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Prenatal Diagnosis of Thalassaemia by Chorionic Villus Sampling: A Clinico- Hematological Study in a Government Medical College of Eastern India

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Abstract: *Thalassemia and other hemoglobinopathies are genetic disorders of hemoglobin, which can be prevented by population screening and offering genetic counselling. It is a preventable disease as proved by countries like Italy, Greece and Cyprus by establishing 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. . Pre natal 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. With this scientific background, the present study is being conducted as a part of State Thalassemia Control Program by Government of West Bengal with an aim to diagnose the genetic status of fetus of carrier parent so that thalassemia can be prevented at that stage only. In the present study,235 cases 0f chorionic villus sampling are studied over a period of one year regarding Age group wise distribution of Mothers , HPLC diagnosis of Mother and father, Timing of Chorionic villus sampling(CVS) and complication , Mutant Allele status and Diagnosis by chorionic villus sampling and the results are tabulated. In our present study, CVS show normal genotype in 110 out of 235 case(46.80%).70 cases(29.78%) came out to be B thal trait.5 cases came out to be of E trait genotype.30 cases(12.76%) came out to have E B thal genotype and 20 cases(8.51%) cases of B thal Major. So it can be concluded that CVS is an acceptable, reliable and safe method of early diagnosis of fetal thalassaemia that helps to prevent birth of the thalassaemia-affected babies with considerable reduction of socio-economic burdens.*

Key words: *Chorionic villus sampling(CVS),Prenatal diagnosis, Thalassemia..*

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I. Introduction

Thalassemia and other hemoglobinopathies are genetic disorders of hemoglobin, which can be prevented by population screening and offering genetic counselling. In India it is estimated that there are over 25 million carriers of this disease[1] . Beta-thalassemia (β-thalassemia/B thal), sickle cell anemia, E-beta thalassemia and hemoglobin D Punjab are the common hemoglobinopathies in the world including India. About 4.5% of world population is affected by hemoglobinopathies[2]

Thalassemia in children, beside physical and emotional suffering, puts a major strain on national resources. The birth incidence calculated for homozygous thalassemics would be 11316 per year in India which are added each year to the existing load of homozygous thalassemics[3]. Majority of these children become transfusion-dependent and have reduced life expectancy. Till date, the most cost-effective way of prevention of the birth of thalassemia-affected babies is prenatal diagnosis (PND). 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[4].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[5]. 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.

Chorionic Villus Sampling (CVS) is one of such prenatal diagnostic method, in which few villi from the chorion frondosum are collected by trans-cervical (TC-CVS) or trans-abdominal (TA-CVS) route. CVS has the advantage of early termination of pregnancy in a relatively safer way in case the results are abnormal. Again, if the CVS result is normal, it is very much reassuring for the couple. Many studies showing the effectiveness of CVS have been done in other countries[6,7,8] .We have not come across a study of notable size on CVS in Eastern India in the literature.

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[9,10] . In 1984, the alternative trans-abdominal approach was introduced[11]. 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 of thalassemia[12].

Haemoglobin E is widespread in the north eastern States[13,14,15]. In eastern India the prevalence of Hb E trait varies from 3-10 per cent in West Bengal[16]. Both Hb E and Hb S when co-inherited with β-thalassaemia result in a disorder of variable clinical severity[17,18,19]. It is also important to identify carriers of δβ- thalassaemia as compound heterozygotes of δβ- thalassaemia and β-thalassaemia can lead to a severe disorder. δβ-thalassaemia carriers are characterized by a modest elevation in Hb F levels (5-20%) with reduced or normal HbA2 levels and hypochromic and microcytic red cells. This phenotype partially overlaps with that of carriers of hereditary persistence of foetal haemoglobin (HPFH) and genotyping of high Hb F determinants is required as these are not infrequent in India[20]. Screening in antenatal clinics is the best way to identify couples at immediate risk of having an affected child. However, experiences in India have shown that only 15-20 per cent of pregnant women come to antenatal clinics in public hospitals in the first trimester of pregnancy when prenatal diagnosis should ideally be done[21,22]. This emphasizes the need for generating awareness in the population for early registration in antenatal clinics as well as among obstetricians to ask for a screening for β-thalassaemia and other haemoglobinopathies along with other investigations which are done routinely. The other target groups for screening in India include high school children, college or university students, high risk communities and extended family members of affected children[23,24,25]. The latter cascade screening approach appears to be a practical way of identifying a larger number of β thalassemia carriers in a cost-effective way in India. β-thalassemia is extremely heterogeneous with more than 200 mutations described worldwide[26]. In India, about 64 mutations have been characterized by studies done at different centres[26,27,28] . Six to seven mutations [IVS 1-5 (G>C), 619 bp deletion, IVS 1-1 (G>T), Codon 8/9 (+G), Codons 41/42 (-CTTT),Codon 15 (G>A), Codon 30 (G>C)] are common accounting for 85-95 per cent of mutant alleles. However, regional differences in their frequencies have been noted[28,29,30] . The prevalence of IVS 1 -5 (G>C), the most common mutation in India varies from 15-88 per cent in different States. Codon 15 (G>A) is the second most frequent mutation in Maharashtra and Karnataka and Codon 5 (-CT) is the third most common mutation in Gujarat. The -88 (C>T) and the Cap site +1 (A>C) mutations are more common in the northern region[29,30].

With this scientific background,the present study is being conducted .This work is being carried out as a part of State Thalassemia Control Program by Government of West Bengal with an aim to diagnose the genetic status of fetus of carrier parent so that thalassemia can be prevented at that stage only.

II. Materials And Methods

Many Thalassemia control units have been established in different district hospitals and medical colleges to cover the maximum number of people to identify Thalassemia carriers by HPLC using Bio Rad Variant II, provide counselling and generate awareness. Samples are also collected from outreach camps in remote areas.

Institute of Hematology and Transfusion Medicine (IHTM), Medical College, Kolkata, is one of the nodal center with the facility to carry out pre-natal diagnosis and has been offering this facility since August 2010.From the Thalassemia control unit of Calcutta National Medical college, samples of chorionic villus biopsy were sent to IHTM for reporting. Whenever the mother was identified as Thalassemia carrier, the father's carrier status was checked and in case of both parents being carriers ,the underlying β- globin gene mutations were identified by routine molecular techniques like ARMS PCR.6 .To identify these anomalies, the polymerase chain reaction-amplification refractory mutation system (PCR-ARMS) technique was used, the beta-Thalassemia mutation was detected by PCR-ARMS. Allele encountered in our study was IVS-I-5 (G-->C) , Codon 6 (A>T) , codon 15 (G- ->A) , FS 41/42 (-CTTT), FS 8-9 (+ G), Codon 30 (G-->C), Codon 26 (G > A).

The B thalassemia is inherited in an autosomal recessive manner. At conception, each sib of an affected individual has a 50% chance of being an asyptomatic carrier and 25% chance of being unaffected and not even a carrier.Heterozygotes(carriers) may be slightly anemic but are clinically asymptomatic.

In the present study,235 cases of chorionic villus sampling are studied over a period of one year regarding 1)Age group wise distribution of Mothers ,2) HPLC diagnosis of Mother and father, 3)Timing of Chorionic villus sampling(CVS) and complication , 4)Mutant Allele status and5) Diagnosis by chorionic villus sampling and the results are tabulated below.

Following are the limitation of CVS[31] :

1.A small percentage of individuals who are carriers or have a disease diagnosis,may have a mutation that is not identified by this method. The absence of a mutation therefore does not eliminate the possibility of positive carrier status or the diagnosis.

2.The error rate of Taq polymerase for base incorporation is 1 in 6000 bases.

3.Note that benign polymorphism are not reported.

4This assay is unable to differentiate between cis and trans mutations.

III. Results

Table 1 Age group wise distribution of Mothers

Age group(yrs)	18-30 yrs	>30-40 yrs	>40 yrs
Mothers(n=235)	215(91.4%)	20(8.51%)	nil

Table 2 : HPLC diagnosis of Mother and father

HPLC diagnosis	Mother(n=235)	Father(n=235)
Thal B trait	200 (85.10%)	190 (80.85%)
E trait	35 (14.89%)	30 (12.76%)
Others	nil	10-EB trait,5-E disease

Table 3 : Timing of Chorionic villus sampling(CVS) and complication

CVS time	No. of cases	Complication
<12 wk	05 (2.12%)	Nil
12-14Wk	210 (89.36%)	Nil
>14 Wk	20 (8.51%)	Nil

Table 4 : Mutant Allele status.

Mutant Allele status	No. of cases(n=235)
Homozygous	30 (12.76%)
Heterozygous	80 (34.04%)
Compound heterozygous	15 (6.38%)
Absent	110 ((46.80%)

Table 5 : Diagnosis by chorionic villus sampling.

Diagnosis	No. of cases
Normal	110 (46.80%)
B trait	70 (29.78%)
E trait	05 (2.12%)
E B thal	30 (12.76%)
B thal major	20 (8.51%)

IV. Discussion

Standard management of Beta 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 thalassemia patients. However, in developing countries where thalassemia is prevalent and health care resources are limited, these forms of management are usually not easily affordable. So prevention is the most effective and least expensive means of dealing with this problem [32].The present study of CVS clearly supports the above notion. Correct prenatal diagnosis can make the parent to take decision regarding continuation of pregnancy/abortion without any health hazard to the mother

As per table 1 ,in our study, we get 91.4% mothers(215 out of 235) are in the age group of 18-30 yrs. Only 8.51% mothers are in the age group of >30-40 yrs.

Table 2 elaborates the HPLC diagnosis of the parent. Out of total 235 mothers(n=235),200 mothers are beta thal trait(85.10%) and 14.89% are E trait as we found in our study. In case of male,80.85% persons are Thal B trait,12.76% are E trait.10 cases are EB trait and 5 cases are having Hb E disease.

Table 3 elaborates the timing of chorionic villus sampling in mothers with occurrence of complication. Most CVS was performed in 12-14 weeks gestational time(210 out of 235 cases).In 20 cases CVS was

performed after 14wk of gestational period(8.51% cases) .In 5 cases CVS was performed below 12 wk of gestational age(2.12% cases). .No complication was encountered in any of the cases. In several studies the sampling success rate of CVS varied between 97-100%, which increased with advanced gestation[33,34]. In one study the procedure failed to obtain an adequate sample in 0.3% cases[35]. In our study, the sampling success rate was 100% as in all cases chorionic tissue was collected.

Table 4 elaborates the mutant allele status in chorionic villus samples.Here, it is observed from the above data set and result that IVS1-5(G-C) heterozygous are the most dominant genotypes in the Kolkata extended city area of Eastern India based state named West Bengal. HBB is located at chromosome 11p15.4.The assay test for mutation is PCR and sequencing. Assay is against common asian mutation,619 bp deletion and mutant nomenclature is IVS1-5(G>C).In the present study,30 cases(12.76%) come out to be homozygous.80 cases are heterozygous(34.04%).15 cases appears to be compound heterozygous(6.38%).Absence of mutant allele is seen in 110 cases(46.80%).

This mutation leads to formation of premature stop codon in the protein sequence as a result of splice site alteration. The resultant protein is truncated and unable to function effectively.

However there are limitations to this test also. A very small percentage of individuals, who are carriers or have a disease diagnosis, may have a mutation that is not identified by this method. Absence of a mutation, therefore does not eliminate the possibility of positive carrier state or the diagnosis. For carrier testing, it is important to first document the presence of a gene mutation in an affected family member, with subsequent targeted mutation analysis of the same mutation in suspected carriers. Furthermore the error rate of the Taq polymerase for base incorporation is 1 in 6000 bases.

In our present study, CVS study shows normal genotype in 110 out of 235 case(46.80%).70 cases(29.78%) came out to be B thal trait.5 cases came out to be of e trait genotype.30 cases(12.76%) came out to have E B thal genotype and 20 cases(8.51%) cases of B thal Major(table 5). In one study, result of CVS showed that among these 28 cases, were diagnosed as thalassemia major and 9 as thalassemia minor. None of the patients reported for any complication after getting CVS done. In another 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 [36].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% [36].

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% [37].

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 [38]. Post CVS fetal loss has been reported from 1.3-3.0 %.[39,40]. In the above mentioned study fetal loss was not observed in any case after the procedure, the findings comparable with our results.

Inconclusive results may be a problem after CVS. One study reported that 3.4% of CVS had inconclusive result [41]. However, in our study, none of the patient followed up had inconclusive results.(Table 5).

A Chinese study reported that 12% of the fetuses had thalassemia major after CVS[42].Conversely, an Iranian study also demonstrated 18% of fetuses were diagnosed to have beta thalassemia major [43]. Similarly, in our study, 8.51 % of the fetuses were diagnosed to have thalassemia major, consistent with the other Asian studies(table 5)

In this study, we also initiated awareness and screening as well as a genetic counselling program mainly in the districts of Kolkata (WB).Colah et al[44] reported that antenatal screening is acceptable in India; however, awareness generation is still a primary requisite. Several programs, with the aim of preventing homozygous b thalassemia, based on carrier screening and counselling of couples at marriage; preconception or early pregnancy, are operating in several at-risk populations in Mediterranean areas[45,46]. Until gene therapy becomes a reality, the only approaches to the control of hemoglobinopathies are prevention and avoidance. Cao et al.[47] reported reduction of the birth rate of thalassaemia major from 1:250 live births to 1:4,000 in Turkey after execution of comprehensive genetic preventive programme based on voluntary screening and nondirective counselling[48]. Our study also show that prenatal diagnosis by CVS in motivated parent can add appreciable momentum to thalassemia control program in our country.

V. Conclusions

Thalassemia is a prevalent condition in the population we studied. Obstetricians have to play important role by generating awareness among the general population as well as screening of antenatal population for thalassemia besides other routine antenatal investigations. CVS is an acceptable, reliable and safe method of

early diagnosis of fetal thalassemia that helps to prevent birth of the thalassemia-affected babies with considerable reduction of socio-economic burdens. Thalassemia is a genetic disorder, if we really want to eradicate it from our society where about 10% of the population is thalassemia carrier this routine screening is the quintessential way which is cost effective and can be performed within a viable time limit.

Limitation of the Study

Though the State Thalassemia Control Programme is going in the right direction but still quite a few obstacles have to be overcome since there are many social obduracy and village women are still obsessed with prejudices and social stigma. Regionally there are sporadic religious obstacle which is yet to be subverted. Despite having a healthy daughter many families opt for a male child and avid for it resulting some times in toll to the health security, a new thalassemia male child is added. They refuse PND in the hope of begetting a male childAnother limitations in this study were that pregnant women present for antenatal care at varied gestational age and uniformity for screening at specific gestational age could not be maintained.

References

[1]. Cao A, Rosatelli MC, Galanello R (1996) Control of beta-thalassaemia by carrier screening, genetic counselling and prenatal diagnosis: the Sardinian experience. Ciba Found Symp 197(137–51): 151–155

[2]. 2.Sandra Ann Carson (2004) b-Thalassemia minor associated with pregnancy complications. J Watch Women's Health

[3]. Nishi Madan, Satendra Sharma, S. K. Sood, Roshan Colah, (Late) H. M. Bhatia. Frequency of β-thalassemia trait and other hemoglobinopathies in northern and western India. Indian J Hum Genet. 2010 Jan-Apr;16(1):16-25.

[4]. Rueangchainikhom W, Sarapak S, Orungrote N. Chorionic Villus Sampling for Early Prenatal Diagnosis at Bhumibol Adulyadej Hospital. J Med Assoc Thai 2008;91(1): 1-6.

[5]. Michael R, Baun D, Vichinsky E. Thalassemia syndromes. In: Behrman RE, Kliegman RM, editors. Nelson textbook of paediatircs. 18th ed. New York: WB Saunders; 2007; 2033-7.

[6]. Tasleem S, Tasleem H, Siddiqui MA, Adil MM, Rashid Y. Prenatal diagnosis of beta-thalassaemia by chorionic villous sampling. J Pak Med Assoc. 2007 Nov;57(11):528-31.

[7]. Laksanavilai U, Piyamongkol W, Sirichotiyakul S, Tongprasert F, Leuwan S, Srisupundit K. Chorionic villous sampling: experience of 636 cases. J Med Assoc Thai. 2013 Apr;96(4):383-8.

[8]. Han J, Pan M, Zhen L, Yang X, Ou YM, Liao C, et al. Chorionic villus sampling for early prenatal diagnosis: experience at a mainland Chinese hospital. J Obstet Gynaecol. 2014 Jun;9:1-4.

[9]. Jackson LG, Wapner RA,Barr MA. Safety of chorionic villus biopsy. Lancet 1986; 1: 674 5.

[10]. Canadian Collaborative CVS-Amniocentesis Clinical Trial Group. Multicentre randomised clinical trial of chorion villus sampling and amniocentesis. First report. Lancet 1989; 1: 1-6

[11]. Smidt-Jensen S, Hahnemann N. Transabdominal fine needle biopsy from chorionic villi in the first trimester. Prenat Diagn 1984; 4: 163-9.

[12]. Syed S, Shafi F, Yasmeen L, Noreen H and Chaudhri R. Pre- Natal Diagnosis of beta – Thalassemia by Chorionic Villous Sampling. Journal of Rawalpindi Medical College (JRMC); 2009;13(2):83-85 83

[13]. Deka R, Reddy AP, Mukherjee BN, Das BM, Banerjee S, Roy M, *et al*. Hemoglobin E distribution in 10 endogamous population groups of Assam, India. *Hum Hered* 1988; *38* :261-6.

[14]. De M, Halder A, Podder S, Sen R, Chakraborty S, Sengupta B, *et al*. Anemia and hemoglobinopathies in tribal population of eastern and north eastern India. *Hematology* 2006; *11* : 371-3.

[15]. Sharma SK, Mahanta J. Prevalence of hemoglobin variants in malaria endemic north east India. *J Biol Sci* 2009; 9 : 288-91.

[16]. Das MK, Dey B, Roy M, Mukherjee BM. High prevalence of Hb E in 3 populations of the Malda district, West Bengal, India. *Hum Hered* 1991; *41* : 84-8.

[17]. Nadkarni A, Ghosh K, Gorakshakar A, Colah R, Moahtny D. Variable clnical severity of Hb E β-thalassemia among Indians. *J Assoc Physicians India* 1999; *47* : 966-8.

[18]. Panigrahi I, Agwaral S, Gupta J, Singhal P, Pradhan M. Hemoglobin E beta thalassemia: Factors affecting phenotype. *Indian Pediatr* 2005; *42* : 357-62.

[19]. Kulozik AE, Bail S, Kar BC, Serjeant BE, Serjeant GR. Sickle cell -β+ thalassemia in Orissa state, India. *Br J Haematol* 1991; *77* : 215-20.

[20]. Nadkarni A, Wadia M, Gorakshakar A, Kiyama R, Colah RB, Mohanty D. Molecular charaterization of δβ thalassemia and hereditary persistence of fetal hemoglobin in the Indian population. *Hemoglobin* 2008; *32* : 425-33.

[21]. Mohanty D, Colah R, Gorakshakar A. editors. *Report of the Jai Vigyan S & T Mission Project on community control of thalassaemia syndromes- Awareness, screening, geneticcounselling and prevention. A National Multicentric Task Force Study of Indian Council of Medical Research, New Delhi; 2008*. New Delhi: ICMR; 2008.

[22]. Colah R, Surve R, Wadia M, Solanki, Mayekar P, Thomas M, *et al*. Carrier screening for β-thalassemia during pregnancy in India: A 7 year evaluation. *Genet Test* 2008; *12* : 181-5.

[23]. Madan N, Sharma S, Sood SK, Colah R, Bhatia HM. Frequency of β-thalassemia and other hemoglobinopathies in northern and western India. *Indian J Hum Genet* 2010; *16* :16-25.

[24]. Modell B, Petrou M. The problem of hemoglobinopathies in India. *Indian J Haematol* 1983; *1* : 1-5.

[25]. Gorakshakar AC, Colah RB. Cascade screening for β-thalassemia: A practical approach for identifying and counseling carriers in India. *Indian J Community Med* 2009; *34* : 354-6.

[26]. Globin Gene Server: *http://globin.cse.psu.edu/*, accessed on October 5, 2010.

[27]. Edison ES, Shaji RV, Devi SG, Moses A, Viswabandhya A, Mathews V, *et al*. Analysis of β-globin mutations in the Indian population: presence of rare and novel mutations and regionwise heterogeneity. *Clin Genet* 2008; *73* : 331-7.

[28]. Kumar R, Tamhankar PM, Panigrahi I, Dalal A, Agarwal S. A novel β-globin mutation (HBB; c: 107 A>G; or codon 35 β(A>G) at alpha -beta chain interfaces. *Ann Hematol* 2009; *88* : 1269-71.

[29]. Old JM, Varawalla NY, Weatherall DJ. The rapid detection and prenatal diagnosis of β-thalassemia in the Asian Indian and Cyproit populations in the UK. *Lancet* 1990; *336* : 834-7.

[30]. Rao VB, Natrajan PG, Lulla CP, Bandodkar SB. Rapid midtrimester prenatal diagnosis of beta-thalassaemia and other haemoglobinopathies using a non- radioactive anion exchange HPLC technique - an Indian experience. *Prenat Diagn* 1997; *17* : 725-31.
[31]. Dehury S,Purohit P,Meher S,Das K,Patel S.Compound heterozygous state of Beta thalassemia with IVS1-5(G>C) mutation in eastern India.Rev Bras Hematol Hemoter.2015;37(3):202-6.
[32]. Cao A, Galanello R. Effect of consanguinity on screening for thalassemia. N Engl J Med. 2002; 347(15):1162-
[33]. Laksanavilai U, Piyamongkol W, Sirichotiyakul S, Tongprasert F, Leuwan S, Srisupundit K. Chorionic villous sampling: experience of 636 cases. J Med Assoc Thai. 2013 Apr;96(4):383-8.
[34]. Choudry A, Masood S, Ahmed S. Feasibility and safety of transabdominal Chorionic Villus Sampling. J Ayub Med Coll Abbottabad. 2012 Jan-Mar;24(1):38-43.
[35]. Han J, Pan M, Zhen L, Yang X, Ou YM, Liao C, et al. Chorionic villus sampling for early prenatal diagnosis: experience at a mainland Chinese hospital. J Obstet Gynaecol. 2014 Jun;9:1-4.
[36]. Tasleem S, Tasleem H, Adil M, Siddiqui MS, Yasmin Rashid. Prenatal diagnosis of ß-Thalassaemia by Chorionic Villous Sampling. JPMA 2007; 57 (11):528-531.
[37]. Asnafi N, Akhavan Niaki H. Pregnancy outcome of chorionic villus sampling on 260 couples with betathalassemia trait in north of Iran. Acta Med Iran. 2010 May-Jun; 48(3):168-71.
[38]. Nasreen K, Azim W and Liaqat J. Beta-thalassemiainstitution based analysis of ethnic and geographic distribution, effect of consanguinity and safety of chorionic villus sampling as a diagnostic, tool for pre-natal diagnosis in selected patients. Pakistan Armed Forces Medical Journal 2010;4
[39]. Rahim MK, Sabih D, Shahid, Baig SM, Azhar A and Bakhtiar M.Prenatal diagnosis of _-thalassemia at minar, multan Nishtar Medical Journal 2009;1 (2):4-9
[40]. Brun JL, Mangione R, Gangbo F, Guyon F, Taine L, Roux D, et al. Feasibility, accuracy and safety of chorionic villus sampling: a report of 10741 cases. Prenat Diagn 2003; 23: 295-301. 11.
[41]. Laksanavilai U, Piyamongkol W, Sirichotiyakul S, Tongprasert F, Leuwan S, Srisupundit K. Chorionic villous sampling: experience of 636 cases. J Med Assoc Thai. 2013 Apr;96(4):383-8.
[42]. He S, Li D, Lai Y, Zhang Q, Que T, Tang Y, et al. Prenatal diagnosis of β-thalassemia in Guangxi Zhuang Autonomous Region, China. Arch Gynecol Obstet. 2014 Jan;289(1):61-5.
[43]. Asnafi N, Akhavan Niaki H. Pregnancy outcome of chorionic villus sampling on 260 couples with beta-thalassemia trait in north of Iran. Acta Med Iran. 2010 May-Jun;48(3):168-71.
[44]. Colah R, Surve R, Wadia M, Solanki P, Mayekar P et al (2008) Carrier screening for beta-thalassemia during pregnancy in India: a 7-year evaluation. Genet Test 12(2):181–185
[45]. Cao A, Rosatelli MC, Monni G, Galanello R (2002) Screening for thalassemia: a model of success. Obstet Gynecol Clin North Am 29(2):305–328
[46]. Cao A (2002) Carrier screening and genetic counselling in betathalassemia. Int J Hematol 763(Suppl 2):105–113
[47]. Cao A, Rosatelli MC, Galanello R (1996) Control of beta-thalassaemia by carrier screening, genetic counselling and prenatal diagnosis: the Sardinian experience. Ciba Found Symp 197(137–51): 151–155
[48]. Sheiner Eyal, Levy Amalia, Yerushalmi Ronit, Katz Miriam (2004) Beta-thalassemia minor during pregnancy. Obstet Gynecol 103:1273–1277

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