

Biochemical tests in pregnancy

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Abstract

Pregnancy is a normal physiological phenomenon associated with marked hormonal and biochemical changes in the maternal circulation which facilitates the metabolic, vascular and immunological adjustments necessary for the fetus to thrive. Abnormal concentrations of these hormones or of other plasma constituents of fetoplacental origin may indicate gestational pathology. The metabolic changes associated with pregnancy are relatively short lived and thus are rarely harmful to the healthy mother. When pregnancy deviates from its normal course there are many biochemical markers which can be used to assess these abnormalities. As biochemistry is only one part of obstetric care the results should be interpreted in conjunction with clinical and medical imaging data.

Key words: human chorionic gonadotrophin, alpha fetoprotein

INTRODUCTION

Prior to the widespread availability of high resolution ultrasound scanning, the diagnosis of early pregnancy failure (such as spontaneous abortion and ectopic pregnancy), of fetal malformation and fetal growth disturbances relied solely on clinical evaluation backed by blood tests on the maternal circulation. There are certain biochemical markers which can be used to assess maternal, placental and fetal health. They help to diagnose maternal conditions such as gestational diabetes and pre-eclampsia, placental conditions like trophoblastic disease and fetal chromosomal abnormalities like Down's syndrome.

Biochemical diagnosis of pregnancy:

Biochemical diagnosis of pregnancy is routinely made by the detection of human chorionic gonadotrophin (beta-hCG) using a latex agglutination technique detecting concentrations >200 i.u/L while a monoclonal antibody enzyme immunoassay will detect concentrations as low as 50 i.u/L.

Also estimation of scavengershaftsprotein 1 (SPI) and pregnancy associated plasma protein A (PAPPA) helps in determining gestational age in early pregnancy.¹

Biochemical monitoring of pregnancy:

Ectopic pregnancy

The incidence of ectopic pregnancy appears to be increasing making accurate diagnosis of this condition increasingly important. Even though definitive diagnosis still depends on laparoscopy, use of additional tests may help reduce the number of unnecessary laparoscopies. Determination of urinary β -hCG and plasma monoclonal

antibody tests are the commonly employed tests for diagnosis of ectopic pregnancy. When the test is positive and an ectopic pregnancy is suspected a quantitative β -hCG (0.15 – 0.8 i.u/L) may be advocated.

In ectopic pregnancies with normal hCG concentrations PAPPA concentrations have been reported to be consistently low. If these observations are confirmed estimation of PAPPA may prove useful as an adjuvant test in the diagnosis of ectopic pregnancy.

Spontaneous abortion

Many studies have reported low concentrations of various hormones and placental proteins in cases of early spontaneous abortion. Measurement of hCG is a valuable adjunct in the evaluation of threatened abortion in the first trimester. If less than 3000 i.u/24 hrs is excreted the fetus is almost invariably dead. Also plasma progesterone concentrations have been reported to be low in such situations.¹

Biochemical assessment of maternal health

Common maternal problems in pregnancy include anemia, urinary tract infection, toxemia, gestational diabetes and pre-eclampsia.

Anemias of pregnancy

Types of anemias that are more prominent in pregnancy include iron deficiency anemia, hemoglobinopathies and megaloblastic anemia. The last variety is quite unusual. Examination of well prepared and well stained blood film helps in the diagnosis of anemia.

Urinary tract infections in pregnancy

The urinary tract stasis and dilation, possible instrumentation or catheterization, and the trauma of childbirth all increase susceptibility of the woman to UTI during or following pregnancy.

The periodic microscopic examination of the urine sediment for white blood cells and bacteria as well as screening procedures to detect significant bacteria helps in the proper diagnosis.

Toxemia of pregnancy

Along with periodic measurement of blood pressure and weight the check for proteinuria is a valuable screening procedure for toxemia, because proteinuria and renal impairment are prominent features of this disease. Toxemia can progress to pre-eclampsia and frank eclampsia (convulsions).²

Diabetes mellitus

Prevalence of gestational diabetes mellitus ranges from 1 to 14 % depending on the populations studied. Screening for gestational diabetes can be carried out at 26-28 weeks gestation. This enables early intervention which results in significant improvements in both fetal and maternal outcomes. The diagnosis can be confirmed by further tests of fasting glucose concentration or 75 g oral glucose tolerance test. These patients should be reassessed in post partum period for evidence of diabetes. The woman's glycated hemoglobin should be maintained in the normal range to ensure optimal fetal outcome.³

Pre-eclampsia

Pre-eclampsia occurs typically in the third trimester and affects 4-8 % of pregnancies. It constitutes a triad of pregnancy associated hypertension, marked proteinuria (>300 mg daily) and pathological edema. It is thus critical to carry out dipstick testing for protein at each antenatal visit together with blood pressure measurement and careful examination for edema. Other findings include rises in serum uric acid, urea and creatinine. Low hemoglobin and platelet concentrations are informative if the patient is suspected to have severe form of pre-eclampsia-haemolysis-elevated liver enzymes-low platelets (HELLP).³

Biochemical assessment of placental health

Biochemical assessment of placental health is important because it helps in diagnosing trophoblastic disease (hydatidiform mole or choriocarcinoma). Maternal serum human placental lactogen and serum or urinary oestriol concentrations which were previously used extensively in the assessment of placental function are rarely used nowadays.

Physiologically serum hCG arising from trophoblastic activity is elevated as early as eighth day after implantation. Concentrations double every 2-3 days and peak at approximately 10 weeks. They then decline and plateau out at lower concentration until parturition.

In addition to confirming pregnancy hCG can be used as a marker to assess various abnormalities in first trimester.

An elevated serum hCG level suggests the presence of multiple pregnancies or gestational trophoblastic disease such as chorionic carcinoma or hydatidiform mole. A hydatidiform mole appears as snow storm on ultra sound. Confirmatory biochemical tests include free β -hCG concentrations because this form of hCG is secreted in disproportionately high amounts. hCG can be used to assess the effectiveness of therapy and monitor for recurrence following surgery for gestational trophoblastic disease. A rapid decline or disappearance of serum hCG is to be expected after surgery. After the second month of pregnancy the fetoplacental unit becomes the major source of estrogen production in the pregnant woman. These estrogens are excreted in the urine and are proportional to the amount and type of trophoblastic disease in the placenta as well as the blood flow through the placenta. Mean excretion in the last 6 weeks is about 16 mg/day with a range of about 20 to 24 mg/day.

Level of urinary estriol less than 12 mg/day, during the last weeks of pregnancy is associated with impending fetal death. Levels below 4 mg/day almost indicate fetal death. Sudden falls in estriol levels from above 12 mg to 4 or 6 mg indicate serious fetal difficulties and prompt delivery must be considered.⁴

Biochemical assessment of fetal health

The major aim of fetal assessment is to ensure satisfactory growths in utero. There are many factors which can cause fetal growth retardation. These may range from poor maternal nutritional state to placental insufficiency and fetal abnormality. Fetal abnormalities that can be detected using biochemical markers include neural tube defects, Down's syndrome, hemolytic disease of the newborn and lung immaturity.

Alpha fetoprotein

It is a fetal protein arising from the yolk sac and fetal liver. It can be detected in maternal serum until 32 weeks of normal gestation.

Neural tube defects

Neural tube defects are among the most common fatal congenital malformations.

In neural tube defects such as spina bifida and anencephaly, the concentration of alpha fetoprotein in the maternal serum is unusually high in the first trimester because cerebrospinal fluid leaks into the amniotic fluid. As a marker of neural tube defects maternal serum alpha fetoprotein, ideally, should be measured between 15 and 18 weeks of gestation. Elevated maternal serum AFP levels are seen in about 85% of open neural tube defects. After maternal serum AFP is found to be elevated the

level of AFP in the amniotic fluid should be determined. Elevated amniotic fluid AFP is about 95% sensitive for open neural tube defects. Any suspicion of a neural tube defect can be further assessed with ultrasound, usually at 18-20 weeks.⁵

Diagnosis of fetal genetic abnormality

Most of the fetal genetic disorders are diagnosed using tissue sampling techniques, although majority of these procedures are performed for fetal karyotyping. Tissue sampling techniques that can be used for the diagnosis are amniocentesis and chorionic villus sampling (CVS). most commonly occurring fetal genetic abnormality is Down's syndrome. Another procedure used for screening of Down's syndrome is maternal serum screening (triple test).

Chorionic villus sampling

As the fetus and the placenta both develop from the same early blastocyst their genetic make-up is identical in the vast majority of cases. Thus, chromosome and DNA analysis of the placenta will provide information about the fetus.

Amniocentesis

Traditionally amniocentesis has been performed at 16 weeks gestation and the result is available 2-4 weeks later. As a result of the late gestation at which the result becomes available earlier amniocentesis is currently under investigation. This new technique can be employed from 10 weeks gestation.

Down's syndrome

Down's syndrome is one of the common causes of fetal growth retardation. It is the result of either partial or total trisomy of chromosome 21 or a major obstetric concern, particularly in older women. Important biochemical markers include alpha fetoprotein, hCG, unconjugated oestriol, pregnancy-associated plasma protein -a, serum inhibin-a and free β -hCG. These markers are used in various combinations and together with ultrasound to increase the detection rate of Down's syndrome.

Between 11 and 13 weeks (that is late first trimester), serum pregnancy-associated plasma protein-A. Free β -hCG and ultrasound assessment of nuchal thickness (the physiological space between the back of the neck and the overlying skin of the fetus) are most commonly used in the assessment of Down's syndrome.

In the second trimester screening for Down's syndrome traditionally employs the triple test of maternal serum hCG, serum unconjugated oestriol and alpha fetoprotein at 15-18 weeks of gestation. Some laboratories also measure serum pregnancy associated plasma protein -A.⁶

Fetal lung maturity

The lungs are among the last of the fetal organs to mature.

Thus, mature lungs usually indicate that the fetus is ready for birth. Fetal lung maturity is evaluated by measuring the amount of surfactant in the amniotic fluid. A deficiency in surfactant leads to the development of respiratory distress syndrome (RDS) in neonates. 75 percent of the surfactant consists of phosphatidyl choline (lecithin), 10 percent consists of phosphatidyl glycerol and the remainder consists of various phospholipids and sphingomyelin. Various assays can be used for measuring the concentration of various components of surfactant. The most popular biochemical assay used to assess FLM is the lecithin/sphingomyelin ratio.

Hemolytic disease of the newborn

In hemolytic disease of the newborn (HDN) the red blood cells of the fetus are coated with maternal IGG antibody and are destroyed in the infant's reticuloendothelial system. Several blood group systems have been associated with HDN, for example, the Rh system, the ABO system, and other groups that form IgG antibodies. At present there are no laboratory procedures that can predict ABO hemolytic disease during the prenatal period.

The objective of prenatal blood studies is to identify women at risk for having babies affected with HDN. Following studies can be done early in the pregnancy: 1) ABO grouping; 2) Rh testing; and 3) screening for unexpected antibodies (indirect coombs' test) 7.

CONCLUSION

Although ultrasound based bio-physical tests are available for the diagnosis of early pregnancy failure, fetal malformation and fetal growth disturbances, biochemical assays still form an important part of the screening of many pregnancies. These biochemical and hormonal tests constitute only one aspect of obstetric care and so the results should be interpreted in conjunction with clinical findings and imaging, particularly ultrasonography

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