

Genetic Research Centre (GRC) is the only permanent Centre of Indian Council of Medical Research catering to the needs of the families having children with mental retardation, birth defects, thalassaemia and reproductive loss. The Genetic Centre aims to reduce fetal mortality and under five mortality by appropriate genetic counseling and prenatal diagnosis of common genetic disorders. It also focuses on adolescent

health. Over the last year we have concentrated our efforts on the following areas:

1. Genetic polymorphism in MTHFR in Neural Tube Defects.
2. Molecular characterization of Fragile X syndrome.
3. Preimplantation Genetic Diagnosis for aneuploidy screening

10.1. Genetic Polymorphism in MTHFR Gene

Principal Investigator	:	Zareen M. Patel
Project Associates	:	Shyla Menon, Rashmi Adhia, Aruna D'souza, Shiny Babu
Duration	:	2005-2008

Neural Tube Defects (NTD) are serious birth defects, which develop during the third and fourth post conceptional week due to failure of embryonic neural tube to close. The etiology of NTD is multifactorial with multiple genetic and environmental modifiers. The prevalence of NTD in India is 3-4 /1000 births while worldwide it is reported to be 1-2 /1000 births.

There are several genetic polymorphisms that are associated with defects in folate and Vitamin B12 dependent homocysteine metabolism. Many of these SNPs have proved useful as markers to identify certain phenotypes. Certain SNPs in MTHFR (C677T, A1298C) have been associated with a variety of multifactorial disorders including Neural Tube Defects.

The results on ICMR study and MRC trial on NTDs highlighted the role of preconceptional folic acid (4 mg) in cases at risk for the disease. However it gave protection in 70 percent of the cases. 30 percent of cases of NTD did not respond

to administration of folic acid. Therefore, as an extension of this MTHFR gene polymorphism has been studied in mothers who are non-responders to folic acid.

The aims and objectives of the study were to screen MTHFR gene polymorphism in normal population, in a cohort of NTD patients who are non-responders to folic acid and to study genetic heterogeneity with respect to the two loci (C667T and A1298C) as risk factors.

For C667T, a PCR product of 198 bp was obtained. On digestion with Hinf3 it yields products of 175bp and 23bp in presence of heterozygosity (C>T). Data on 320 subjects screened revealed (80%) were wild type C/C, while (20%) CT showed heterozygous C/T. No homozygous TT was found.

The study can help in genetic counseling and can also help highlighting in the role of MTHFR gene in the etiology of NTD and other genetic disorders.