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Case Report

Unusual false-negative serum human chorionic gonadotropin detected by qualitative immunoassay: A case report of two Iraqi women

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Abstract

Human chorionic gonadotropin (hCG) is a human pregnancy hormone that plays a crucial role in the promotion, maintenance, and establishment of pregnancy. Measurement of hCG in early pregnancy is the first and most common test. Blood is considered to have more concentration of hCG than urine, so early detection of pregnancy test is more advised in serum than urine, but this study showed two Iraqi pregnant women with false-negative hCG result in the blood, whereas it was positive in urine, with persisting pregnancy symptoms. This study is considered the first report regarding this finding. In spite of hCG in serum being regarded the most standard test for pregnancy, the results of this study call for attention to the importance of early diagnosis of pregnancy through test in urine, and it must be made compulsory to avoid risks toward pregnant women and fetus with false-negative hCG result in serum.

Keywords: false-negative human chorionic gonadotropin, human chorionic gonadotropin, qualitative immunoassay, rapid human chorionic gonadotropin immunoassay

Introduction

Human chorionic gonadotropin (hCG) is the fundamental investigation for identification of early pregnancy as well as certain early complications. hCG is a glycoprotein with two asymmetrical subunits called alpha and beta that are joined with noncovalent bonds. In blood and urine, there are many variants of hCG, as intact hCG as well as free alpha and free beta subunits [1].

hCG has special features that recognize it from other hormones as strong acidic glycoprotein with large sugar proportion; in addition, it has many functions that control pregnancy and cancer [2].

As hCG is made by cells found in the placenta, it is called the human pregnancy hormone, which maintains and nourishes the fertilized egg in the uterine wall. The level of hCG in serum and urine is increased highly through the first trimester of pregnancy and then declines.

Case report

In October 2018, two women attended a private laboratory in Babil, Iraq, for pregnancy tests. The first woman was a 31-year-old health worker, whereas the other was a 26-year-old housewife. The two cases were observed by chance when the women attended the private laboratory for hCG test in urine sent by a gyno-doctor, with 5 weeks after the last conception. Pregnancy test was done in urine by a standard qualitative hCG immunoassay by two diffrent kits 'CTK biotec': Hannover, Germany and 'ACON Laboratories': San Diego, USA. The result was positive in urine.

Then after a few days, the same women returned to the laboratory for molar pregnancy and diluting serum hCG test. An unusual and unexpected result was reported, as absolute negative result in the blood. Serum was then tested again with

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the same kits used previously in the urine test with the same result. Urine was obtained from the women again for hCG test, and the result was positive in the urine.

Clear pregnancy symptoms appeared in the two pregnant women, such as amenorrhea, nausea, and vomiting, whereas negative serum HCG result persisted at that stage. Ultrasound and color Doppler examination confirmed that the uterus is gravid with a normal pregnancy fetus at 5 weeks and 4 days. At 8 weeks of pregnancy, the ultrasound showed positive cardiac action. At 14 weeks, active fetal movement, breech presentation, a normal amount of amniotic fluid, fetal sex was male for first case and female for the second case, and also no gross congenital abnormalities for both fetuses were reported.

The test was repeated until 2 months of pregnancy, and positive hCG result in urine and false-negative result in serum for both cases persisted. Some other tests were done, such as complete blood count, blood group type, Rubella test, urine culture, urinalysis, hepatitis B and C, sexually transmitted infections such syphilis, and all these investigations were normal or negative; moreover, Cytomegalovirus (CMV), and toxoplasma tests were done. Follow-up pregnant women ended until delivery to provide information about the health of mothers and fetuses development. Male and female babies were in good health for the first and second cases, respectively. All information included in this study was obtained from the two pregnant women with complete agreement.

Discussion

Point-of-care testing for quick pregnancy detection in a mature female is common in health care units and emergency. Rapid hCG commercial immunoassay is available in both blood and urine. Blood hCG is regarded as the gold standard test to detect early pregnancy test and is more accurate than urine because early hCG level is higher in serum than urine in the first days after fertilization, although false-positive results have been detected in blood for many reasons, such as prostate cancer, malignancy tumors, pituitary hCG, biochemical hCG, as well as heteroantibodies, but in these two case reports, urine hCG was positive, whereas serum was negative.

A study in Belgium among 20 acute care hospitals showed there were no false-positive results in urine to detect the accuracy of qualitative urinary hCG assays [3].

Many studies mentioned that false-positive results of hCG in urine are not recorded, which agrees with this study. Some searches showed false-negative urine hCG result because of elevated levels of beta-core fragment hCG in urine samples [4]. Another study revealed that rapid test of urine qualitative hCG immunoassays may not be preferred in the presence of markedly high hCG levels presented in molar pregnancy [5].

Many molecules of hCG and related forms are observed in urine and serum of pregnant women such as nicked hCG, not a nicked hormone, hCG without C-terminal, free beta subunits, free alpha subunits, and beta core fragments [6]. Depending on the differences in hCG forms, tests detecting pregnancy in urine as a qualitative immunoassay must have the ability to capture several types of hCG molecules, and this will provide a more accurate and sensitive assay for a pregnancy test in urine samples [7].

Heterothallic antibodies were responsible for the false-positive results in 12 women diagnosed as having post-gestational choriocarcinoma based on persistently positive hCG test results without pregnancy. Diagnosis of choriocarcinoma must be modified to include a compulsory investigation of hCG in urine [8], to reflect the role of hCG urine to detect false-positive result in serum owing to heterothallic antibodies.

Conclusion

As false-negative pregnancy test result in the blood (serum or plasma) may have dangerous outcomes and serious risks of pregnant and fetal mortality and morbidity, this finding highlights the value of early detection of pregnancy test in urine that must be compulsory to prevent and avoid unexpected risks. Hence, repeating the pregnancy test in urine in spite of negative results in blood should be tried in all cases where pregnancy is likely but the pregnancy test remains negative. Early uterine scan is very important in such a case because some pregnancy investigations may not test all variants of hCG, and therefore show false-negative results. More studies with a large number of samples are required to prove this finding by comparing all tests in serum with urine, and this may open a new window of discovery regarding hCG never seen before by understanding the accurate causes beyond hCG positivity in urine and negativity in serum.

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Conflicts of interest

There are no conflicts of interest.

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