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Cell free fetal DNA (cffDNA): An excellent method for early non-invasive prenatal diagnosis

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Objective of antenatal care is to ensure a normal pregnancy culminating in delivery of healthy baby and healthy mother. A quality antenatal care aims at identification and screening of high risk cases and prevention, early detection and timely management of complications. Prenatal screening and diagnosis is routinely offered in antenatal care and is considered to be important in antenatal counseling about the continuation of pregnancies affected by chromosomal or genetic disorders. Prenatal testing is now part of established obstetric practice in countries where facilities are available. It has two categories, Prenatal screening which is done in all antenatal women to determine risk of having Down syndrome and Prenatal diagnosis which is done in high risk cases to provide a definitive diagnosis of a particular disorder.

Diagnostic testing is done by chorionic villus sampling between 11 to 14 weeks gestation or amniocentesis after 15 weeks. This approach to obtaining fetal DNA currently provides the gold standard test for prenatal diagnosis. However, these invasive procedures carry a risk of miscarriage of around 1%.[(1)] To reduce this risk of miscarriage and allow earlier testing Search for a reliable and convenient method for non-invasive prenatal diagnosis has long been going on. Some researchers have investigated using fetal cells obtained from the cervical mucus[(2)] but most research has focused on detection of genetic material from the fetus present in the maternal circulation.

Cell-free fetal DNA in maternal blood represents extracellular DNA, originating from trophoblastic cells. It is probably a product of apoptosis (programmed cell death), resulting in fragmentation and ejection of chromosomal DNA from the cell.[(3)] However, majority of cell-free DNA in maternal blood is of maternal origin with cell-free fetal DNA representing only 3% to 6% of the total cell-free circulating DNA. Cell free fetal DNA consists predominantly of short DNA fragments rather than whole chromosomes. In the maternal blood fetal DNA can be detected from the 4th week of gestation and the concentration increases with gestational age.[(4-5)] As against fetal cells, cffDNA is rapidly cleared from the maternal circulation with a half life of 16 min and is undetectable 2 hour after delivery.[(6)] Although the majority of work to date has focused on cffDNA, both types of cffNA, i.e. DNA and RNA, could potentially be used for the NIPD of specific genetic characteristics of the fetus. Clinical applications of cffDNA analysis in prenatal screening include aneuploidy, Rh D status, fetal sex determination, single gene disorder, and diseases associated with abnormal placentation.

Ethical Issues

As the test is simple and can be used very early without any risk to the mother, cffDNA can be used for fetal sex determination and can be misused in a country like India (because of the wide preference of a male child). In near future, this technology may be applied to detect other genetic traits also present in the mother, for e.g. BRCA1/2 mutations in breast cancer, which may be possibly diagnosed prenatally using cffDNA. The addition of tests for increased possibility of developing adult-onset diseases is ethically more risky than testing for inherited or congenital disorders, because there is a possibility that the disorder may never develop.

In conclusion, we can say that early NIPD of the genetic status of a fetus can be detected from 4 weeks gestation by analysis of cffDNA in maternal circulation which is highly specific and sensitive in detection of aneuploidy, Rh status, single gene disorder, and sex linked diseases. High levels of cffDNA can predict disorders like preeclampsia and measures to prevent complications can be initiated early. Further research in analysis of cffDNA will be useful in many diagnostic areas.

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