The clinical significance of Non-invasive Prenatal Genetic Screening (NIPT) in Pregnancy -A Single Centre Experience

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BACKGROUND & AIM

NIPT test is used to screen the fetal abnormalities due to the presence of chromosomal aberrations in the developing foetus. NIPT is next generation sequencing based technique which uses the cell-free fetal DNA (cfDNA) extracted from maternal blood.

- **Aim**: We present a single-centre study of 376 singletons and 13 twin gestations (10 plus to 20weeks) screened in the age group of (22-48yrs) for chromosomal abnormalities using NIPT test.
- The **clinical indications for patients** who underwent NIPT test were increased risk of trisomies, increased nuchal translucency or increased risk in biochemical markers investigations, previous child born with Down syndrome and advanced maternal age. The patients were referred after sonographic and biochemical investigations by the concerned clinician. The clinical history and family history of any genetic disease or any other disease were noted.

METHODS

- Cell free DNA was extracted and concentration was measured using Qubit dsDNA quantification assay kit. NIPT protocol using NGS was performed as per the manufacturer's instructions using Illumina/Thermo platform and sequencing data was analyzed through the analysis run with specific pipeline version. The written informed consent forms were obtained from all the patients. The results were interpreted using software and Z score in the results.

RESULTS

The higher value of the Z-score confirms the risk of presence of aneuploidy. The z-score for chromosomes **13, 18, and 21** is between -6<Z score<2.8 shows low risk pregnancy. For chromosome **1-22**, low risk lies in the reference range of -6<Z score<6. The average fetal fraction was 12.11 in all pregnancy cases. **The high-risk cases (n=5)** were genetically counseled and further invasive tests Quantitative fluorescent polymerase chain reaction (QFPCR) and Chromosomal Microarray (CMA) using amniotic or chorionic villi samples were recommended by the clinician with regular clinical follow-up

Table 1 Demographic and clinical characteristics/indications of High Risk Cases

Case ID	Fetal Fraction	Clinical Indications	Gestation	Type of Pregnancy	Chromosomal Aneuploidy detected in NIPT
CHR01	12.79%	Aneuploidy screening in view of high risk of Trisomy 21 (1:5) in quadruple marker	20 weeks and 2 days	Singleton	Trisomy 21 Genetic counselling and clinician's recommendations of QFPCR and CMA with regular followup
CHR02	11.02%	Advanced maternal age; Trisomy risk in maternal serum screening	15 weeks and 2days	Singleton	Trisomy 3 Genetic counselling and clinician's recommendations of QFPCR and CMA with regular follow-up
CHR03	11.94%	Aneuploidy Screening; Increased NT-2.2mm,	17 Weeks 04 Days	Singleton	Trisomy 21 Genetic counselling and clinician's recommendations of QFPCR and CMA with regular follow-up
CHR04	8.41%	USG indicative of increased NT3.5mm Advanced maternal age.	14 weeks	Singleton	Trisomy 13 Genetic counselling and clinician's recommendations of QFPCR and CMA with regular follow-up
CHR05	8.3%	Advanced maternal age	10 weeks and 5 Days	Singleton	Trisomy 21 Genetic counselling and clinician's recommendations of QFPCR and CMA with regular follow-up

DISCUSSION & CONCLUSION

The NIPT is a **screening test,** not a diagnostic test. PCPNDT act (1994) is followed for NIPT in India (1). Management of a patient with a high-risk pregnancy is multidimensional and supportive with genetic counselling to reduce the psychological distress and anxiety (2). This test benefits the patients by omitting the need of undergoing painful invasive procedures and helps in clinical decision making. Our study indicates that NIPT is an effective approach to rule out chromosomal anomalies at an early stage in prenatal screening so that early interventions can be planned for high risk pregnancy as per the recommendations of American College of Medical Genetics and Genomics (**ACMG) statement, 2013**. NIPT is a very safe and effective screening test currently used as a second-tier test for high-risk pregnancy in India (2,3).

References:

1. Pre-Conception and Pre-Natal Diagnostic Techniques (Prohibition of Sex Selection) Act (PCPNDT Act 1994)
2. American College of Obstetricians and Gynaecologists' Committee on Practice Bulletins—Obstetrics; Committee on Genetics; Society for Maternal-Fetal Medicine. Screening for Fetal Chromosomal Abnormalities: ACOG Practice Bulletin, Number 226. Obstet Gynecol. 2020 Reference three
3. Gregg AR, et al. ACMG statement on noninvasive prenatal screening for fetal aneuploidy. Genet Med. 2013;15(5):395–398.