, 95% CI = 66 – 86%) controls, after learning about PND, had utilized PND for thalassaemia in subsequent pregnancies. Once again there was a statistical difference ($p < 0.01$) between those who received genetic counselling and those who did not. In both the groups, 30 (17%) individuals, including 20 (15%) cases and 10 (24%) controls, had prior knowledge regarding PND but did not utilize the facility in the following pregnancy. The reasons cited by those 30 individuals have been illustrated in Figure 1.

Once the information regarding PND had been conveyed to the study population, 128 (95.5%, 95% CI = 91 – 100%) cases and 40 (95.3%, 95% CI = 86.2 – 100%) controls showed willingness to use PND in future pregnancies. With respect to TOP, following PND, 122 (91%, 95% CI = 84 – 98%) cases and 40 (95.3%, 95% CI = 86.2 – 100%) controls were ready to accept it as a possible solution in the case of an affected fetus. The religious verdict on TOP was acceptable to 122 (91%, 95% CI = 84 – 98%) cases, and 42 (100%, 95%

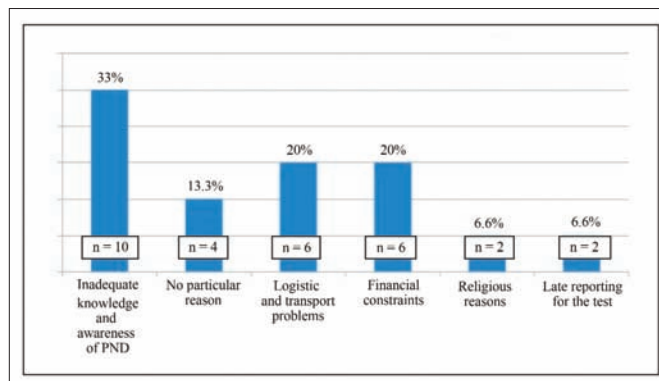


Figure 1: Frequencies and percentages of reasons for non-utilization of prenatal diagnosis amongst individuals with apparent awareness about PND in both groups.

Table I: Statistical significance of results of various parameters assessed in cases and controls.

Parameters assessed	Results		
	Cases (not counselled)	Controls (counselled)	Statistical significance (p-value)
Awareness about availability of PND.	70 (52.2%)	42 (100%)	p < 0.001
Knowledge of appropriate gestational age for PND (10 weeks).	52 (39%)	40 (95.3%)	p < 0.001
Utilization of PND in subsequent pregnancies.	50 (37.3%)	32 (76%)	p < 0.01
Acceptability towards termination of pregnancy (TOP).	122 (91%)	40 (95.3%)	p = 0.072
Acceptability of religious verdict on TOP.	122 (91%)	42 (100%)	p = 0.072

Table II: Calculation of odds ratio for subsequent PND use in both groups by using 2 x 2 table.

Comparison groups	Outcome		
	Positive (PND used)	Negative (PND not used)	Total
Genetically counselled (controls)	32 (A)	10 (B)	42
Not counselled (cases)	50 (C)	84 (D)	134
Total	82	94	176

$$\text{Odds Ratio (OR)} = A \times D / B \times C = 32 \times 84 / 10 \times 50 = 2688 / 500 = 5.376$$

CI = 98 – 100%) controls. Only 12 (9%, 95% CI = 2.1 – 15.9%) cases refrained from sharing their views on the religious verdict. No statistically significant difference (p = 0.072) was found between the two groups in the acceptability towards PND, TOP and Islamic verdict on TOP. The statistical significance of the difference in the results of two groups is depicted in Table I.

The calculated odds ratio for subsequent PND utilization was 5.37, which shows a significant positive relation between genetic counselling and PND utilization. Details of the calculation of odds ratio are given in Table II.

DISCUSSION

The advent of PND has been a major milestone in preventing thalassaemia. Pakistan, despite being a third world country, offers a high quality PND service for thalassaemia affected patients with a minimal chance of miscarriages related to chorionic villous sampling¹¹ and a negligible rate of misdiagnosis.⁸ Though this service is not available on a wider scale, it is still being underutilized on the level at which it is being provided. The goal of this study was to assess the role of genetic counselling in PND utility, to identify the reasons as to why the service was not being used optimally and to recommend some practical measures to improve its utility. The response of thalassaemia affected families towards PND and TOP were used to help us reach the goal. It was tried to analyze the role played by genetic counselling in the whole picture and, therefore, the study sample was divided in two groups, on the basis of receiving genetic counselling or not.

The major contributors towards the underutilization of PND services were the lack of awareness of the disease, its genetic nature and the availability of PND itself. Other important factors include financial constraints, transport and logistics problems. Previously conducted local studies have also recognized un-

awareness as one of the main hurdles to the utility of PND. The results showed a high rate of unawareness towards PND (47.8%) and its appropriate timing (61%) in the group who had not received genetic counselling. In contrast, all the individuals (100%) who had received genetic counselling were fully aware of the test and the majority (95.3%) had a clear understanding about the appropriate timing of the test during pregnancy. The PND utilization in subsequent pregnancies was also much higher (80%) in the controls as compared to the cases (37.3%). The statistically significant higher rates of awareness about PND, its timing, and its utility in the control group clearly reflect the importance and efficacy of genetic counselling in controlling thalassaemia. De Montalembert *et al.* reports that 50 – 70% of the parents of children with sickle cell disease, requested for PND after being counselled on it, hence emphasizing the role of genetic counselling yet again.¹²

Lack of awareness and knowledge about PND has been an established impediment to the facility.¹³ The aim should be to bridge the gap between the availability of PND and its utility, and with genetic counselling we can ensure that this gap is indeed reduced. It will require an initial effort of training health care providers but will turn out to be effective in the long-run. A number of participants showed surprise and displeasure for not being offered genetic counselling at various health strata, which includes health care providers such as paediatricians, general practitioners, transfusion service providers, and non-government organizations (NGO's). This makes awareness and education based campaigns, particularly targeting health care professionals, an absolute necessity. Educational campaigns for the affected families should also be arranged to create awareness about the basics of the disease, its management and prevention. Therefore, coverage should include everyone, from a highly qualified doctor to an illiterate common man.

Financial constraints, logistics and transportation problems are other major reasons for people not utilizing the facility to its maximum potential.¹⁰ Majority of the Pakistani population cannot afford the cost of test which is quite substantial, this was well reflected in this study as 20% of the study population with awareness about the test, did not opt for it due to financial problems. Since the test is available only at a limited number of diagnostic centres in few major cities across Pakistan,

therefore, logistic problems and transportation limitations are also very important impediments towards the test utilization. This was also well reflected in this study when 20% of study population did not utilize the test despite having knowledge about the test. The solution to these problems include test subsidy and widespread availability, therefore, addressing these financial and logistic problems will be an uphill task for a resource-constrained country like Pakistan.

As opposed to the general concept, religion was not found to play a pivotal role in hindering the utility of PND or TOP, as is evident by data shown in Figure 1. Positive responses to PND, TOP and the religious verdict on TOP were seen in the majority (> 90%) of the study population in both the groups. Ahmed *et al.* reports a better response and decision-making ability towards selective TOP after clearly conveying the Islamic perspective on the subject. The involvement of religious authorities has been advocated for acceptance of PND in Muslim countries.¹⁴ These results reconfirmed the already documented prevalent consanguineous marriages in the Pakistani society.¹⁵

Non-collection of test reports and miscommunication of the results over the telephone due to logistics and transportation issues resulted in the birth of β -thalassaemia major children in two of the families who had used PND. Some of the parents were confused as to whether or not PND was required in every pregnancy, and some even had subsequent normal children without PND, thereby thinking that the test was not an essential requirement in every pregnancy. Therefore, these individuals with apparent knowledge of the test, had misunderstandings and misconceptions which again adds to the lack of awareness of the general population.

Subsidizing the test can be a practical option to tackle the financial issue related to the problem. As far as the rest of the constraints are concerned, most can be categorized under the heading of unawareness. The solution to that, as already mentioned, is creating awareness. The method is to make genetic counselling a necessary part of dealing with a genetic disorder. Counselling should cover all aspects of the disease, from the basic pathology to the most appropriate preventive measures. It should be done in a confidential, compassionate and non-directional manner since the final decision and responsibility regarding TOP always lies with the parents.¹⁶ Local studies have indicated scanty knowledge about thalassaemia as a negative factor for decision-making in PND and thalassaemia screening.¹⁷ Even countries where finances and infrastructure are not a major hurdle to PND, lack of knowledge or superficial knowledge of PND has been a known impediment to its utility.¹⁸ Therefore, the role of genetic counselling is of prime importance in ensuring a better utility of PND facilities.

A National thalassaemia control program should be in place to provide resources and supervise activities for an effective prevention of thalassaemia. A National thalassaemia prevention program has yielded productive results in Greece.¹⁹ Countries like United Kingdom have demanded PND provision as part of National policy.²⁰ Since cost and logistics are important impediments towards test utility; therefore, cooperation of the government and support by international agencies and NGO's for prevention programs is a requirement for developing countries.

CONCLUSION

The study reflects a very positive attitude of genetically counselled thalassaemia affected families towards PND. For better utilization of PND, genetic counselling services should be available at all health strata.

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