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Original Article

How accurate are placental growth factor, urate, lactate dehydrogenase and proteinuria in diagnosing preeclampsia and its severity?

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ABSTRACT

Objective: The objective was to assess the diagnostic accuracy of serum and urinary placental growth factor (sPlGF and uPlGF, respectively), urate, lactate dehydrogenase (LDH), and proteinuria for diagnosing and differentiating between women with preeclampsia and women with a normal healthy pregnancy, gestational hypertension, and gestational proteinuria.

Study design: Urine and blood samples were taken from pregnant women diagnosed with late-onset severe preeclampsia (30 patients), mild preeclampsia (30 patients), gestational hypertension without meeting the criteria for preeclampsia (30 patients), gestational proteinuria without meeting the criteria for preeclampsia (30 patients), and healthy pregnant control women (30 patients). A receiver operating characteristic (ROC) curves analysis was performed to evaluate the diagnostic accuracy and to select the optimal cutoff points for different markers.

Results: sPlGF is the best test for differentiating women with severe preeclampsia from women in all of the other groups ($p = 0.001$). However, there was no significant difference between sPlGF and proteinuria in the 24-h urine collection ($p = 0.329$) in this differentiation. uPlGF can be used to differentiate women with severe preeclampsia from women in all of the other groups. However, proteinuria in the 24-h urine collection is better than uPlGF for this differentiation ($p = 0.013$).

Conclusion: sPlGF and uPlGF can be used to diagnose women with severe preeclampsia and should be considered at least as important as proteinuria in the diagnosis of preeclampsia. A large study that considers the cost-effectiveness of adding these markers to the diagnosis of preeclampsia should be conducted before our recommendation is applied.

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Introduction

Preeclampsia remains a potentially serious complication of pregnancy that is responsible for a significant amount of maternal and perinatal morbidity and mortality worldwide [1,2].

The etiology of preeclampsia remains elusive, although the leading theory is that defects in placental implantation and function ultimately manifest as the development of preeclampsia [3]. Consequently, much effort has been directed toward the identification of maternal serum and urinary manifestations of altered placental function to aid the prediction and diagnosis of preeclampsia [4–7].

Researchers have examined various placental markers to determine whether they may be of value in the prediction and diagnosis of preeclampsia [4–10]. Placental growth factor (PlGF) is an important regulator in the human placenta and can be isolated from the maternal circulatory system and maternal urine [4–10]. Changes in the circulating concentrations of this and other factors may represent abnormal placental development in preeclampsia. In fact, decreased concentrations of circulating free PlGF have been found during clinical preeclampsia and before the onset of preeclampsia [6,7]. Hyperuricemia is associated with a diagnosis of preeclampsia, and this condition characterizes a population that is prone to adverse maternal and fetal outcomes [11]. No randomized trials have been conducted that compare the diagnosis of various hypertensive conditions of pregnancy using different placental markers to the gold standard diagnostic tool.

Aim of the study

The primary outcome measure was the assessment of the accuracy of serum PlGF (sPlGF), urinary PlGF (uPlGF), urate, and lactate dehydrogenase (LDH) in the diagnosis of and differentiation between women who have been diagnosed with late-onset severe preeclampsia (>34 weeks) and those with a normal healthy pregnancy, gestational hypertension, and gestational proteinuria and mild preeclampsia after 34 weeks of gestation. The secondary outcome measures included the ability to use the above-mentioned markers to determine the adverse maternal and fetal outcomes (cesarian section and preterm birth).

Materials and methods

This study was performed at the Security Forces Hospital (SFH), which is a tertiary care hospital in Riyadh, Saudi Arabia, between November 2010 and November 2012.

The study was approved by the scientific and ethics committee of the hospital. This study involved 254 pregnant women. All of the patients received antenatal care and were delivered at SFH. The gestational age was confirmed based on the menstrual date and/or ultrasonographic examination prior to 20 weeks' gestation.

Urine and blood samples were taken from 30 patients who had been diagnosed and admitted with late onset severe preeclampsia (all of the cases were between >34 and ⩽38 weeks' gestation).

Urine and blood samples were also taken from the other 224 pregnant women at the same gestational age as the severe preeclampsia patients (>34 to ⩽38 weeks' gestation). Women who had already been diagnosed with mild preeclampsia (mPE; 30 women), gestational hypertension that did not meet the criteria for preeclampsia (30 women), or gestational proteinuria that did not meet the criteria for preeclampsia (30 women) and healthy pregnant control women (30 women) were also included in our study.

The exclusion criteria included any patient whose diagnosis had been changed or upgraded from one of the above five groups to another group. The exclusion criteria also included any patient who delivered at <37 weeks except in cases of severe preeclampsia, patients with multiple pregnancies, patients with IUGR or IUFD in all groups except the sPE group, patients with known chronic hypertension and/or renal disease, and patients with structural or chromosomal anomalies detected in utero or after birth.mPE was defined according to well-established criteria: blood pressure of at least 140/90 mmHg on at least two occasions 4–6 h apart and urinary excretion of at least 300 mg of protein in 24-h urine specimens [12,13] after 34 weeks of gestation.

Blood pressure measurements were performed using a mercury sphygmomanometer, and the Korotkoff V was used to determine the diastolic pressure [13].

Late-onset (>34 weeks of gestation) sPE was defined as preeclampsia in addition to a blood pressure of at least 160/110 mmHg on at least two occasions 4–6 h apart, proteinuria of more than 5 g in a 24-h urine volume, and/or persistent 3 + proteinuria on dipstick testing [12]. Other diagnostic criteria for sPE included intrauterine growth restriction (less than the 5th percentile, with or without reversed or absent uterine artery end-diastolic flow), persistent cerebral or visual disturbances (e.g., headache and vision changes), epigastric or right-upper-quadrant pain, pulmonary edema, oliguria (urinary output of less than 500 mL per 24 h), altered liver function tests (aspartate aminotransferase [AST] and alanine aminotransferase [ALT], more than twofold higher than normal), and/or thrombocytopenia (less than 100,000 cells/μL) [12,13].

Gestational hypertension was diagnosed if the patient exhibited hypertension and no other signs or symptoms to suggest preeclampsia [12].

Gestational proteinuria was defined as proteinuria of more than 300 mg of protein in a 24-h period of urine collection without other signs or symptoms to suggest preeclampsia [12].

The healthy pregnancy controls were defined as those patients with term delivery and with no history of illness, no documented concerns of hypertension, no renal disorder, and no proteinuria before or during the current pregnancy. Moreover, they also had no gestational diabetes, no preterm labor, and no growth restriction during the current pregnancy.

All biological samples (serum and urine) were collected in a serum separator tube at >34 to ⩽38 weeks of gestation before the patient received any medication, such as fluids, antihypertensive drugs, or magnesium sulfate. All of the participants provided informed consent.