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Original Article

Use of Chorionic Villous Sampling for Prenatal Diagnosis of Beta Thalassaemia: Attitudes and Practices of Parents

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Abstract

Background: To assess the attitudes and practices of parents of Beta-Thalassaemia Major children regarding Chorionic Villous Sampling (CVS), as prenatal diagnosis in subsequent pregnancies.

Methods: In this cross-sectional study a pre-designed questionnaire was used to evaluate the socio-demographic profile and attitudes of parents of 210 registered thalassaemic children, regarding CVS.Only those parents who had one or more pregnancies after the index case were included in the study. Results were entered and analyzed on SPSS version 20.

Results: After the index case, 36.2% parents underwent CVS in all subsequent pregnancies . The common reasons not to utilize this facility were lack of knowledge (47.7%), careless attitude (41.7%), family pressure (4.4%) and financial issues (1.5%). Religious reason was not found in any of the cases. Majority of the families (54.3%) belonged to lower middle class financial status. There was a significant association between CVS practice and educational level of the mother and genetic counselling at the time of diagnosis of index case. In future pregnancies, 52.8% parents had no planning, while 15.7% showed interest in undergoing CVS in next pregnancies.

Conclusion: Despite the availability of CVS in the country, very few families had opted for it; the major reasons being lack of knowledge, careless attitude and family pressure. As against the common thought, religious reason was not a significant factor.

Key Words: Prenatal diagnosis, Chorionic Villous Sampling, Beta-Thalassaemia Major.

Introduction

Beta-Thalassemia Major (BTM) is an autosomal recessive, inherited disorder of haemoglobin synthesis, caused by reduced or absent synthesis of beta globin chains, resulting in life-threatening anaemia and requiring regular blood transfusion for survival. It is common in the Mediterranean, Indian subcontinent, and Middle East regions. Approximately, 5000-9000 children with β-thalassemia are born annually in Pakistan with an estimated carrier rate of 5-7%.[1] Both the parents of an affected child are carriers, having a single copy of mutated beta globin gene. At each conception, the child has 25% chance of being affected, 50% chance of being an asymptomatic carrier, and 25% chance of being normal.[2] High fertility and birth rate, low educational status, trends of consanguineous marriages and lack of awareness are some of the reasons that have made this disease highly prevalent in Pakistan.[3] The mainstay to control this preventable disease is by population screening, appropriately timed genetic counselling, prenatal diagnosis and option of terminating affected pregnancies.[1] The preferred method for prenatal diagnosis is detection of beta- chain mutation by polymerase chain reaction (PCR) of fetal DNA obtained by chorionic villous sampling (CVS). This technique can prevent the birth of an affected child in developing countries in which Beta-thalassaemia is very much prevalent. This facility initially reported in 1994, is now available at many centers in the country and offered to all couples at risk for a child with BTM. CVS is performed at 10-12 weeks of gestation by trans-abdominal route, and after seeking appropriate level of training and performance of initial procedures under supervision, it is a simple, easy to apply, useful, and fairly safe technique. In comparison to estimated total cost of the long-term treatment of beta -thalassaemia, cost required for CVS and laboratory diagnosis of Beta- thalassaemia mutation is minimal. In cases where fetus is detected to be homozygous for Beta -thalassaemia mutation, termination is done soon after the diagnosis, usually from 13-16th weeks of gestation which is usually uneventful and without any untoward complications.[4]

Subjects and Methods

This was a cross-sectional descriptive study, which was based on a pre-designed structured questionnaire. It was conducted in the Thalassaemia Center, Children

Hospital, Pakistan Institute of Medical Sciences (P.I.M.S) Islamabad, Pakistan from January to March 2017. Parents of 210 registered patients of BTM, who had history of at least one pregnancy after the index case, were included in the study. Parents having children with any other haemoglobinopathy, Beta-Thalassaemia Intermedia and those having only a single child were excluded from the study. A carefully designed questionnaire was used to collect data from either of the parents available with the child at the time of interview, regarding socio-demographic status, number of thalassaemic children, family history and previous knowledge of thalassaemia,provision of genetic counseling at the time of diagnosis of first thalassaemic child, parents' future pregnancy plan and approximate treatment related expenses. They were also inquired if they had opted for CVS or not; and if not, reasons for not opting. All data was entered and analyzed using SPSS version 20 and a p-value of <0.05 was considered statistically significant.

Results

(54.3%) belonged to lower middle class (Table 1). Majority can not bear the expenses more than 10,000 per month (Table 2). The total number of children in the families under study ranged from 2 – 10, with majority parents (31.9%) having 3 children. Out of those, number of children suffering from BTM ranged from 1-4. Most of the families (63.3%) had 1 thalassaemic child, followed by 2 in 66 (31.4%) of the families. Only 22 (10.5%) parents had previous knowledge about the mode of inheritance of thalassaemia, regardless of the family history. None of the parents had received pre-marital screening and no parent reported any complication following CVS. The 2 major reasons among parents not practicing CVS testing in 1 or more pregnancies, were lack of proper knowledge about CVS in 64(47.7%) and careless attitude in 56 (41.7%) (Table 3). Majority (52.8%) had no planning, 66(31.4%) were practicing family planning methods and 33(15.7%) desired 1 or more children in future after undergoing CVS prenatally. There was significant association between the trend of opting for CVS among the parents and educational level of the mother (p=0.008). Similarly, if the parents were offered good genetic counseling at the time of diagnosis of first thalassaemic child, there was a higher trend of practicing CVS in the subsequent pregnancies (p <0.05). However, neither the educational level of the father nor the financial status of the family had any significant association with the CVS practice.

Table I : Socio-demographic profile of families

		N	%
Residence Province-wise distribution (n=210)	Punjab	106	50.4
	Federal Capital	54	25.7
	KPK	32	15.2
	AJK	16	7.6
	FATA	01	0.4
	Sindh	01	0.4
Educational Status (n=210) Mothers:	Uneducated	72	34.3
	Under-primary	09	4.3
	Primary	27	12.9
	Under-matric	24	11.4
	Matric	46	21.9
	Inter	16	7.6
	Graduate	10	4.8
	Masters	06	2.9
Fathers:	Uneducated	40	19.0
	Under-primary	12	5.7
	Primary	21	10.0
	Under-matric	30	14.3
	Matric	65	31.0
	Inter	18	8.6
	Graduate	15	7.1
	Masters	09	4.3
Financial status (with average monthly income) n=210	Poor (<5000 Rs.)	38	18.1
	Lower Middle (5000-15,000 Rs.)	114	54.3
	Middle (15,000-50,000 Rs.)	55	26.2
	Upper Middle (>50,000 Rs.)	03	1.4

Table 2: Treatment related expenses per month (Pkr)

	No. of Families	No (%)
<1000 Rs	76	36.1%
1000-5000 Rs	89	42.3%
5000-10,000 Rs	27	12.8%
>10,000 Rs	18	8.5%

Discussion

About 3% of the world's population carries the genes for beta thalassaemia; the carrier rate in Pakistan ranges between 5-8%. Around 5000 children are diagnosed annually with BTM in Pakistan; consanguinity being one of the major factors leading to its high prevalence in the country.[5]In a family having a patient of BTM (extended family) the prevalence of carrier is more than 30%.[6]

As in many other developing countries in Asia, β-thalassaemia increases the burden for healthcare services in Pakistan and with limited available national resources, it is very difficult to provide safe

Table 3. Knowledge, attitudes and practices among parents regarding prenatal diagnosis by CVS.

		No	%
Genetic Counseling offered(n=210)	Yes	140	66.6
	No	70	33.3
CVS undergone after the index case (n=210):	Never	97	46.2
	In some pregnancies	37	17.6
	In all pregnancies	76	36.2
Reasons for not opting for CVS (n=134)	Lack of proper knowledge	64	47.7
	Careless attitude		
	Family Pressure	56	41.7
	Financial reason	06	4.4
	Health Concerns	02	1.5
	Non-availability of one parent	02	1.5
		02	1.5
	Transportation problem	01	0.7
	Late diagnosis of index case	01	0.7
Termination of pregnancy sought after diagnosis of Thalassemia major on CVS (n=32)	Yes	27	84.3
	No	05	15.7

blood transfusion and iron chelation therapy to each and every patient. [7] Multidisciplinary approach is needed to treat this disease but it is difficult due to shortage of resources and poor coordination among the existing facilities.[8] Bone marrow transplantation, the only curative option, is extremely expensive and unaffordable for most Pakistani patients. Therefore, prevention is the most effective and the least expensive option available, to deal with β-thalassemia in our country. [7]

Different strategies to prevent thalassemia include parental awareness, population screening, genetic counseling, and prenatal diagnosis. Creating awareness and educating parents is a cost-effective tool in preventing and improving the quality of life of patients with thalassemia. [8,9] The developed countries are more focused at preventing the disease by detection of thalassemia carriers and marriage counseling.[10,11] In Cyprus, the incidence of BTM cases dropped by 96% through preventive programs. [12] The provision of CVS sampling in the first trimester of pregnancy makes it more acceptable. It is preferable to do CVS before 120 days (17 weeks) of pregnancy. In one study, almost all prenatal diagnoses were carried out in the first trimester with >95% of women opting for termination of pregnancy in case of BTM fetus. [13] In case of homozygous fetus, termination is physically and emotionally more feasible and acceptable in the earlier stages of pregnancy. The results of one study showed that the performance of CVS test was reliable; especially considering the validity and predictive value in the diagnosis of thalassaemia major. Thus, couples with thalassemia trait can safely undergo this test to prevent the birth of the children with major thalassaemia.[14]

In Pakistan, Punjab Thalassaemia Prevention Programme (PTPP) has been started by the Government of Punjab to provide free Prenatal Diagnostic service (Collection of chorionic villous sample and mutation analysis) which is catering whole of the province through its field officers, especially covering the districts of Rawalpindi, Mianwali, Jhelum, Gujrat, Chakwal, Khoshab, Sargodha and Attock. People from Khyber Pukhtoon khwa , Gilgit Baltistan and Azad Jammu and Kashmir are also taking advantage through this initiative .[15]

In our study, most of the patients, 106 (50.4%) were residents of Punjab province, followed by 54 (25.7%) from Federal Capital Islamabad and 32 (15.2%) from KPK. The Thalassemia Center at PIMS Islamabad has more than 1500 patients of thalassaemia registered and caters for the transfusion services of many of the patients from these parts of the country. Regarding the educational level of the parents, majority of the mothers, 72(34.3%) were uneducated and majority of the fathers, 65(31%) had received formal education up to matric level. This is comparable to other studies done in the same context in different settings in Pakistan. Ali S. et al. [10,16,17]

Positive family history for thalassemia was found in 26% cases. Despite a high rate of consanguineous marriages in our country, the prevalence of positive family history is low in present study. Most of the families, 114 (54.3%) belonged to lower-middle class with an average income of Rs. 5000-15,000/month. The maximum number of parents that is 89 (42.3%) spent between Rs. 1000-5000/month on the treatment of their one or more thalassaemic children. The expenditures included money spent on travelling, food, stay and medicines. Majority of the patients were supported by The Bait-ul-Maal Pakistan as well as by Hospital Zakat Funds. In a study conducted in India, they found that the average annual cost of treatment was $137.9±47.8, the expenditure included amount spent for blood transfusion and related expenses, iron chelation therapy (if prescribed), folate and calcium supplementation therapy, investigations (viz. serum ferritin level, Hb estimation), splenectomy (if done in

last 1 yr), vaccination for Hepatitis B and others like treatment costs for adverse effects of transfusion.[18]

A study from Iran showed that proper genetic counseling teams consisting of a doctor and a professional with a BSc. degree in health studies were established in designated accessible urban health posts in every city.[19]A formal genetic counseling session should include explanation of the nature and prognosis of the disorder and available treatment options, estimation and communication of genetic risk for parents and providing options for avoiding them including technique of prenatal diagnosis and associated problems and supporting the individual or couple in making the decision that is right for them.[20] In present study a significant association between genetic counselling and undergoing CVS testing ($p < 0.05$). In the present study, only 76 (36.2%) parents had undergone CVS in all subsequent pregnancies, while the majority 97 (46.2%) had never opted for CVS testing. Another study showed that after the index case, 72% families did not undergo prenatal diagnosis of thalassemia by CVS.[21] Common reasons in our study were lack of awareness about prenatal testing (47.7%) and careless attitude by the parents (41.7%). Despite the fact that majority of the families belonged to lower middle class, financial reasons were found in only 1.5% of the cases. This might be because CVS is done free of cost now at few Government-based Centers. In spite of the common notion in our country that termination of pregnancy is not religiously permitted, our study showed no significant relationship between not undergoing CVS and religious reasons. In one study comparable to ours, CVS was not advised in 48% families and there were 24% families in which it was advised but they did not opt for it. [21] In another study 37.5% knew about prenatal diagnosis but did not use it.[22]

Termination of pregnancy (TOP) was done in 84% of families after the diagnosis of thalassemia on CVS. In the rest, reasons for not opting TOP were delay in collecting report and reaching hospital in time especially in those patients who belong to far flung areas where there is no local specialized center for prenatal diagnosis. In a study conducted in Saudi Arabia, the attitude towards abortion was greatly affected by religious values. [23]Another study in Egypt showed that the change in attitude towards termination of pregnancy was related to good counseling of the religious aspects towards prenatal diagnosis and termination of pregnancy.[24]In comparison, a study done to assess attitudes towards prenatal diagnosis and termination of pregnancy for thalassemia in pregnant Pakistani women in the North of England showed influence by various other factors, similar to our findings. [25] It can therefore be concluded that religion should not be taken as a proxy for their attitudes either for or against termination of pregnancy.

Conclusion

1.Beta-Thalassemia Major poses a major burden of disease in our country, and prevention is the only way to reduce its incidence.

2. Prenatal Diagnosis by Chorionic Villous Sampling is a safe procedure to detect cases, but non- utilization of this facility is evident, due to lack of awareness. Religious reasons were not found in any of our cases.

3.Specialized genetic counseling sessions at the time of diagnosis of thalassaemia child regarding family screening and prenatal diagnosis emphasizing on its long term benefits should be carried out.

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