Journal of Advances in Science and Technology

Vol. VIII, Issue No. XV, November-2014, ISSN 2230-9659

RULE OUT ANEUPLOIDIES AND BIRTH DEFECTS' THROUGH MATERNAL SERUM BIOCHEMISTRY MARKERS

AN INTERNATIONALLY INDEXED PEER REVIEWED & REFEREED JOURNAL

www.ignited.in

Journal of Advances in Science and Technology
Vol. VIII, Issue No. XV, November-2014, ISSN 2230-9659

Rule out Aneuploidies and Birth Defects' Through Maternal Serum Biochemistry Markers

Sreedhar Mayavan[1]* Dr. Kanachana Chinnappan[2] Dr. Sai Shalini[3]

[1]Research Scholar KEISIE International University

[2]M.B.B.S., MD (Biochemistry)

[3]M.B.B.S., M.D (Path)

Abstract – There have been a number of studies evaluating the association of aneuploidy serum markers with adverse pregnancy outcome. Pregnancy is a time of great anticipation and anxiety for parents, but some parents are more Apprehensive that their baby may be born with a severe physical or mental disability. In fact, about one in forty babies could suffer from a congenital abnormality. Abnormalities can range from something now correctable, like a cleft lip. To something severely disabling like congenital Heart disease. Recent advances in medicine make it possible to give pregnant women a lot of Information about their babies before birth. For majority of parents to be, prenatal testing (PNT) provides reassurance; for a minority the test results may indicate a problem with the Baby's growth or development. As a result, studies which evaluate the association of biomarkers with a broad definition of a given condition may underestimate the ability of such markers to identify pregnancies that are destined to develop the more severe form of the condition.

Keywords: Aneuploidy, Serum, Growth, Development, Medicine, Biochemistry, Maternal, Markers, Birth etc.

----------♦----------

INTRODUCTION

Pregnancy is a time of great anticipation and anxiety for parents, but some parents are more Apprehensive that their baby may be born with a severe physical or mental disability. In fact, about one in forty babies could suffer from a congenital abnormality (Macri, Weiss, 1982). Abnormalities can range From something now correctable, like a cleft lip. To something severely disabling like congenital Heart disease. Recent advances in medicine make it possible to give pregnant women a lot of Information about their babies before birth. For majority of parents to be, prenatal testing (PNT) provides reassurance; for a minority the test results may indicate a problem with the Baby's growth or development. Prenatal diagnosis has its beginning in 1966, when Steele and Brag (UK Collaborative Study, 1982). showed that the constitution of chromosome complement of a fetus could be determined by analysis of cultured cells from the amniotic fluid. Because the association between late maternal ages an increased risk of Down syndrome was already well known, their report led directly to the development of prenatal diagnosis as a medical service. This project mainly focuses on the non-invasive prenatal diagnosis of a wide range of genetic defects. The non-invasive screening of the fetus is mainly done by maternal serum screening (MSS). Collection of maternal blood sample is invasive in a limited sense. However, collection of maternal blood for testing is a fairly common and routine procedure and it is noninvasive as far as the fetus is concerned. It does not involve any risk like fetal loss or infection. It is therefore considered as a non-invasive procedure. The quality of the non-invasive prenatal screening is significantly enhanced by the use of ultrasound imaging. It is very important to note that the non-invasive tests like maternal serum screening (MSS) and ultrasound are tests for screenings and not diagnostic tools. The tests are helpful in ruling out the probability of many diseases, which includes many genetic disorders. These tests enable pregnant women to get an estimate of the probable risk that the fetus has genetic abnormality. If the risk for a particular disorder is high, the parents are advised to carry out confirmatory tests like invasive tests to confirm the disorder. If a disorder is detected, the parents to be have a choice to decide between the possible courses of action (Krantz, *et. al.,* 1996). The courses include:

(1) In utero treatment;

(2) Delivery at a special centre for immediate postnatal treatment; or

(3) Termination of an affected fetus, i.e. abortion.

Many parents are distressed and terrified to undergo invasive prenatal testing as it is invasive and carries chances of fetal loss. Hence in general many parents prefer noninvasive testing to invasive testing.

REVIEW OF LITERATURE:

Prenatal screening for birth defects was initially implemented using a single biochemical marker (alpha-fetoprotein) to identify a single condition (open neural tube defects, ONTDs) in the second trimester of pregnancy (Macri, Weiss, 1982, UK Collaborative Study, 1982) Over the course of the last 30 years, the field has evolved so that multiple ultrasound and biochemical markers across the first and second trimesters are used to identify patients at risk not only for ONTDs but also for Down syndrome and trisomy 18/13 (Krantz, *et. al.,* 1996. Askie, *et. al.,* 2007. Orlandi, *et. al.,* 1997. Krantz, *et. al.,* 2000). In addition, there have been a number of reports (Goetzl, 2010. Davenport, Macri, 1983. Spencer, Nicolaides, 2002) regarding the effectiveness of the serum markers to identify pregnancies at high risk for additional adverse perinatal outcomes leading to a number of reviews and consensus opinions (Cuckle, *et. al.,* 2005). The purpose of such reviews was to evaluate serum markers which were already being used in aneuploidy screening to see if there was any additional benefit in identifying other conditions beyond the primary outcomes being screened. These reviews focused on improving pregnancy management through the use of additional counseling and follow-up ultrasound examination since the effectiveness of treatments for these other conditions was not well-established.

1- General Principles for Genetic Screening:

Both at the national and supranational levels, guidelines have been elaborated with a view to the developments in genetic screening and the ethical issues raised by it. All these documents deal with the question as to which requirements apply to screening programmes. In any genetic screening programme, guidelines should be established governing its aim, limitations, scope, and ethical aspects, as well as the storage and registration of data or material, the need for follow-up (including social consequences), and the risk of side effects. The two most frequently citied objectives of genetic screening are to reduce the prevalence of the disorder and to inform individuals and couples at risk about their reproductive choices. Particular attention is being paid to the rights of participants in terms of informed consent, confidentiality, and data protection.

2- Types of Genetic screening:

There are two types of genetic screening:

(1) Genetic screening before birth: this includes screening on fetal cells in maternal blood, maternal serum screening, ultrasound screening, screening on fetal cells obtained after amniocentesis or CVS, preimplantation genetic diagnosis. The major reason for genetic screening before birth is to detect genetic disorders during early pregnancy. Information can be provided to enable couples to consider to termination or continuation of the pregnancy, while the early diagnosis would allow appropriate plans to be made for treatment and follow-up.

(2) Genetic screening after birth: this includes neonatal screening, carrier screening at antenatal clinics, preconception carrier screening, cascade screening, school-age careening, and adults screening. Genetic screening after birth has two purposes. First, it can confirm that the person tested has or does not have, certain genetic characteristics, with implications for own future health. The second reason for an adult to be tested is to see if their children will be at risk.

3- Different Types of Prenatal Diagnosis:

Both invasive and non-invasive methods are currently used for prenatal diagnosis. Amniocentesis and chorionic villus sampling (CVS) both are invasive procedures associated with a small but finite risk of fetal loss. Thus, the use of amniocentesis or CVS is indicated for only a small percentage of pregnant women selected for specific reasons for invasive prenatal diagnosis. In contrast, a combination of maternal serum screening (MSS) Also called triple screening and ultrasonography scanning can be used for fetal evaluation in low-risk as well as in some high-risk pregnancies because both are non-invasive and without risk to the fetal. MSS can help to identify fetuses at increased risk of open NTDs, some chromosomal abnormalities including Down syndrome, and other disorders. Ultrasonography, in addition to its function in assessment of gestational age and fetal growth, enables the diagnosis of a number of morphological abnormalities, many of which are genetic in origin, at early gestational ages. If an antenatal screening test suggests the pregnancy is at a high risk of a condition, a definitive diagnostic test will be offered to the woman. Women who have had a previous fetal abnormally or who have a family history of an inherited of an inherited condition may be offered these diagnostic tests from the outset of pregnancy. It is not easy to apply invasive testing for mass population screening. Besides being expensive, invasive testing is both labor intensive and requires highly skilled operators.

a. Non-invasive prenatal diagnosis (NIPD)

b. Invasive prenatal diagnosis

Sreedhar Mayavan[1]* Dr. Kanachana Chinnappan[2] Dr. Sai Shalini[3]

Amniocentesis:

Amniocentesis refers to the procedure of removing a sample of amniotic fluid Trans abdominally by a syringe. The amniotic fluid contains cells of fetal origin that can be cultured for diagnostic tests. Before amniocentesis, ultra sonographic scanning is routinely used to conform fetal viability, gestational age, and the number of fetuses, structural normality, and the optimal position for needle insertion by establishing the position of the fetus and placenta. Amniocentesis is performed on an outpatient basis typically at the 15th to 16th week of gestation; however, the procedure has been performed at a much earlier stage in pregnancy, as early as 10 to 14 weeks. In addition to fetal chromosome analysis, the concentration of AFP (alpha-fetoprotein) can also be assayed in amniotic fluid. The major complication associated with midtrimester amniocentesis is a 0.5 to 1 percent risk of including miscarriage over the baseline risk of approximately 2 to 3 percent for any pregnancy at this stage of gestation. Other complications are rare, including leakage of amniotic fluid, infection, and injury to the fetus by needle puncture.

- Advantages
- Chromosome analysis
- AF-AFP levels to rule out ONTD
- Risk of miscarriage is low compared to CVS. (0.5%)
- Highly reliable results 99+%
- Familiar
- Long standing reputation
- NTD detection
- Disadvantages
- Late in gestation
- Decision making
- Mom feels movement
- Fear of needles
- Needle invades the sac

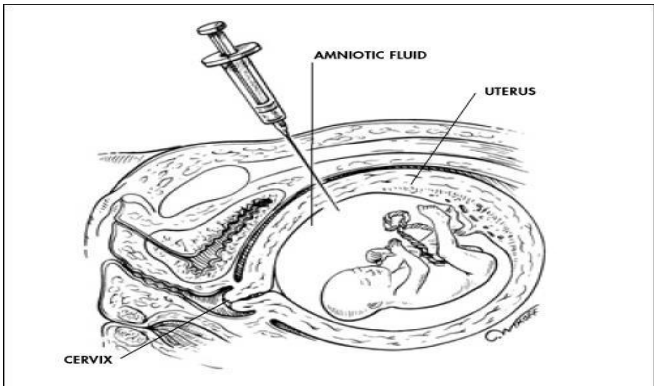

Figure: Amniocentesis in a sixteen-week pregnancy. Ultrasound monitoring helps the doctor make sure the needle avoids the baby and the umbilical cord.

CONCLUSION:

Optimally, a risk-based approach similar to that used in aneuploidy screening would be used for each disease state, in which consistent definition of the disease state, continuous multiple marker likelihood estimates and consistent estimates of a priori risks based on maternal characteristics were incorporated. Additionally, refinements to the risk based on follow-up assessments after the completion of serum screening could further improve the process. Moving forward, the goal should be to develop and implement high-performance direct screening protocols for specifically defined adverse outcomes. When evaluating the adoption of cffDNA testing for aneuploidy, clinicians should ensure that they continue to utilize existing screening protocols or new direct screens to identify pregnancies at risk for adverse outcomes. Otherwise, there may potentially be an increase in the overall morbidity and mortality in the population.

REFERENCES:

Askie, L.M.; Duley, L.; Henderson-Smart, D.J., Stewart, L.A. (2007). A meta-analysis of individual patient data Lancet, 369, pp. 1791–1798.

Cuckle, H.; Benn, P.; Wright, D. (2005). Down syndrome screening in the first and/or second trimester: Semin. Perinatol, 29, pp. 252–257.

Davenport, D.M.; Macri, J.N. (1983). The clinical significance of low maternal serum alpha-fetoprotein. Am. J. Obstet. Gynecol., 146, pp. 657–661.

Goetzl, L. (2010). Adverse pregnancy outcomes after abnormal first-trimester screening for aneuploidy. Clin. Lab. Med., 30, pp. 613–628.

Krantz, D.A., Hallahan, T.W., Orlandi, F., Buchanan, P., Larsen, J.W., Jr., Macri, J.N. (2000). First-trimester Down syndrome screening using dried blood biochemistry and nuchal translucency. Obstet. Gynecol., 96, pp. 207–213.

Krantz, D.A.; Larsen, J.W.; Buchanan, P.D.; Macri, J.N. (1996). First-trimester Down syndrome screening: Free beta-human chorionic gonadotropin and pregnancy-associated plasma protein A. Am. J. Obstet. Gynecol., 174, pp. 612–616.

Macri, J.N., Weiss, R.R. (1982). Prenatal serum alpha-fetoprotein screening for neural tube defects. Obstet. Gynecol., 59, pp. 633–639.

Orlandi, F.; Damiani, G.; Hallahan, T.W.; Krantz, D.A.; Macri, J.N. (1997). First-trimester screening for fetal aneuploidy: Biochemistry and nuchal translucency. Ultrasound Obstet. Gynecol., 10, pp. 381–386.

Spencer, K., Nicolaides, K.H. (2002). Prenat Diagn., 22, pp. 877–879.

UK Collaborative Study (1982). Estimating an individual's risk of having a fetus with open spina bifida and the value of repeat alpha-fetoprotein testing. Fourth report of the UK collaborative study on alpha-fetoprotein in relation to neural tube defects. J. Epidemiol. Community Health, 36, pp. 87–95.

Corresponding Author

Sreedhar Mayavan*

Research Scholar KEISIE International University

E-Mail – sreedhar.mayavan@hotmail.com