Abstract

Objective: To evaluate the practices and attitudes of parents of thalassemia major patients towards chorionic villous sampling (CVS).

Patients & Methods: A cross-sectional study was conducted at thalassemia centre at Pakistan Institute of Medical Sciences in the months of July and August 2011. Information regarding CVS was taken from parents of 100 registered β thalassemia major patients. Parents with no history of pregnancy after index case, parents of α thalassemia patient and those with other haemoglobinopathies were excluded from study. Results were entered and analyzed on SPSS version 17.

Results: After the index only 28 families underwent prenatal diagnosis of thalassemia by CVS. There were 72 families in which CVS was not done. Out of these it was not advised in 48 families and there were 24 families in which it was advised but they did not opt for it. Various reasons for this included health, religious and social issues and also the risk of miscarriages. When they were asked for CVS in future pregnancies, majority (67%) said yes but 33% were still not convinced to go for CVS in future.

Conclusion: Prenatal diagnosis of β-thalassemia by CVS is available in Pakistan for over a decade but its use remains limited. The main reasons for the limited use were that either they were not advised, or they did not opt for it for cost, health, social and religious issues. There is a need to impart awareness of the procedure particularly addressing the above mentioned issues.

Key words: prenatal diagnosis, thalassemia screening, chorionic villous sampling

Introduction

Thalassemia is the most common autosomal recessive single gene disorder caused by different genetic lesions that variably impair globin chain synthesis. About 3% of the world population carries gene for beta-thalassemia. In Pakistan, the carrier status is estimated around 5-7%. If both parents are carriers of thalassemia, in every pregnancy there is 25% chance for fetus to be diseased. It is a preventable disease as proved by countries like Italy, Greece and Cyprus. They were amongst the first to establish successful national programs resulting in significant reduction in the births of affected children. The main prevention strategies comprise of targeted screening of thalassemic families, extended family screening, screening before marriage and prenatal diagnosis for thalassemia. Over the last decade, techniques of first trimester fetal tissue sampling have enabled diagnosis of many genetic disorders to be made early in pregnancy thus allowing patients to have the option of a pregnancy termination if the fetus is affected. CVS and amniocentesis are prenatal diagnostic procedures used to detect certain fetal genetic abnormalities. Prenatal diagnoses of single gene disorders and chromosomal abnormalities by CVS is now known and well established procedure. Early diagnosis is important to prevent any possible complications. CVS was used as a rapid means of prenatal diagnosis of genetic disorders in 1980. In Pakistan prenatal diagnosis for β thalassemia was introduced in 1994. The advantage of procedure is the diagnosis of disease in early pregnancy (7-12 weeks) and thus early termination of pregnancy is associated with lower morbidity and decreased psychological trauma.

CVS is a technique for retrieval of fetal cells from developing pregnancy during the first trimester. Transcervical approach, was used initially and was first to be started clinically in Europe and Northern America. In 1984, the alternative trans-abdominal approach was introduced. This technique, offered benefits of lowered risk of infection and higher patient acceptability. To-date all over the world multiple studies have demonstrated high efficacy, safety and acceptability of this procedure, and to be the gold standard for prenatal diagnosis.

Prenatal diagnosis of thalassemia by CVS though a routine procedure to be carried out in many countries, is still not a
common practice in our country. Factors identified for this under utilization are lack of awareness, poor access, delay in seeking advice and high cost.

The aim of the current study was to determine the practices and attitudes of parents of thalassemia major children towards prenatal diagnosis of thalassemia by chorionic villous sampling.

Patients & Methods

This was a cross-sectional questionnaire based descriptive study conducted at Thalassemia centre, Pakistan Institute of Medical Sciences (PIMS), Islamabad in the months of July and August 2011. Parents of one hundred registered patients of ß thalassemia major and with a history of at least one pregnancy after that thalassemic child were included in the study. Patients with α thalassemia or any hemoglobinopathy were excluded. Diagnosis of ß thalassemia major was done on the basis of history and Hb electrophoresis. A properly designed questionnaire was devised to collect information from parents (mother/ father or both). Parents were asked about consanguinity, their screening status, screening of other children, if they had CVS advised or done, if advised and not done, what were the reasons. Results were entered on SPSS version 17 and analyzed.

Results

Among 100 thalassemic children, 67 were males and 33 were females with male to female ratio of 2:1. Age range was from 1-22 years with mean age of 9.03 ± 5.58 SD years. Eighty eight parents gave the history of consanguinity and 12 children were the product of non consanguineous marriage. Most of the patients belonged to Punjab (74%) followed by KPK (24%) and 2 patients belonged to Baluchistan Province.

Among 100 registered thalassemic children 73% parents have been screened for thalassemia and 27% still not been screened. The reason being either registered recently or have not gone for it despite being advised. Almost all the parents gave history of screening for thalassemia after the diagnosis of first thalassemic child. None of the parents gave history of screening before marriage. Total no of children in these 100 families (including siblings) was 356. Among them 133 (37%) were diagnosed as thalassemia major. Out of 100 families, 78 families had 1 thalassemic child, 11 had 2 thalassemic children and 11 had 3 thalassemic children. 177 (49.7%) children were diagnosed as thalassemia minor and 46% children were normal.

After this index case CVS was done 28 families, once in 24 families and twice in 4 families. 72 families did not go for CVS. Out of these 72 families it was not advised in 48 families and there were 24 families in which it was advised but they did not opt for it.

Result of CVS showed that among these 28 cases 5 were diagnosed as thalassemia major, 9 as thalassemia trait and 14 were normal. None of the patients reported for any complication after getting CVS done. Parents who had thalassemic children were counselled and advised for termination of pregnancy and 4 parents agreed to it.

There were 24 cases in which CVS was advised but they refused to get it done. Various reasons were mentioned by parents as shown in Table 1.

### Table 1. Demographic and Other Parameters in Studied Population (n 100)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total No of Children</td>
<td>356</td>
</tr>
<tr>
<td>No of thalassemic children</td>
<td>100</td>
</tr>
<tr>
<td>No of children in these 100 fams (including siblings)</td>
<td>356</td>
</tr>
<tr>
<td>No of children diagnosed as thalassemia major</td>
<td>133 (37%)</td>
</tr>
<tr>
<td>No of children diagnosed as thalassemia minor</td>
<td>177 (49.7%)</td>
</tr>
<tr>
<td>No of children diagnosed normal</td>
<td>147 (41%)</td>
</tr>
</tbody>
</table>

Parents were also asked if they will go for CVS in future pregnancies. As shown in table 1, 67% said yes but 33% were still not convinced to go for CVS in future.

### Discussion

Thalassemia is the world's most common hereditary disorder. In Pakistan about 5000 homozygous thalassemic children are born every year. Standard management of ß-thalassemia includes blood transfusion and iron chelating therapy (to control the deleterious effects of progressive iron overload). Bone marrow transplant from HLA-identical siblings in patients who have no evidence of iron overload results in disease-free survival and has significantly improved not only the survival but also the quality of life for
thalassemic patients. However, in developing countries where thalassemia is prevalent and health care resources are limited, these forms of management are usually not easily affordable. In Pakistan, for instance, patients who receive regular transfusions are not able receive drugs for iron chelation. Moreover, bone marrow transplantation is not easily available and is quiet and expensive option for cure of thalassemic children. So prevention is the most effective and least expensive means of dealing with this problem.8

The main prevention strategies comprise of providing appropriate information of disease and ways of prevention not only to public but also to health professionals. This prevention can be achieved by screening and counseling of families at risk and screening of general population prior to marriage.9 Premarital screening alone has tremendously decreased the birth prevalence of β-thalassemia major.10 Prevention and control of thalassemia requires a well-planned program of population screening and genetic counselling. Prevention of new births of thalassemic children can be implemented by prenatal diagnosis with selective termination of pregnancy in case of homozygous fetus.11 WHO guidelines on control of haemoglobinopathies provide useful guidelines to develop a national programme to control β-thalassemia in our country.12 Such programmes involve identification of individuals carrying a gene for β-thalassemia, counselling of these carriers and prenatal diagnosis by CVS in situations where both parents are carriers.13

Discouraging cousin marriage and family marriages is another way of preventing disease. In our study consanguinity has been reported in 88% couples. These findings are comparable with another study done in Lahore on awareness of thalassemia prevention by CVS. Consanguinity was reported in 82% of their cases. In the same study among thalassemic children 64% were males and 36% were females, the findings comparable to our result (67% males and 33% females). Similar, male preponderance and 36% were females, the findings comparable to our result same study among thalassemic children 64% were males 82% of their cases. In the other study done for intrauterine diagnosis of thalassemia major by CVS in 60 couples with thalassemia trait, 28 (47%) were homozygous for beta-thalassemia, 8(13%) thalassemia minor and 24 (40%) cases were normal.19 In the same study 4 (2%) out of 60 women had a spontaneous fetal loss after the chorionic villous sampling. In another study done in Iran on outcome of CVS in 300 women, 18% fetuses turned out to be of thalassemia major and rate of spontaneous abortion was 1.4%.20 In our study however out of 28 pregnancies in which CVS was done, none gave the history of any complications. In another study done on geographic distribution and safety of CVS, out of 223 cases in which CVS was done 43% were Thalassemia minor, 38% thalassemia major and 19% were normal and rate of pregnancy loss after CVS was 2%.21 Syed S reported pregnancy loss in 2/137 (1.5%) cases. Another study done in Multan on DNA analysis of post CVS samples revealed that 12(20%) out of sixty fetuses studied were homozygous for thalassemia and all the couples opted for termination of pregnancy.22 Post CVS fetal loss has been reported from 1.3-3.0 %.23, 24 In the above mentioned study fetal loss was not observed in any case after the procedure, the findings comparable with our results.

Conclusion

Prenatal diagnosis of β-thalassaemia by chorionic villous sampling is a safe procedure being available in Pakistan for over a decade but its use remains limited. In this study 2/3rd of families did not go for CVS in subsequent pregnancy. The main reasons being either they were not advised, cost, health, social and religious issues. There is a need to impart awareness of the procedure particularly addressing the above mentioned issues. Both patients and doctors should be made aware of Fatwa given for PND and subsequent
termination of pregnancy (if required) and safety of procedure.

References
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