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Review Article

Overview of Inception and Viability of Genetic Amniocentesis

Sohail S[1]*, Riaz R[2], Majid A[2], Ali M[3], Sohail F[4], Saadat S[2], Rana H[2] and Hassan U[5]

[1]MS Microbiology, University of Central Punjab, Pakistan
[2]MBBS, Allama Iqbal Medical College, Pakistan
[3]MS Biotechnology, University of Central Punjab, Pakistan
[4]BS Microbiology, Government College University, Pakistan
[5]MBBS, King Edward Medical University, Pakistan

***Corresponding author:** Shehreen Sohail, MS Microbiology, University of Central Punjab, Pakistan

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Abstract

Clinical procedures that took both time and effort in terms of prior diagnosis are being aided by technology and significant advancements in recognizing and predicting outcomes long before they actually take place. The aim of prenatal diagnosis is to detect fetal structural and genetic abnormalities. That is why it is possible to talk in the unborn fetus about preventing and detecting inherited and congenital illnesses. The most comprehensive and intrinsic makeup shared by all and therefore a vital subject to comparative analysis even before birth is the unmistakable nucleotide sequence that directs all physical and chemical changes. Amniocentesis involves taking out a small sample of amniotic fluid from the sac surrounding the fetus and analysis of its composition, so in essence genetic amniocentesis refers to examination of genetic abnormalities that might be prevalent in the developing fetus This permits taking decisions concerning about the progress of pregnancy to be made before viability. Comparatively less commonly, amniocentesis is performed in the beginning of third trimester instead of earlier testing. Advanced genomic study technologies such as Chromosomal Microarray Analysis (CMA) provide much more accurate and detailed information about the fetus. The ideal site for amniocentesis for localization should be determined by an ultrasound scan but in the absence of this facility, a site may be selected after careful palpation of the gravid uterus. Trisomy, Micro deletions/ micro substitutions can be detected by genetic amniocentesis. Fluorescence in Situ Hybridization is a dependable and brief technique for identifying maximum chromosomal variations and has now been carried out as a routine symptomatic strategy for the discovery of fetal irregularities.

Keywords: Sequencing; Amniocentesis; Genetic; Amniotic fluid; Fetomaternal; Fetus

Introduction

As much as science and medicine has progressed over the last century in an exponential manner, genetics or the study of gene makeup has been pivotal to deep understanding and cures of ailments stemming from womb. The clarity has grown which is remarkable both in terms of present achievements and future promises. Liquid biopsies, represent one of the latest and most efficient trends in oncology and genetics. The main principle for the execution of this technique is to make use of the fact that DNA fragments from tumors and solid formulations can be found in tiny amounts in the blood and other extracted fluids [1]. Soon after the completion of the Human Genome Project in 2003, analysis and research in genetics has mainly progressively focused on the study along with sequencing of genomes and prevalent congenital conditions, with the primary aim of improving the understanding of genetic basis of medical ailments and identifying actionable alterations in chromosomal structures. The integration and development of Next-Generation- Sequencing (NGS) techniques readily available since 2006, allowed for a cost- and time-saving sequencing of DNA, leading to a "genomic era" of research and treatment. It was termed as next generation sequencing impact in pharmacogenomics. These dubbed "pharmacogenomics" provided a considerable step forward in the evolving Personalized Medicine (PM) by enabling the early detection of driver mutations as well as different resistance mechanisms, precise calculation and quantification of existing mutational burden, vast number of germline mutations which settled the foundation of a new approach in medicinal care [2].

The advanced genomic study which includes microarray analysis (CMA) give us the most accurate and latest information about the fetus where it is compared with chromosomal analysis, which is traditional G- banded [4]. Some genetic and chromosomal anomalies occur in multiple gestations like Mendelian disease as compared to normal single pregnancies. It is very important to go for parental amniotic diagnosis in case of multiple pregnancies [5]. Downs syndrome can be studied and diagnosed in the fetus with the advancement in fetus study and diagnosis.

Amniocentesis

A baby floats in a bag of fluid in the womb of mother. That sac of bag is called amniotic sac. Amniocentesis is a procedure in which during pregnancy some of fluid is taken from amniotic sac for genetic testing. There can be many genetical reason for which this testing is done. Amniocentesis before 15 weeks has been introduced and is practiced widely in many prenatal diagnosis centers. There are major and vital anatomical differences between the condition and appearance of fetus, which are observed during 15-16 weeks, when

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amniocentesis is clinically performed, and in the ongoing first and early second trimester of fetal gestation. This is mainly because of the existence of extraembryonic coelom and the comparatively small amount of amniotic fluid in initial phase of pregnancy [6]. The ideal site for amniocentesis for localization should be determined by an ultrasound scan but in the absence of this facility, a site may be selected after careful palpation of the gravid uterus.

Amniotic Fluid

The fetus in the womb is surrounded by amniotic fluid. It contains the skin of the baby and the waste products of the baby. A complete set of baby's DNAs can be found in each cell in the amniotic fluid. This can help to evaluate the health of the developing baby and diagnose the potential problems of the cell samples obtained during amniocentesis. Amniocentesis gives medical professionals important information about a baby's chance of developing one or more legacy or pregnancy-long conditions. When a serious abnormality is identified, amniocentesis allows parents to decide if the pregnancy should continue.

Detection Procedure for Amniocentesis

Selection by abdominal palpation

There are three sites from which amniotic fluid may be aspirated with relative ease. The easiest of these is the suprapubic approach. The bladder must be emptied just before the procedure. The fetal presenting part can be displaced from the pelvic brim by gentle pressure and amniocentesis performed. However, this approach may not be possible if the presenting part is engaged. Alternative sites for amniocentesis are between the fetal limbs and behind the fetal neck but traumatic taps are more likely.

Selection by ultrasound

The maternal abdomen is scanned using real time ultrasound. An accessible pool of liquor is located and measurements made in all three dimensions. The depth of the pool from the skin is measured on the monitor and the optimal angle for needle entry determined. If a biopsy probe is available, amniocentesis can be done under real time ultrasound guidance. The proposed site is marked with either a skin marking pencil.

Amniocentesis Procedure

The procedure is carried out under complete aseptic and uncompromising conditions. It is good practice to explain the procedure to the patient once again, maintain a conversation during the procedure and warn her before every step that may cause momentary dis-comfort. Scrub and gown as for any aseptic surgical procedure. Prepare the area around the proposed puncture site with povidone iodine and cover the surrounding area with sterile towels. Infiltrate the site with 2% lignocaine, using a 24g needle superficially and a 22g needle later for the deeper planes. Infiltration with local anesthetic should extend to the visceral peritoneum. If the depth of entry has been calculated by ultrasound, insert the 20g spinal needle with stiletto to the predetermined depth. The stiletto is withdrawn and fluid aspirated. It prevents blockage of the needle during its passage through maternal tissues. However, minimal adjustments of the needle position may occasionally be required to ensure the free flow of amniotic fluid. The operator will experience a sudden 'give' in resistance to the passage of the needle when the amniotic sac is entered. If the tap is bloody or dry, the needle and stiletto should be withdrawn completely and amniocentesis may be attempted at another site. After the procedure is done, completely cover the puncture site [7].

Genetic Analysis of Amniotic Fluid

Parental diagnosis can be done by taking amniotic fluid from the fetus by the process of genetic amniocentesis. In amniocentesis, the amniotic fluid is used for biochemical analysis and also biochemical assays can be done from the fetal cell [8].

Prevalent method for the preparation analysis of amniotic fluid samples

Amniotic fluid uses a technique in which the cells are harvested, cultured and then analyzed for further responses. In this case cells remain adherent during chromosome banding and harvesting as well. Coverslips are mounted on the microscope to get a magnified image after banding process is finished. In this case, we can observe individual colonies arising from a separate cell of the amniotic fluid taken from the fetus. In-situ technique should be done for uncommon cells as compared to the flask method so we can recognize cell mosaicism in the amniotic liquid sample. This result ultimately in less time for each process.

Passaging cells from coverslips

If the cells required for extra examination which includes metaphase FISH and DNA study didn't result in a suitable amount of metaphase chromosome arrangements then in this case, we can need some more extra cells for further examination by passing them through unused cultured dish to new coverslips for extra metaphase chromosome arrangements including FISH and in some cases to a new flask in which cells are used as a source for further DNA analysis.

Culturing cells directly from amniotic fluid

In the process of culturing cells directly from amniotic fluid we grow cells in the flask so that we can provide exact and appropriate DNA and for the further biochemical studies. The transfer of cells to the flask is done, so that examination of cells can be done in the case if flasks are being shipped. This procedure includes lifting cells from the flasks by trypsinization. Additional passaging of cells is required if same process is to be performed on spot [8].

Detection of Amniotic Defects

Detection of anomalies

The following genetic anomalies and disorders can be detected and acted upon by genetic amniocentesis.

Trisomy

Different techniques as Fluorescence *in situ* hybridization (FISH) with the evolution of array of comparative genomic hybridization, in addition to quantitative analytic polymerase chain reaction assays are usually applied to the uncultured amniocytes that are dully obtained from cultures. After these, Conventional and easier cytogenetic analysis is applied to cultured amniocytes. Along with that, Interphase FISH is applied to uncultured urinary cells postnatal. Trisomy 13, 15, 17 and 21 (Downs syndrome) can be detected by genetic amniocentesis [9]. It can help immensely with early detection

and development of any treatment plans prior to birth [10].

Micro deletions/micro substitutions

Sequencing, after aspiration of amniotic fluid has been shown to almost all the time deliver high dependability, accurateness, and reproducibility for earlier detection of fetal chromosome number variations in those obtained prenatal samples. Before this procedure was introduced, there was effectively no way to establish an advanced estimate of small anomalies or changes in the nucleotide makeup. Its physical and clinical utility as a first-tier diagnostic method has been effectively analyzed and demonstrated in a large cohort group of pregnant women that were with reference to statistics, randomly referred for fetal chromosome testing. In all these samples taken, Micro deletions and micro substitutions can be detected substantially by these techniques and contribute to early treatment plans [11].

Prenatal Analysis of Amniocytes

Prenatal analysis is another diagnostic method in order to detect any type of chromosomal abnormalities, congenital defects during second trimester of pregnancy. The birth defects can be recognized through this method. Fluorescent fluorescence *in situ* hybridization (FISH) testing for pre-birth aneuploidy screening (13, 18, 21, X, Y) can likewise be performed. Cytogenetic investigations on the amniotic liquid are viewed as almost 100% exact and Chorionic Villus Examining (CVS) is viewed as over 99% solid for the location of enormous fetal chromosome irregularities. Be that as it may, unobtrusive or secretive irregularities including microdeletions for the most part can be recognized uniquely with the utilization of targeted FISH testing.

Fluorescence *in situ* hybridization

It can be done on uncultured amniocentesis or by CVS tests. The results are usually available on the next day. The test does not distinguish between all chrome abnormalities; in chromosome 21, 18, 13, X and Y, this FISH test explicitly takes a gander. It allows the FISH test to detect most basic chromosome irregularities, particularly the condition of the Down syndrome. Furthermore, the FISH test is ready to identify the child's sex. The FISH test is typical, in any case the child will return to the complete chromosome test in maximum ten days without having DOWN disorder, and possibly with no chromosomal irregularity. There still have chance of a rare chromosomal abnormality being distinguished around then. Assuming the FISH test returns as unusual, this implies that there is a chromosomal anomaly present. An ultrasound is performed before the procedure to ensure that it is appropriate and possible to perform the Amniocentesis. The size of the fetus will be measured. The position of the placenta is then mapped and the amount of amniotic fluid assessed. Some fetal abnormalities may be visible at this stage.

The amniocentesis is then carried out in the ultrasound room, which normally takes one to two minutes. It's usually not local anesthetic because the thickness of the amniocentesis needle is very similar to that of the needles for blood tests, the thickness and not the length of the needle is the cause of the inconvenience. Most people say that your arm's amniocentesis is less uncomfortable than a blood test.

Complications

Following complications can occur during the process of fluid extraction for analysis and prenatal determination of chromosomal aberrations.

Trauma

The most common complications are trauma to the fetus and placenta but ultrasound guidance reduces the risk. If the cord is in a fixed position (e.g., around the neck and in oligohydramnios where there is unprecedented fixation of the cord due to decreased production of amniotic fluid), the risk increases. Injury to the maternal soft tissues can also occur. If the procedure has been traumatic, as you have observed, monitor the fetus closely for any distressing signs that may arise. In such cases, it is good practice to examine the newborn for puncture marks [8].

Fetomaternal transfusion

This may occur following amniocentesis. Where indicated, do a Kleihauer-Betke test to quantify the volume of foe to-maternal transfusion and administer anti-D immunoglobulin where appropriate to prevent a transfusion reaction that might endanger fetal survival [12].

Infection

This can be one of the most common and dangerous outcomes by result of invasive procedures performed on fetus. Intrauterine sepsis may occur after amniocentesis. It usually results from an omission of aseptic technique and can be easily avoided with a little extra care towards precautions. Rarely, infection occurs because of trauma to the maternal bowel during procedures.

Abortion and preterm labor

Abortions and preterm labor may also occur following amniocentesis. Studies in Britain have shown that fetal wastage in women is higher in those who had undergone mid-trimester amniocentesis (2.6%) than in controls (1.1%) who did not undergo the procedure. However, preterm labor may have occurred for reasons other than those related to amniocentesis.

Anomalies in the newborn

There is an apparent increase in certain anomalies in the newborn following mid-trimester amniocentesis. These include respiratory problems at birth and postural deformities. The loss of amniotic fluid volume may restrict fetal breathing and body movements that were normal before the procedures were performed. Such anomalies may be clipped by using small caliber needles for amniocentesis [7].

Leakage amniotic fluid

Amniotic liquid leaks through the vagina after amniocentesis. In maximum cases, the measure of liquid lost is little and stops inside multi week, and the pregnancy is probably going to proceed typically.

Injury with needle

The child may move an arm or leg into the way of the needle during this procedure. Severe needle wounds are uncommon in most of the cases.

Rh sensitization

The blood cells of the baby enter the bloodstream of the mother in some cases during amniocentesis. After amniocentesis you will have an injection of the blood product called Rh immune globulin, if you have a Rh-negative blood and if you have no Rh-positive blood

antibody then in this case it prevents your body from producing Rh antibodies which can cross the placenta and harm the red blood cells of your baby.

Conclusion

While the trends in behavior and attitudes are not what they were a few decades ago, there is still a great amount of apprehension regarding prenatal testing and medical decisions [12]. According to surveys, around 78-80% of parents are willing to get through the process of prenatal p in the form of amniocentesis or chorionic villus sampling (CVS), women at that time experienced decrease in the risk of giving birth to a baby born with a major birth defect but it in some cases there is still a slightly higher risk of fetus developing any chromosomal abnormality. Emotional Stress and Anxiety was clinically elevated in these individuals and usually recorded at its highest at the pre-counseling stage, though it returned to near normal levels over time in a controlled manner.

These elaborative findings suggest that women who participate willingly in prenatal counseling and testing may be a possible subject to experience various level of distress and unrealistic perceptions of their potential risk and may want to take advantage of steps that have been particularly designed to lessen these states [8]. The current examination utilizing FISH tests explicit for chromosomes 13, 18, 21, X, and Y can possibly discover answers rapidly and less parental tension and of controlling further abnormalities. Prenatal tests have moved to non- invasive methods for determining the fetal risk for genetic disorders without the risk of error in recent years. Modern high-performance molecular technologies and cell-free fetal DNA discovery in maternal plasma have led to new methods for fetal aneuploidy screening. The treatment of amniocentesis is relatively safe and reliable. However, the risk of fetal loss following amniocentesis is probably slightly higher approximately 0.5 percent.

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