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Serum Markers and Adverse Maternal: Fetal Outcomes

Alka Patil[1], Hetashvi Sudani[2], Priyanka Agrawal[3], Aakanksha Deshmukh[4]

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Abstract

The goal of every obstetrician should be to give the best prenatal care to the fetus to achieve optimal perinatal outcome. The early assessment of patient specific risks of pregnancy complication has the purpose to improve pregnancy outcome. The first trimester and second trimester Screening tests have high predictive value for adverse pregnancy outcomes. Women should be adequately counseled for the disorders to be screened. Estimation of serum markers has vital role in counselling women and consideration of increased fetal surveillance. With innovations like serum markers obstetricians have the opportunity to improve pregnancy outcomes with effective treatment.

Keywords: Serum Markers, Tripple Test, Quadruple Test, Non-invasive Testing, Adverse Pregnancy Outcomes.

INTRODUCTION

Birth is not only about making babies. Birth is about making mothers strong, competent, capable mothers who trust them selves and know their inner strength. *Barbara Katz Rothman*

The goal of every obstetrician should be to give the best prenatal care to the fetus to achieve optimal perinatal outcome. Screening in pregnancy is of surveying a population of women with markers to identity those at higher risk for a particular disorder. Such women can then be offered further diagnostic tests and appropriate treatment to reduce their risk and or complications arising from the disease or condition. Biochemical markers are the building blocks of screening test.[1]

Over the course of the last 30 years, the field has evolved so that multiple ultrasound and biochemical markers during first and second trimesters are used to identify patients at risk not only for ONTDs but also for Down syndrome and trisomy 18/13.[2]

The early assessment of patient specific risks of pregnancy complications has the purpose to improve pregnancy outcome and to individualize the patient and disease specific approach.[3] The first and second trimester screening test have a high predictive value for APOS such as preterm labour, preterm premature rupture of membranes, IUGR, GDM, Pre-eclampsia. In women with no evidence of chromosomal abnormality or neural tube

Authors Affiliation:
[1]Professor & HOD, [2-4]Junior Resident, Department of Obstetrics and Gynecology, ACPM Medical College, Dhule 424002, Maharashtra, India.

Correspondence Author:
Alka Patil, Professor & HOD, Department of Obstetrics and Gynecology, ACPM Medical College, Dhule 424002, Maharashtra, India.

E-mail: hetashvipatel92@gmail.com

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defects, the presence of atleast one abnormal test result is associated with an increased risk of fetal and neonatal mortality.

First Trimester Screening Test

Double marker test which involves nuchal translucency, hCG and pregnancy associated plasma protein A.

Second Trimester Screening Test

1. Triple test includes
   - Maternal serum Alpha fetoprotein (AFP)
   - Human chorionic gonadotropins (hCG)
   - Unconjugated estriol (uE3)
2. Quadruple test include inhibin A with triple test. Explanation of underlying mechanisms have been based on abnormal placentation and perfusion. Although in most cases these complications occur in later stages of pregnancy, most of them are potentially predictable in Early pregnancy screening programs.[4]

Early diagnosis enables obstreticians and perinatologists after counselling regarding continuation of pregnancy or termination and decide on timing and place of delivery.

Counselling Before Screening

All couples who are being offered screening should be counseled about why test is done and helped to understand the interpretation of results. They should also be aware about the follow up of positive results.

First Trimester Testing

The level of HCG is elevated and that of PAPA is decreased in Down's syndrome but both are decreased in trisomy 18 and trisomy 13. In the second timester, while AFP, UE3 and PAPP-A are lower levels of beta HCG and inhibin A are higher in women whose fetuses have Down's Syndrome.

Second Trimester Testing

Second trimester maternal serum screening is best offered between 15 and 20 weeks of gestation and involves the analysis of three analytes (Triple test) or four analytes (Quadruple test).[5]

1. **Beta Human Chorionic Gonadotropin (Beta Hcg)**

The biochemical evidence of pregnancy event precedes our ability to see pregnany Sonographically. B HCG is detectable 8 days after conception. In multiple gestations, B-HCG may be above discriminatory zone, yet no yolk sac may be seen. Continued observation is required.

Table 1: Low level of Papp-A

Miscarriage
Preterm
Small for gestational age
NICU admission
Still birth
Low Apgar score at 5 min

Serial B-HCG determinations are appropriate to exclude ectopic pregnancy with B-HCG level < discriminatory zone.[6,7]

2. **Pregnancy Associated Plasma Protein A (Papp-A)**

The association between PAPP-A or beta-hCG levels and various adverse Obstetric outcomes has been explained by the fact that both hormones are produced in the placenta soon after implantation,

Table 2: Abnormal unconjugated estriol with unfavourable pregnancy outcomes

Preterm birth
Smith - Lemli – Opitz syndrome
Pregnancy loss
Aromatase Deficiency
Pre-eclampsia
Fetal adrenal insufficiency

and low levels could possibly reflect abnormal placentation.[8]

3. **Unconjugated Oestriol (uE3)**

Estriol is the principle estrogen derived from the placenta, the fetal adrenal gland secretes dehydroepiandrosterone sulfate (DHEAS). The placenta converts DHEAS to estriol, and then diffuses into the maternal circulation. uE, is first detected at[9] weeks and peaks at 31-35 weeks of gestation. In second trimester, it is reported that decreased uE, was related to Down's syndromes, trisomy 18 syndromes and neural tube defects.

The low levels of UE3 in pregnant women who developed into pre-eclampsia may result from the pathological change of pre-eclampsia, for example, in sufficient placental perfusion result in attenuation of placenta function, and then the

Table 3: Variable affecting serum AFP

Cigarrete smoking
Gestationa age at delivery
Z score of Neonate in previous Pregnancy
Interpregnancy interval
Maternal weight
Gestational Age assessment
Parity status

conversion of DHEAS and the secretion of UE.[9]

4. **ALPHA FETOPROTEIN (AFP)**

Alpha Fetoprotein is a fetal glycoprotein that is initially produced in fetal yolk sac. Fetal AFP diffuses across placental barrier into maternal Circulation.[1]

Table 4: Elevated levels of AFP

Neural tube defects
Abnormal vault defects
Oesophageal atresia
Duodenal atresia
Renal anomalies
Multiple pregnancy
Intrauterive fetal dealth.
Placental Chorioangioma
Maternal hepatoma and Teratoma
Low maternal weight

Table 5: Low Levels of AFP

Chromosomal Trisomies (Trisomy 21,18)
Insulin dependant Diabetes Mellitus
Overestimated gestational Age
Gestational trophoblastic disease
High maternal weight

Excretion of AFP in the fetal urine results in high levels of AFP in the amniotic fluid. Transfer of AFP to the Maternal serum occurs via the placenta and transamniotically. The interpretation of MSAFP screening test is gestational age dependant and should be performed at 15th to 20 th week of pregnancy, serial tests are required.[10]

5. **INHIBIN A**

During pregnancy, inhibin A is mainly synthesized and secreted by placental syncytiotrophoblasts, which is involved in the regulation of various hormones in the placental local regulatory axis.

INHIBIN IS RELATED TO

- Endometrial decidualization
- Embryo implantation
- Proliferation
- Differentiation of trophoblasts.

It affects the occurrence, development and maintenance of pregnancy. Inhibin A can affect fetal growth and pregnancy outcome. The level of inhibin. A reached the first peak at 8-10 weeks of pregnancy, was relatively stable at 14-30 weeks, increased gradually from the third trimester of pregnancy to full term, and reached the highest level at delivery.

The Increase of inhibin A is associated with the occurrence of preeclampsia, and fetal malformation and fetal growth. The increase of inhibin-A in the second trimester of pregnancy may reflect the abnormality of placental development in the early stage of pregnancy and may cause obvious clinical manifestations in the third trimester of pregnancy. The unfavorable environment in the early stage of the uterus leads to the restriction of intrauterine growth of the fetus and leads to premature delivery.[11]

DISCUSSION

Normal pregnany is associated with delivering

Table 6: Adverse Fetal Outcomes

Congenital malformations
Intrauterine fetal death
Chromosomal Trisomies (trisomy 21 and trisomy 18,13)
Small for gestational age
Still birth
Intrauterine growth retardation
Fetal macrosomia and shoulder dystocia
Low Apgar score at 5 min
Fetal adrenal insufficiency

Table 7: Adverse Material Outcomes

Pre-eclampsia
Gestational diabetes mellitus
Insulin dependent Diabetes Mellitus
Placenta Accreta
Spontaneous abortion
Preterm delivery
Gestational trophoblastic disease

healthy baby with out complications prenatal, intra -natal, postnatal period. Yet there may be many adverse fetal and maternal outcomes. Ethically, it is essential to detect them earliest with prompt interventions and information to patient.

Women should be adequately counseled for the disorders to be screened and the difference between screening and diagnostic tests. Screening tests pick up high risk cases from the population and are not diagnostic tests and follow up by confirmatory tests may be necessary. The serum markers tests are non invasive and pose no risk to mother or baby.[12]

Interpretation of Screening Tests

Results of maternal serum screening are Received as a positive or negative and are in a ratio. An abnormal or positive screening test means the couple needs to consider a diagnostic test for conformation of the report. An abnormal result can also be observed if the pregnancy is older or younger than the actual gestational age and ultrasound should confirm the same. The values can also change in multiple gestation.[12]

First trimester screening: Free B-HCG and pregnancy associated plasma protein-A (PAPP-A) are the markers used most commonly and have the highest efficacy and consistency.

The benefits of moving prenatal diagnosis to an early gestational age are many. These include providing information regarding the pregnancy to the patient at a time when reproductive choices can be made with a great deal of privacy. If desired by the patient first trimester pregnancy termination can be performed with less maternal risks compared to procedure done later in pregnancy.[13]

In Case of multiple test results for example serum testing, even if abnormal level of maternal level of serum AFP is found, it is usually not due to neural tube defect, but because of other causes and it can alert the physician to other pregnancy complications. The detection of abnormalities by other tests can significantly alter the case of affected fetuses and allow them to be born in hospitals where specific neonatal care can positively influence longterm survival and health.[14]

Management of Screen Positive Pregnancy

A screen positive result provoked anxiety in the couple. Detailed counselling and explanation of the results are important. A screen positive result does not mean that the fetus is affected however, a screen positive test requires follow up with invasive tests for karyotyping to confirm or rule out aneuploidy. Based on gestational age CVS or amniocentesis should be offered.[5]

CONCLUSION

Pregnancy and childhood are attended by certain risks to the mother and foetus. The aim is to improve our management of high risk situations and optimise the outcome of pregnancy. Estimation of serum markers has vital role in counselling women and increased fetal surveillance. Clinician's must balance the potential benefits of non-invasive testing while not missing other adverse outcomes. With innovations like estimation of serum markers, obstetricians have opportunity to improve pregnancy outcomes with effective treatment. Detailed counselling and explanation of the results are important.

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