ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 8, Issue – 3, June – 2023 , Page No. : 124 – 127

Prenatal Screening and Diagnosis of genetic disorders - Need of the hour

[1]Dr. Sanjeev Sharma, Indraprastha Apollo Hospital, New Delhi.

[2]Dr. Kunal Sharma, Dr. Baba Sahib Ambedkar Medical College and Hospital, Delhi.

[3]Dr. Kapil Sharma, SGRD Medical College, Baba Farid University of Health Sciences.

[4]Dr. Vandana Sharma, Gene strings Diagnostics, New Delhi.

Corresponding Author: Dr. Sanjeev Sharma, Indraprastha Apollo Hospital, New Delhi.

Citation this Article: Dr. Sanjeev Sharma, Dr. Kunal Sharma, Dr. Kapil Sharma, Dr. Vandana Sharma, "Prenatal Screening and Diagnosis of genetic disorders - Need of the hour", IJMSIR- June - 2023, Vol – 8, Issue - 3, P. No. 124 – 127.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Due to the increasing burden of genetic diseases caused by advanced maternal age, consanguineous marriages, and lifestyle factors prenatal genetic testing plays a vital role.

The prenatal genetic tests are of two types screening and diagnostic. Prenatal screening tests such as NIPT evaluate a pregnancy with high risk or low risk. The genetic diagnosis tests such as PGD are used to detect any chromosomal aneuploidy or any monogenic con dition inherited in the developing fetus.

Opting for a genetic test depends on the clinical indication of the patient or couple planning for pregnancy. The major clinical indications are advanced maternal age, family history of a disease, consanguineous marriage, previous pregnancy with any genetic ab normality, or a previous child with an intellectual dis order or any other disorder such as thalassemia, etc. The availability of next-generation sequencing techniques has made it possible to evaluate the whole genome of a developing fetus.

However, their implementation is associated with ethical considerations and following the recommended guidelines in reprogenetics medicine.

Keywords: Advanced Maternal Age, Consanguineous, Screening, Diagnostic, Pregnancy, Next Generation Sequencing, Genome

Introduction

A healthy pregnancy with the outcome of a healthy baby is the desired dream of every couple. Due to advanced lifestyle and many other factors clinical and environ mental people opt for delayed pregnancy and it usually crosses 35 years which falls under advanced maternal age.

The chromosomal abnormalities in a newborn are a very traumatic situation for the parents as well as in later ages of a child to deal with. More than 3% of pregnancies are identified with structural anomalies in the fetus with a burden of genetic disorders in newborns such as Down syndrome, beta-thalassemia, and neural tube defects in India.

Approximately 21,400 children with Down syndrome, 9000 with beta-thalassemia and 5200 with sickle cell

disease have been reported to be born in India every year [1,2]. There are certain screening tests done in India which include triple test, quadruple test, and first-trimester double-marker test with or without nuchal translucency (NT). The detection rate for these serum screen tests with NT is 82 per % and for quadruple tests is 80 % [3].

This review article is focused to provide brief information about the available screening and diagnostic tests to be considered to make correct decisions timely and for a good outcome of pregnancy.

With increasing awareness and availability of whole genome sequencing at low cost various noninvasive and invasive prenatal genetic screening and diagnosis techniques have been in use in current clinical practice. These include cytogenetic tests such as karyotyping and FISH, genetic screening and diagnosis tests e.g., NIPT, chromosomal microarray, preimplantation genetic screen ing, career sequencing, and many others using Next generation sequencing techniques.

Karyotype is based on culture, harvesting, giemsa staining (G-banding) and microscopic evaluation of blood cells and is used to see the copy number variants (CNVs) and balanced chromosomal abnormalities as the mainstay of cytogenetic testing from decades. FISH includes hybridization of samples and labeled with fluorescent probes and is used to diagnose many types of chromosomal abnormalities in patients.

Microarray technology involves restriction digestion of a sample fragmentation labeling, hybridization, staining, and washing of arrays which are further scanned and analyzed. Microarray has enabled access to sub micro scopic CNVs, deletions, and duplications. The test is recommended for mental retardation and autism as a first-tier test.

NIPT is a genetic screening test that uses cell-free fetal DNA extracted from fetal cells in maternal blood circulation and informs whether the pregnancy is at low or high risk for chromosomal aneuploidies e.g., Trisomy 13, Trisomy18, Trisomy 21, and sex chromosomal aneuploidies. NIPT test includes low-coverage massively parallel whole-genome sequencing of circulating cell-free fetal (ccf) DNA extracted from pregnant women's blood plasma. Total ccf DNA is sequenced, and the reads are aligned to reference the human genome and analyzed further. A proportional score with specific sensitivity and specificity of each chromosome can be calculated ploidy status of chromosomes is reported. The test is specifically designed for Trisomy 21, trisomy18, and Trisomy13 and sex chromosomes aneuploidies.

NIPT is a safe, easy, noninvasive test and does not carry the risk of miscarriage which is associated with amniocentesis and CVS. In NIPT the high-risk pregnancy is clinically advised to opt for AF and CVS tests such as Microarray and others as required by the clinician.

Whole exome sequencing is used to sequence the protein-coding regions or exons using NGS technique and is used for molecular diagnoses of causal genetic variation in foetuses with structural anomalies in com parison with conventional cytogenetic methods.

Quantitative fluorescent polymerase chain reaction (qf-PCR) is performed using a set of str markers for chromo somes 13, 18, 21, x, and yon amniotic fluid, blood, or chorionic villi samples. A carrier sequencing test is done if a patient or anyone partner of the couple has a family history of a genetic disorder e.g., thalassemia, sickle cell anemia, or cystic fibrosis — they belong to an ethnicity that has a higher risk of a particular condition the carrier sequencing determines the status whether the child will be born with the disease or not.

Preimplantation genetic screening/PGS for aneuploidies is a test used to identify whether the child is normal or abnormal. In the PGS test the embryo biopsy is done on

day 5 or day 6, 5-7 trophectoderm cells are taken under instructed lab conditions in a media and subjected to NGS. The trophectoderm represents the genetic makeup of a developing fetus and it is an invasive test done in high-risk pregnancies and during IVF treatment if the mother or the couple has a previous clinical history or any clinical indication for the test to be done e.g., if the mother is older than 35 years. The fetus's genome is sequenced and aligned with the normal human genome and if any chromosomal abnormality is observed the embryo is not implanted after informing the results to the patient. The preimplantation genetic diagnosis or PGD test is done for rare or monogenic conditions is done if the patient has any previous history of that disorder running in the family and the fetus is saved with prior testing and diagnosis.

Newborn screening or NBS is another test in clinical practice which is used a baby's blood to detect abnormalities that may cause certain health conditions such as inborn errors of metabolism. This is important to diagnose in the early phase as treatment can be initiated to avoid further complications.

Pretest and post-test counseling of pregnant women plays an important role in genetic diagnosis and screening. These tests are done as per ACMG (The American College of Medical Genetics and Genomics) and ACOG [4,5] (The American College of Obstetricians and Gynecologists) guidelines and in India PCPNDT act regulates the genetic tests and sex determination is not allowed because of the increasing incidence of abortion of female fetus [6].

Patient consent is of utmost importance for any clinical decision-making. They should be made to understand all the genetic test results associated with pros and cons. This will help in decreasing the incidences of common genetic disorders and congenital disabilities.

Conclusion

Genetic disorders are a lifelong problem that deteriorates the quality of life of an individual and its associated persons economically, physically, mentally, and socially. There are several prenatal screening and diagnosis tests available but awareness about the requirement of tests to be done, pre-and post-test counseling, and approaching the physicians for these tests at the right gestational age is very crucial.

Sometimes there is confusion regarding which prenatal screening test to be done in which case, due to the availability of novel and advanced techniques com mercially available in the market. The lacunae in the system is due to the absence of definite guidelines and awareness about these tests in the country.

The requirement is to create a high end technically sound clinical infrastructure with NGS technology and spread mass-scale awareness for important prenatal genetic tests to be adopted and to be made available to the public in a cost-effective way with pre and posttest counseling. This will definitely help to reduce the burden of genetic disorders in India.

References

1. Verma IC, Saxena R, Kohli S. Past, present & future scenario of thalassaemic care & control in India. Indian J Med Res. 2011;134:507–21.

2. Phadke SR, Puri RD, Ranganath P. Prenatal screening for genetic disorders: Suggested guidelines for the Indian Scenario. Indian J Med Res. 2017 Dec;146(6):689-699.

3. Benn P, Borrell A, Chiu R, Cuckle H, Dugoff L, Faas B, et al. Position statement from the Aneuploidy Screening Committee on behalf of the Board of the International Society for Prenatal Diagnosis. Prenat Diagn. 2013;33:622–9.

4. https://www.news-medical. net/ news/ 2022 1216/ ACMGs-new-guideline-strongly-recommends-the-use-of – non invasive-prenatal-screening-for-fetal-chromosome-abnormalities.aspx

5. https://www.acog.org/womens-health/faqs/prenatal-genetic-screening-tests

6. https://www.indiacode.nic.in/bitstream/123456789/8399/1/pre-conception-pre-natal-diagnostic-techniques-act-1994.pdf