Prenatal Diagnosis of Thalassaemia

Genetics Resource Centre (GRC)

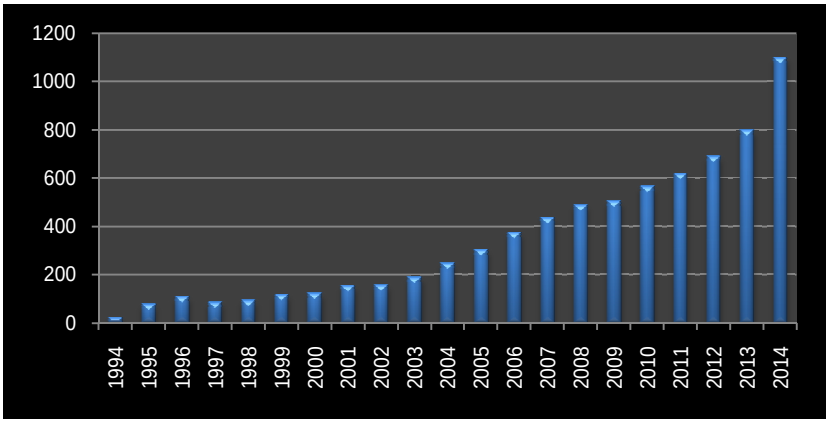
Prenatal diagnosis is done to know about the status of disease in fetus before it is born. It is usually done to know about a genetic disorder or congenital malformation in the fetus. The basic objective is to provide an informed choice to the parents. If the fetus is healthy then the parents are reassured. When the fetus has a serious genetic abnormality or malformation then the parents have the choice to either terminate the pregnancy or to accept the child with genetic abnormality.

Prenatal diagnosis can be done by either invasive or non-invasive methods. The commonest non-invasive method is by ultra-sound examination. Several congenital malformations may be suspected as early as 12 weeks of gestation and confirmed by 18 weeks. A more recent addition to the list of non-invasive prenatal diagnosis is by testing of fetal DNA abnormalities in the maternal blood. The invasive method of prenatal diagnosis involves fetal sampling by Chorionic Villus Sampling (CVS) or amniocentesis. The fetal sample may be tested for a large number of single gene disorders or chromosomal defects.

GRC offers comprehensive facility for invasive prenatal diagnosis of many common single genetic disorders like thalassaemia, cystic fibrosis, Duchenne Muscular Dystrophy and trisomies 13, 18 & 21. GRC provides comprehensive facility under one roof for fetal sampling and the genetic testing.

Thalassaemia major is a difficult and expensive disease to treat. The births of children with thalassaemia major can be prevented by early prenatal diagnosis and selective termination of the affected pregnancies. The first step in prenatal diagnosis involves identification of the Beta thalassaemia mutation in the father and the mother. In the next step the fetal sample is taken and is tested for the parent's mutations. It usually takes about a week to get the result. The error rate in prenatal diagnosis is around 0.5%.

In 1994 Pakistan became the first Muslim country to start a clinical service for prenatal diagnosis of thalassaemia. The fetal sample was taken by Dr. Yasmeen Rashid at Lady Wellington Hospital Lahore and its DNA testing was done by Dr. Suhaib Ahmed at the Armed Forces Institute of Pathology (AFIP), Rawalpindi. Since then over 8,000 prenatal diagnoses for thalassaemia have been done in Punjab and Khyber Pakhtunkhawa. In the last couple of years over 90% of the workload of prenatal diagnosis of thalassaemia has shifted to GRC. In 2014 GRC did over 1000 prenatal diagnoses for thalassaemia. It forms almost 80% of the total number of prenatal diagnoses for thalassaemia done in Pakistan.



Prenatal diagnosis has become a popular choice for the couples having children with genetic disorders who wish to have healthy children. However, financial constraints and lack of awareness about availability of prenatal diagnosis amongst the medical community and the affected parents are the two most common reasons for underutilization of prenatal diagnosis in Pakistan.

Who needs prenatal diagnosis for thalassaemia?

Prenatal diagnosis is required by the couples who already have a child affected by thalassaemia. It is also advisable for the couples who do not have previously affected child but who both have thalassaemia trait. If in a couple one parent has thalassaemia trait and the other parent is normal then they do not require prenatal diagnosis. Thalassaemia carrier testing is technically difficult therefore when one of the parents has thalassaemia trait the other parent must be tested with best possible means to ensure detection of typical as well as atypical (silent) forms of thalassaemia.

What are the chances of error in prenatal diagnosis?

The experience of over 8000 prenatal diagnoses done at AFIP and GRC has shown that the chance of error in prenatal diagnosis is around 0.5%.

What are the limitations in prenatal diagnosis of thalassaemia?

Prenatal diagnosis of thalassaemia is possible in nearly all of the couples. Occasionally we may come across a couple in whom the disease causing mutation is not identified. In such couples the diagnosis can be done by linkage analysis or genomic sequencing. More commonly we come across a situation in which the previously affected child is wrongly labeled as thalassaemia. If CVS is done in such a couple then we are unable to complete the test because the request was wrongly initiated. It is therefore important that before requesting prenatal diagnosis for thalassaemia or any other disease the previously affected child's illness must be correctly identified.

Can the CVS done at another place be sent to GRC for testing?

Yes the CVS can be done at any place and the sample can be sent to GRC for testing. The sample should be collected in sterile normal saline. It should be dispatched without unnecessary delay so that it reaches GRC within 24 hours of collection. The sample should be accompanied by request form clearly showing the indication and the blood samples of the parents.

What samples are required?

In addition to the fetal sample we require 2 ml blood in EDTA of the father, the mother and the previously affected child (if any). If the father's sample is not available for some reason then the test can be completed by obtaining the affected child's blood. The test cannot be completed if the sample of the father as well as the affected child is not available.

Is termination of pregnancy for genetic disorders permissible in Islam?

Most religious scholars in Pakistan, including Molana Mohammad Taqi Usmani, agree that Islam permits termination of pregnancy for a serious genetic disorder in the fetus provided it is done before 120 days (17 weeks) of gestation.