

The role of laboratory medicine for health during pregnancy

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ABSTRACT

Pregnancy produces profound physiological changes that increase in significance as it progresses. These changes include hormonal changes, metabolic changes, increases of plasma volume up to 50%, alterations to the balance of the coagulation system in favour of clotting, and GFR increases to a peak 50% above pre-pregnancy levels. Since healthy physiological changes occur during pregnancy, different reference intervals may be needed. First antenatal screens usually include Complete blood count, Blood group and antibody screen, rubella antibody status, syphilis serology, Hepatitis B serology and HIV abs testing. Additional testing in early pregnancy may be added to the first antenatal screen such as varicella, Chlamydia and vitamin D tests. The most important test in the second antenatal testing screen is gestational diabetes screening and protein detection in urine to rule out preeclampsia. Screening for Down syndrome, other chromosomal abnormalities and neural tube defects is recommended for all pregnant women above the age of 35 years. Additionally, 37 weeks into pregnancy, a swab to detect Group B streptococcal (GBS) infection is recommended.

INTRODUCTION

Human Pregnancy is not a disease, it is a physiological condition; pregnancy produces profound physiological changes that become more significant as pregnancy progresses.

The hormonal changes starts from the **ovaries**, and then later the **placenta**. The first hormone to make its appearance after conception is human chorionic gonadotropin (hCG) then followed by hormones include estrogen, progesterone, prolactin, renin and human placental lactogen. It is also worth mentioning that adequate levels of circulating thyroid hormones are of primary importance for normal reproductive function, all these changes are accompanied by growing uterus with gradual mechanical effect.

Metabolic changes are also due to an increased insulin production, and pregnancy is associated with insulin resistance caused predominantly by human placental lactogen. This facilitates placental glucose transfer and any carbohydrate load will cause a greater than normal increase in plasma glucose.

Plasma volume increases progressively throughout normal pregnancy; most of this 50% increase occurs by 34 weeks' gestation and is proportional to the birth weight of the baby. Because the expansion in plasma volume is greater than the increase in red blood cell mass, there is a fall in haemoglobin concentration.

Changes in the coagulation system during pregnancy produce a physiological hypercoagulable state. The concentrations of certain clotting factors, particularly VIII, IX and X are increased. Fibrinogen levels rise significantly by up to 50% and fibrinolytic activity is decreased. Concentrations of endogenous anticoagulants such as antithrombin and protein S decrease. Thus, pregnancy alters the balance within the coagulation system in favour of clotting.

During pregnancy renal vasodilatation increases renal blood flow early during pregnancy, this increase cardiac output (CO), GFR and renal plasma flow (RPF) by 50%, also an increase in Renin & Aldosterone level promotes Na⁺ retention leading to volume overload.

The kidneys face remarkable demands during pregnancy, GFR rises early to a peak of 40% to 50% that of pre-pregnancy levels, resulting in lower levels of serum creatinine, urea, and uric acid. There is a net gain of sodium and potassium, but a greater retention of water, with gains of up to 1.6 L.

Clinicians should be aware of the role of pregnancy specific reference ranges and how these can assist correct diagnosis and management in pregnancy. Appropriate pregnancy reference intervals help clinicians to avoid interpreting normal results as pathological and help them to identify when results are truly abnormal.

REVIEW

Tests included in the first antenatal screen

- Complete blood count
- Blood group and antibody screen
- Rubella antibody status
- Syphilis serology
- Hepatitis B serology
- HIV

Although the first antenatal screen usually occurs early in pregnancy, it may be requested at any stage of pregnancy, i.e., if a woman presents for the first time late in pregnancy, she should still receive a first antenatal screen.

Complete blood count

Anaemia is most common medical disorder especially in underdeveloped countries which

increases maternal morbidity and mortality; it is well accepted that there are three main causes:

- Decreased erythrocyte production as in iron, vitamin B₁₂ and folate deficiency.
- RBCs destruction as in hemoglobinopathies.
- RBCs loss as in any haemorrhage.

Gestational age should be considered when assessing haemoglobin, as levels decrease during pregnancy due to haemodilution caused by increased plasma volume. The lower limit for haemoglobin is usually 12 g/dL, but for pregnant women the lower limit is usually reported as 10 g/dL.

Pregnancy causes a two- to three-fold increase in the requirement for iron, not only for haemoglobin synthesis but also for the foetus and the production of certain enzymes. There is a 10- to 20-fold increase in folate requirements and a two-fold increase in the requirement for vitamin B₁₂.

The platelet count tends to fall progressively during normal pregnancy, although it usually remains within normal limits. In a proportion of women (5–10%), the count will reach levels of 100–150 × 10⁹ cells/L by term and this occurs in the absence of any pathological process

Blood group and antibody screen

Identifying ABO blood group, rhesus D status and red cell antibodies in pregnant women is important to prevent “haemolytic disease of the new-born” in subsequent pregnancies. If the foetus is rhesus D-positive (and the mother is negative), the mother may form anti-D antibodies, which may affect a subsequent rhesus D-positive foetus. Haemolytic disease of the new-born in subsequent pregnancies.

Recently Non-invasive prenatal genetic testing (NIPT) is used to determine foetal rhesus D status and prevent rhesus D negative mothers from undergoing unnecessary prophylactic treatment, this allows to prevent the risk of

foetal anaemia and haemolysis when the mother is serologically RhD negative and the foetus is RHD positive.

Rubella antibody status

All pregnant women should be screened for rubella antibodies. Congenital Rubella Syndrome occurs when the rubella virus infects the developing foetus, especially during the first trimester when up to 90% of affected infants will be born with a birth defect, e.g. deafness, eye defects, heart defects, mental retardation. The risk of birth defects is decreased when infection occurs after 20 weeks' gestation.

The aim of screening is to identify women who have not been immunized or have diminished immunity and are susceptible to contracting rubella, so they can be immunized in the post-natal period to protect future pregnancies. Rubella antibody titers should be measured in each pregnancy as levels may decline and fall below protection levels.

Syphilis serology

All pregnant women should be screened for syphilis, mothers infected with syphilis can experience long-term morbidity and the complications for pregnancy are significant; 70 to 100% of infants will be infected and one-third will be stillborn.

Treponema Elisa Screen assay is used to screen for syphilis as this can detect primary or secondary infection.

Hepatitis B serology

Up to 85% of infants born to mothers infected with hepatitis B (particularly mothers who are HBeAg positive, i.e. with active infection), will become carriers and will be more likely to develop chronic liver disease, including cirrhosis, liver failure or liver cancer. Transmission of the hepatitis B virus from mother to infant can be

prevented by administration of the hepatitis B vaccine and immunoglobulin to the infant at birth, therefore screening is important.

HIV screening

All pregnant women should be screened for HIV. Women who are HIV positive can be given treatment to reduce the risk of HIV being transmitted to their infant (risk reduced from 32% to less than 1%). Interventions to reduce mother-to-child transmission of HIV infection include antiretroviral therapy, elective caesarean section delivery and the avoidance of breastfeeding.

If a patient is considered at risk for HIV, hepatitis C screening should also be considered.

Additional testing in early pregnancy

Consider checking varicella antibody status in pregnant women with no (or uncertain) history of illness (i.e. chicken pox or shingles) or vaccination. Contracting varicella during pregnancy is associated with a significant risk of harm to both mother and infant.

Testing for chlamydia and gonorrhoea should be considered for those who may be at increased risk based on age (e.g. less than 25 years) and sexual history.

Vitamin D is required for normal bone growth development in the foetus. Mothers with known vitamin D deficiency or at risk for deficiency (e.g. dark-skinned women, women who wear a veil) should receive vitamin D supplementation.

Blood tests included in the second antenatal screen

At 26–28 weeks' gestation, a second round of blood tests, commonly referred to as the second antenatal screen includes:

- 50 g glucose tolerance test (the "polycose" test)
- CBC
- Blood group antibodies

Screening for gestational diabetes

Gestational diabetes affects 5–8% of pregnant, it is recommended that testing for gestational diabetes occurs for all women between 26 and 28 weeks of gestation.

A 50 g glucose tolerance test (the polycose test) is used to screen for gestational diabetes. A 50 g glucose load is given to the non-fasting patient, and a glucose level is determined after one hour. Women with an elevated result should be followed up with a 100 g oral glucose tolerance test (OGTT).

Repeat CBC and antibody screening

The CBC should be repeated at 28 weeks' gestation, to check haemoglobin and platelet levels (see commentary in previous section on how to interpret and manage these levels in pregnancy). Antibody screening should also be repeated at 28 weeks' gestation.

Proteinuria in pregnancy can also be a sign of preeclampsia if it's accompanied by high blood pressure. Preeclampsia is a condition that only occurs in pregnancy and causes high blood pressure. It usually occurs after week 20 of pregnancy and can happen in women who didn't have high blood pressure before pregnancy. It can lead to serious complications with mother and baby that can sometimes be fatal.

Additional tests during pregnancy

Sub-Clinical urine infection

It is recommended that all women have a mid-stream urine culture at the time of the first antenatal screen, again at the second antenatal screen and then at 36 weeks' gestation, to exclude a sub-clinical urine infection (asymptomatic bacteriuria).

Screening for Group B streptococcus

Group B streptococcal (GBS) infection is a significant cause of serious neonatal infection.

Approximately 15–25% of women will be carriers, and one in 200 of these women will have infants who develop neonatal sepsis.

Women may have a vaginorectal culture collected at 35 to 37 weeks' gestation.

Testing for Down syndrome and other genetic conditions

Screening for Down syndrome, other chromosomal abnormalities and neural tube defects is recommended to all pregnant women above the age of 35 years.

First trimester screening is based on the combination of results of the following:

The PAPP-A and β hCG tests must be taken between nine and 13 weeks' gestation (ideally between 10 and 12 weeks), and the NT scan carried out after 11 and before 14 weeks' gestation.

Second trimester screening can be offered to all women who present after 14 weeks' gestation but before 20 weeks, who have not completed first trimester screening (bloods are ideally taken between 14 to 18 weeks gestation). This serum screen measures β hCG, alpha-fetoprotein (AFP), unconjugated estriol (μ E3), and inhibin A.

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