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UPDATE ON THE PRENATAL GENETIC SCREENING 2023

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Abstract:

Background: *The benefits of prenatal genetic screening include the ability to assess the risk of genetic disorders, with NIPTs offering high detection rates and low false-positive rates. Recent advances, such as AI algorithms, promise enhanced accuracy and personalized prenatal care. However, risks, such as the potential for parental pressure to terminate pregnancies based on genetic findings, must be carefully considered.*

Objective: *To highlight technological advancements that enhance accuracy, reduce the risk of miscarriage, and revolutionize screening for chromosomal aneuploidies besides addressing challenges and limitations*

Method: *Comprehensive research of prenatal genetic screening. PUBMED and Google Scholar search engines were the main databases used for the search process, and articles were collected from 2000 to 2023. The terms used in the search were: Prenatal, Genetic, and screening.*

Conclusion: *prenatal genetic screening has undergone transformative changes with the advent of advanced technologies, such as next-generation sequencing (NGS) and non-invasive prenatal tests (NIPTs), offering more accurate and comprehensive screening options. These developments, including Chromosomal Microarray Analysis (CMA) and cell-free fetal DNA (cffDNA) testing, have significantly improved the detection of chromosomal aneuploidies while reducing the risk of miscarriage associated with invasive procedures.*

Keywords: *Prenatal, Genetic, screening.*

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INTRODUCTION:

Prenatal genetic screening has undergone significant changes over the years. The introduction of next-generation sequencing (NGS) has revolutionized the field, allowing for more accurate and comprehensive screening. Non-invasive prenatal tests (NIPTs) such as Chromosomal Microarray Analysis (CMA) and cell-free fetal DNA (cffDNA) have emerged as fundamental clinical approaches for pregnant women's screening [1]. These tests have reduced the risk of miscarriage associated with invasive techniques and have improved the detection of chromosomal aneuploidies [2]. Prenatal exome sequencing (pES) and genome sequencing (pGS) have also become important tools in prenatal genetic diagnosis, providing incremental diagnostic yield for fetuses with structural birth defects [3]. The use of cell-free DNA (cfDNA) testing has further expanded prenatal screening, offering high accuracy for identifying genetic conditions like trisomy 21, 18, and 13 [3]. However, it is important for providers to stay updated on the research support behind each type of genetic test and for professional organizations to adapt their testing approaches accordingly

Prenatal genetic screening poses several challenges and limitations. Clinicians struggle to keep pace with the rapidly growing availability and accessibility of these tests, making it difficult to provide accurate and up-to-date information to expectant and new parents [4]. The introduction of advanced technologies like chromosomal microarray analysis (CMA) and non-invasive prenatal screening (NIPS) has complicated decision-making regarding the most appropriate testing for each pregnancy [5]. Uncertain results, such as variants of unknown or uncertain significance and secondary findings, present a key challenge in interpreting genetic diagnoses made during pregnancy [6]. Additionally, the wide range of testing options available, including ultrasonography, maternal serum analytes, and cell-free DNA, requires discussions with multiple specialists and can make pre- and posttest counseling complex [7]. These challenges highlight the need for ongoing research and education to address the limitations of prenatal genetic screening and ensure that clinicians can effectively navigate the complexities of these tests in the clinical setting.

BENEFITS AND RISKS:

Prenatal genetic screening offers several benefits and risks. The benefits include the ability to assess the risk of the fetus being affected by a genetic disorder, such as Down syndrome, and the detection of a broad range of genetic disorders [8]. Noninvasive prenatal screening using cell-free DNA (cfDNA) offers a higher detection rate for trisomy 21 with a low false-positive rate [9]. Additionally, the use of deep neural networks in prenatal screening algorithms has shown promising results in detecting high-risk fetuses affected by genetic diseases [10]. However, there are also risks associated with prenatal genetic screening. These include the potential for pressure on parents to terminate pregnancies based on the identification of genetic conditions [11]. Furthermore, the accuracy and utility of some testing options, particularly for rare conditions, need further research and validation [12]. It is important for healthcare providers to provide pretest and post-test counseling to patients, discussing the benefits, limitations, and nature of the screening tests, and referring patients for genetic counseling when appropriate.

TYPES OF PRENATAL GENETIC SCREENING:

Prenatal genetic screening can be divided into different types. One type is ultrasonography, which uses ultrasound imaging to assess the fetus for any abnormalities. Another type is maternal carrier screening, which evaluates the mother's carrier status for specific genetic disorders. Maternal serum assays are also used for screening, which involve analyzing specific biochemical markers in the mother's blood to detect aneuploidy. Additionally, there is a newer type of screening called cell-free fetal DNA (cffDNA) testing, which involves analyzing fragments of fetal DNA in the mother's blood to detect aneuploidy, microdeletion, and copy number variants. This technology has revolutionized prenatal screening due to its ease of administration and accuracy for certain genetic conditions [3,13].

Recent advances in prenatal genetic screening include the development of non-invasive techniques such as non-invasive prenatal tests (NIPTs) and the use of artificial intelligence (AI) algorithms. NIPTs, such as Chromosomal Microarray Analysis (CMA) and cell-free fetal DNA (cffDNA) testing, have revolutionized the screening methods for chromosomal aneuploidies, reducing the risk of miscarriage associated with invasive procedures [2,14]. AI algorithms have been used to predict embryo ploidy status in in vitro fertilization (IVF) procedures, offering a non-invasive alternative to the current gold standard, preimplantation genetic testing for aneuploidy (PGT-A) [6]. These algorithms have shown promising results in predicting ploidy status using embryonic images and clinical parameters, and the integration of AI into microscopy equipment and Embryoscope platforms is expected to facilitate non-invasive genetic testing [2]. Additionally, advances in sequencing of

circulating cell-free DNA have transformed obstetric care, reducing the need for invasive diagnostic procedures like amniocentesis for genetic disorders [15]. Overall, these advancements in prenatal genetic screening have the potential to improve detection rates, reduce risks, and enhance personalized prenatal care [Table1].

	Ultrasound	Amniocentesis	Chorionic Villus Sampling (CVS)	Cell-free fetal DNA (cffDNA)
Establishment	1960s	1960s	1980s	2011
Type	Screening	Diagnostic	Diagnostic	Screening
Uses	To identify physical sign of genetics problems	Identifies chromosomal abnormalities, inherited disease, and nervus system defects	Identifies chromosomal abnormalities and inherited diseas	Assess the risk of chromosomal abnormalities
Procedure	A probe transmits high-pitched sound waves into the belly.	A needle through the belly extracts amniotic fluid.	A needle through the belly or a catheter through the cervix suctions cells from the placenta	A blood sample is taken from the mother
How it works	measures the nuchal fold thickness	Analyze the fetal cells in the amniotic fluid	Analyze the placental cells	Analyze fetal DNA in the maternal blood
Performed at	11-14 weeks	15-20 weeks	10-12 weeks	10 weeks or later
Risk	None invasive	Miscarriage .001%	Miscarriage .002%	None invasive
Accuracy	Abnormal test must be confirmed with diagnostic test.	99%	98-99%	99% of down syndrome. Up to 50% of +ve are false +ve.

Table: The difference between prenatal genetic screening[16,17]

Cell-free fetal DNA (cffDNA) testing is a non-invasive prenatal diagnostic test that involves the detection and analysis of fetal DNA in the mother's blood. It has been used for various purposes, including prenatal sex determination, screening for fetal pathologies, and paternity testing. CffDNA can be obtained from maternal plasma and has been shown to be a reliable source of fetal genetic material. The testing is based on the presence of fetal DNA fragments in the maternal blood, which can be isolated and analyzed using molecular techniques such as Next Generation Sequencing (NGS). CffDNA testing has been validated for its diagnostic value in screening for chromosomal abnormalities and monogenic diseases in the fetus. It offers a non-invasive alternative to invasive procedures such as amniocentesis and chorionic villus sampling, reducing the risk of complications for both the mother and the fetus [18-20].

LIMITATIONS OF CURRENT PRENATAL GENETIC SCREENING:

Current prenatal genetic screening has several limitations. One limitation is the risk of miscarriage associated with invasive sampling methods such as chorionic villus sampling and amniocentesis [4,5]. Another limitation is the delay in result preparation with standard screening tests [4]. Additionally, there are concerns about the accuracy and diagnostic scope of screening tests, as well as the potential for clinically uncertain findings [21]. Furthermore, the accessibility and availability of these tests have grown exponentially, making it challenging for clinicians to keep pace [22]. It is important for clinicians to be aware of the benefits and limitations of prenatal genetic screening and to offer comprehensive pretest and posttest genetic counseling to expectant parents.

CONCLUSION:

In conclusion, prenatal genetic screening has undergone transformative changes with the advent of advanced technologies, such as next-generation sequencing (NGS) and non-invasive prenatal tests (NIPTs), offering more accurate and comprehensive screening options. These developments, including Chromosomal Microarray Analysis (CMA) and cell-free fetal DNA (cffDNA) testing, have significantly improved the detection of chromosomal aneuploidies while reducing the risk of miscarriage associated with invasive procedures.

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