SAFETY AND EFFECTIVENESS OF TRANSABDOMINAL CHORIONIC VILLOUS SAMPLING FOR PRENATAL DIAGNOSIS OF β-THALASSEMIA

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ABSTRACT

Objectives: To assess safety and effectiveness of trans abdominal, chorionic villus sampling(CVS) for pre-natal diagnosis of B-thalassemia.

Material & Methods: This is prospective observational study conducted over a period from Jan 2018 to Dec 2018 in Rehman Medical Institute of Peshawar-Pakistan. Total of 50 patients were recruited in study. All couples who were carriers of thalassemia trait or had previous child with thalassemia major were included. Patients with multiple gestation, active vaginal bleeding before procedure, gestational age > 16 weeks, recurrent unexplained abortions, medical disease such as overt diabetes, chronic hypertension and patients who refused termination in case of positive diagnosis were excluded from the study A written consent about the CVS procedure, its complications and decision for termination in case of positive diagnosis was taken from all couples. Period of gestation was calculated by booking ultrasound and LMP and procedure was performed between 10-14 weeks. The procedure was conducted in interventional radiology unit of RMI through Trans abdominal route under aseptic technique and local anesthesia (5-10ml of 2% xylocaine).

Results: DNA analysis of chorionic villus sampling showed that 17(34%) fetuses had thalassemia major, 10 fetuses (20%) thalassemia trait and 23 (46%) had no Beta Thalassemia mutation. Twentyeight (56%) couples had consanguineous marriages. Only one patient (2%) had procedure related spontaneous miscarriage. None of sample was reported as insufficient or in adequate.

Conclusion; Trans abdominal approach for chorionic villus sampling is a safe and effective tool for prenatal diagnosis of thalassemia major provided done with skilled hands.

Key words: Thalassemia, CVS, transabdominal.

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INTRODUCTION

Beta thalassemia is the most common heterogeneous autosomal recessive hereditary disorder in Southeast Asian, African, and Mediterranean descent. More than 270 million persons worldwide are heterozygous carriers of hereditary disorders of hemoglobin (Hb), and at least 300,000 affected homozygotes or compound heterozygotes are born every year.[1] The annual incidence among Asian populations is 1: 1000 birth.[2] The approximate prevalence of β-thalassemia trait in Pakistan is around 5-7%, (around ten million people are carriers in total population) and every year about 5000 new cases are born.[3] Dr Yasmeen Rashid, Health Minister Punjab mentioned this figure up to 6000/year in thirteenth national thalassemia conference which means 17 affected children are born each day.[4] The only treatment available is supportive with regular blood transfusions and iron chelation, with definitive treatment of bone marrow transplant only a possibility and hope for few. This high prevalence may put huge burden on our existing health resources and psychological stresses on families. The only way out is to prevent birth of thalassemia children by following RCOG and ACOG recommendation which includes carriers screening, genetic counselling and pre-implantation genetic diagnosis (PGD).[1,5]

Prenatal diagnosis by DNA analysis can be performed using fetal cells obtained by chorionic villus sampling (CVS) or amniocentesis[6] and cell-free fetal DNA (cffDNA) from maternal plasma.[7,8] The advantage of non-invasive cff DNA technique over other invasive (CVS, Amniocentesis) procedure is that it can be performed at

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early stage of 6 weeks gestation and so termination of pregnancy can be offered at early stage with less maternal complications and less mental stress but it is expensive. [9] Likewise, CVS can be offered in first trimester (10-12weeks) in comparison to amniocentesis, which cannot be performed before 16 weeks, which is too late to decide for termination of pregnancy. Both CVS and Amniocentesis being invasive are also associated with fetal complications like miscarriages (0.5%–1.0% of CVS and 0.25%–0.50% for amniocentesis), preterm delivery and fetal limbs deformity.[10] The additional disadvantages of CVS are: difficult cytogenetic analysis, the possibility of contamination with maternal cells and the risk of mosaicism. CVS is also acceptable in our religious fatwa which states, if continuation of pregnancy becomes life threatening then abortion can be carried out within 120 days of the pregnancy but no later than that.[11,12] In the background of risk factors, the invasive procedures are offered to only high-risk group after primary screening testing. CVS can be performed both through trans abdominal(TA-CVS) or transvaginal approach depending upon operator comfort. Initially we use to send our patients to Islamabad and Lahore for CVS as no center in KPK was offering this service, but since 2018 Rehman medical institute has started this procedure. The aim of this study is to evaluate the risk of fetal loss, fetal malformations and other post procedure adverse outcomes in patients undergoing TA -CVS.

MATERIAL & METHODS

This is prospective observational study conducted over a period of one year from Jan 2018 to Dec 2018 in Rehman Medical Institute of Peshawar-Pakistan. Total of 50 patients were recruited in study. All couples who were carriers of thalassemia trait or had previous child with thalassemia major were included. Patients with multiple gestation, active vaginal bleeding before procedure, gestational age > 16 weeks, recurrent unexplained abortions, medical disease such as overt diabetes, chronic hypertension and patients who refused termination in case of positive diagnosis were excluded from the study A written consent about the CVS procedure, its complications and decision for termination in case of positive diagnosis was taken from all couples. Period of gestation was calculated by booking ultrasound and LMP and procedure was performed between 10-14 weeks. The procedure was conducted in interventional radiology unit of RMI through Trans abdominal route under aseptic technique and local anesthesia (5-10ml of 2% xylocaine). Before procedure ultrasound was performed to confirm fetal viability, number of fetuses and placental localization. A Co-axial Chorion Biopsy needle set with an outer guide and an inner aspiration needle was used. A special chorionic biopsy double needle was used to obtain sample. The outer needle (20G) was introduced through the abdomen into the uterine wall with the right hand while holding the USG probe in the left hand to visualize the needle tip. As soon as the needle entered the placenta, the stilette was then removed and inner needle (18 G) was introduced through the outer needle. A 20 ml disposable syringe containing 1ml sterile normal saline was attached to inner needle and its plunger pulled half way back to create suction, the chorionic villi were aspirated by agitation of the aspiration needle and by applying suction force through a syringe. The inner needle was then removed and villi flushed into a sterile petri dish containing normal saline. The outer needle was left in place because in case of inadequate specimen a second or a third attempt could be made. Once sufficient sample was obtained, the outer needle was removed and the puncture site sealed with bandage. Patients were kept under observation for one hour after procedure and then discharged home with instructions to report in case of warning signs like abdominal cramps, vaginal bleeding or leaking. Regular outdoor follow up was done. Specimens were sent to Armed Forces Institute of Pathology (AFIP), Rawalpindi, Punjab for DNA analysis for β-thalassemia. Chorionic villi were investigated by genomic amplification of B-globin gene by polymerase chain reaction (PCR). Results were collected in 7 days. Data were collected in terms of age, parity, and complication like miscarriage, result of chorionic villous sample and need for termination and entered in SPSS 20 for descriptive analysis. The purpose was to assess the safety in terms of procedure related mischarges and effectiveness in terms of adequate tissue sampling.

RESULTS

A total of 50 patients were included in study. 36(73%) patients were less then 30 years of age. Parity was more than 4 in 33 (66%) ladies (Table1). Chorionic villus sampling showed that 17 (34%) fetuses had thalassemia major, 10 fetuses (20%) were diagnosed to have thalassemia trait and 23 (46%) had no Beta Thalassemia Mutation (Table 2, fig-1). Twenty-eight (56%) couples had consanguineous marriages (Table 3, fig-2). 25 (50%) patients were lost to follow up.11(22%) reached term pregnancy and delivered healthy babies. Out of 17 major thalassemia patients, 5 (29.4%) refused termination of pregnancy and 12 (70.6%) accepted it (Table 4). Only one patient had spontaneous miscarriage after the procedure. All patients had single successful attempt and no sample was reported as insufficient or inadequate.

Table 1: Demographic Data.

AGE	Frequency & % ages
<30	36(72%)
>30	14((28%)
Total	50(100%))
PARITY	
<4	17(34%)
>4	33(66%)
Total	50(100%)

Table 2: DNA Analysis.

	Count of S. NO	%Age
Beta Thalasemia Major	17	34%
No Beta Thalasemia Mutation	23	46%
Trait	10	20%
Grand Total	50	100%

Table 3: Marriage status for consanguinity.

Marriage status for consanguinity	No of Patient	%Age
consanguineous marriages	28	56%
Nonconsanguineous marriages	22	44%
Grand Total	50	100%

Table 3: Follow up and outcome of patients after CVS.

Follow up status	No of Patients	%Age
Continued Pregnancy	5	10.00%
Delivered	11	22.00%
Lost Follow up	25	50.00%
Top	12	18.00%
Grand Total	50	100.00%

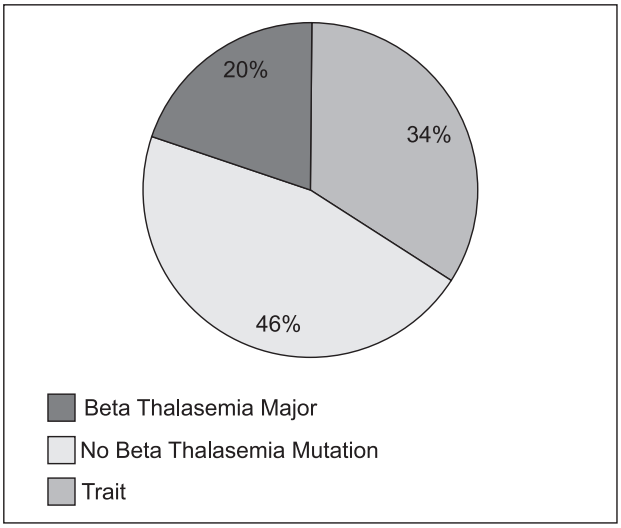

Figure 1: DNA Analysis.

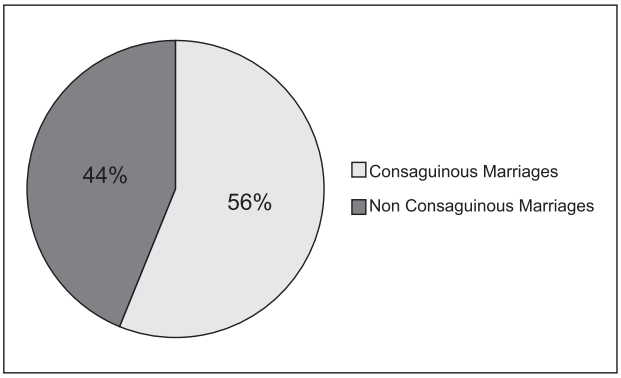

Figure 2: Consanguineous Marraiges.

DISCUSSION

Beta Thalassemia is most common hematological disorder, with approximate prevalence of 5-7% in Pakistan. The mean age of a thalassemia child in Pakistan is 10 years.[13] Just to live these 10 years their supportive therapy like blood transfusion, chelating agent is putting a lot burden on our health resources. The definitive treatment of bone marrow transplant is a hope for only few fortunate, who can afford it, so the only way to stop it is to offer carrier screening and prenatal genetic diagnosis for at-risk couples and to reduce birth of thalassemia major. Countries like Iran and Cyprus have observed a reduction of 96% in incidence through adaptation of these recomendation.[14]

The Total number of patients in our study were 50 with 73% patients <30 years comparable to one study where (77%) of patients were less than 30 years[15] Consanguineous marriages were observed in 28(56%) couples (including first and second degree relative), which is very much comparable with same figure of 56% to a study conducted on Muslim majority community of Pakistan.[16] Another study reported it to be 75%.[15]

One study detected no thalassemia mutation in 24 cases, heterozygote for thalassemia having a single mutation in 8 cases and 28 fetuses were homozygous for beta-thalassemia, which were subjected to termination.[17] These results are very much comparable to our study.

Procedure related spontaneous miscarriage was observed in only one out of 50 patients (2%). One study reported three patients with pregnancy loss of 1.9% in first trimester TA-CVS.[18] A Chinese study on 1355 women with first trimester TA-CVS, reported the fetal loss in 1.54%.[19]

CONCLUSION

Trans abdominal approach for chorionic villous sampling is a safe tool for prenatal diagnosis of thalassemia major provided it is done in skilled hands.

RECOMMENDATIONS

As Beta thalassemia is common problem of Pakistan with low health resources and where consanguineous marriages are normal, carrier screening and chorionic villous sample should be offered to all at-risk couples.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Shams S: Main Idea, Write up.

Raza F: Data Collection.

Nawaz A: Data interpretation, Bibliography.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.