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Original Research Article

PIGF and Pre-eclampsia Risk in a Group of Iranian Pregnant Women

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Abstract

Pre-eclampsia is an abnormal situation, characterized by hypertension and proteinuria in pregnancy due to widespread endothelial dysfunction. This disorder is a major cause of maternal morbidity and mortality in worldwide. Pay attention to significant incidence of pre-eclamptic toxaemia (PET) in pregnancy -as a physiologic phenomenon-, research about pathophysiology and invent of tests for early detection is important in Primary Health Care. Amongst, studies have been shown role of some angiogenic factors such as VEGF, PIGF (Placental Growth Factor) … in pathogenesis of PET. Many of these studies have indicated alleviation of VEGF and PIGF level in maternal blood circulation. These factors play a role in placental vessels development. In fact, serum that is got patients with disorder induces many physiological changes in endothelial cells indicating the presence of a circulating imbalance. Judging from these reasons, we examined relation between PIGF and PET risk in pregnant women. We studied 96 pregnant women (with one risk factor such as first pregnancy…) which were referred to Imam Hussein Hospital, SBMU, Tehran. In this study, PET has been associated with low levels (< 100 pg/mlit) of PIGF (P-value=0.007). Our study supports possible role of PIGF in pre-eclampsia occurrence. Results of this and other similar studies may use establishing early diagnosis test for PET. This can help to decrease maternal and neonatal morbidities and mortality.

Keywords: PIGF (Placental Growth factor), Pre-eclampsia, Pregnancy

INTRODUCTION

Pre-eclampsia occurs in 5-10 percent of pregnancies. It is one causes of maternal mortality alongside infection and vaginal bleeding (Khan et al., 2006; Campbell et al., 2006). Pre-eclampsia is one type of hypertension (HTN) (with undesirable effects on organs) in pregnancy (Airoldi and Weinstein, 2007; Lindheimer et al., 2009). This condition is detected with blood pressure≥ 140/90 along with proteinuria ≥300mg/24h or presence of 30mg/dlit protein (1positive in dips Tick) in urine sample (Organization, 2005). Higher levels of urine protein or higher increased blood pressure, also headache and epigastric pain help to diagnosis, reliably. Although, 10% of cases occur as Atypical type without HTN and proteinuria and with other complications (Lindheimer et al., 2009). Young women with first pregnancy often lay low with PET (3-10 percent), but in older women disorder might be accompanied with chronic hypertension. Some risk factors besides the maternal age (adolescents or older than 35 years) include: African-American race, genetics, obesity (Nilsson et al., 2004). Clinical manifestations of this disorder include maternal cardiac, renal and liver dysfunction also fetal IUGR, placenta abruption and fetal death (Walker, 2000; Maternal Consortium, 1999). There isn't definite diagnosis test about it, now. Many studies have been done inventing a screening test such as angiogenic factors e.g. PIGF.

Table 1. Number of pregnant women with different levels of serum PlGf. In this table 100pg/mlit has been used as the cut off.

PlGF	Frequency	percent	Total
≤ 100 pg/mlit	31	32.29	31
> 100 pg/mlit	65	67.7	65
Total	96	100	96

Table.2. Relation between serum levels of PlGF and pre-eclampsia in pregnancy. In this table, levels of studied factor have been associated with PET. In fact, many of patients (n=7) were with levels **≤ 100 pg/mlit.** Three of them were with **> 100 pg/mlit.** Statistical analysis showed significant difference in levels ≤100pg/mlit and PET in patients and non-patients. (P-value=0.007).
P-value<0.05 is significant.

	Pre-eclampsia				P-value : 0/007	
PlGF	**Yes**		**NO**		**Total**	
≤ 100 pg/mlit	22/6%	7	77/4%	24	100%	31
> 100 pg/mlit	%4/6	3	95/4%	62	100%	65
Total	10		86		96	

PlGF is increased constantly along pregnancy, peaked at 28-32 weeks and then decreased. . Several studies have shown levels of PlGF< 42pg/mlit in 15-18 weeks or PlGF< 100pg/mlit in 20-22 weeks may increase risk of pre-eclampsia (Maynard et al., 2003). Therefore, determination of levels of PlGF early in pregnancy in serum may help to predict risk of PET (Stepan and Faber, 2006; Troisi et al., 2003).

PlGF

Placental growth factor is a protein that is encoded by the *PGF* gene and is located on14q24.3 (Maglione et al., 1993). Alternatively spliced transcripts encoding different isoforms have been found for this gene. Placental growth factor (PGF) is a member of the VEGF (vascular endothelial growth factor) sub-family - a key molecule in angiogenesis, during embryogenesis. The main source of PGF during pregnancy is the placental trophoblast.

MATERIALS AND METHODS

In this research, we studied 96 Iranian pregnant women referred to the Imam Hossein Hospital of SBMU, Tehran, Iran. In this Prospective Cohort study, patients were selected in 15-22 weeks of pregnancy with one of risk factors included: first pregnancy, chronic hypertension, chronic kidney disease, diabetes mellitus, previous PET, obesity, age less than 18 or more than 35, previous fetal death, mole hydatid form and systemic lupus erythematous. Information about goals and performance details were explained for patients and all subjects participated with informed consent. Peripheral blood samples of patients were prepared in non-heparinized tube, then, measurement of serum levels of PlGF was done by IBL kits (TECAN Company). We used PlGF levels= 100pg/mlit as a cut off that means levels≤100pg/mlit were supposed with increased risk of PET. All of subjects were followed up and presence of PET, delivery condition, age and weight of neonate recorded. Also, patients were followed in postpartum period by visiting regularly and assessing the sign and symptoms of postpartum preeclampsia till 6 weeks. Unprepared data were analyzed with SPSS software. P-value<0.05 was considered significant.

RESULTS

At first, we selected 100 pregnant women, but four of them were excluded because of spontaneous abortion and end of pregnancy for Down syndrome. Finally, participants group included to: 54 of them > 35, 2 of them < 18, 54 with first pregnancy, eight with Diabetes mellitus, nine of them with chronic hypertension and four with previous fetal death. After, evaluation of PlGF levels; among all 31 of pregnant women had ≤ 100pg/mlit. There were 10 patients with the diagnosis of PET at the time of termination with term fetus, seven with ≤ 100pg/mlit and three of them with >100 pg/mlit. That is to say, in our study prevalence of PET was 10%. Collected data has been shown in table 1 and table 2. Also, this study showed differences of PlGF amounts increase (raise or decrease) along of pregnancy by term of pregnancy (Figure 1.) although, there is not significant conclusion (P-value=0.339).

Also, we analyze sensitivity and specificity of PlGF on ROC curve. If the levels of PlGF would be 90-94 pg/dlit, sensitivity of test is 96%. But, specificity is low (Figure 2).

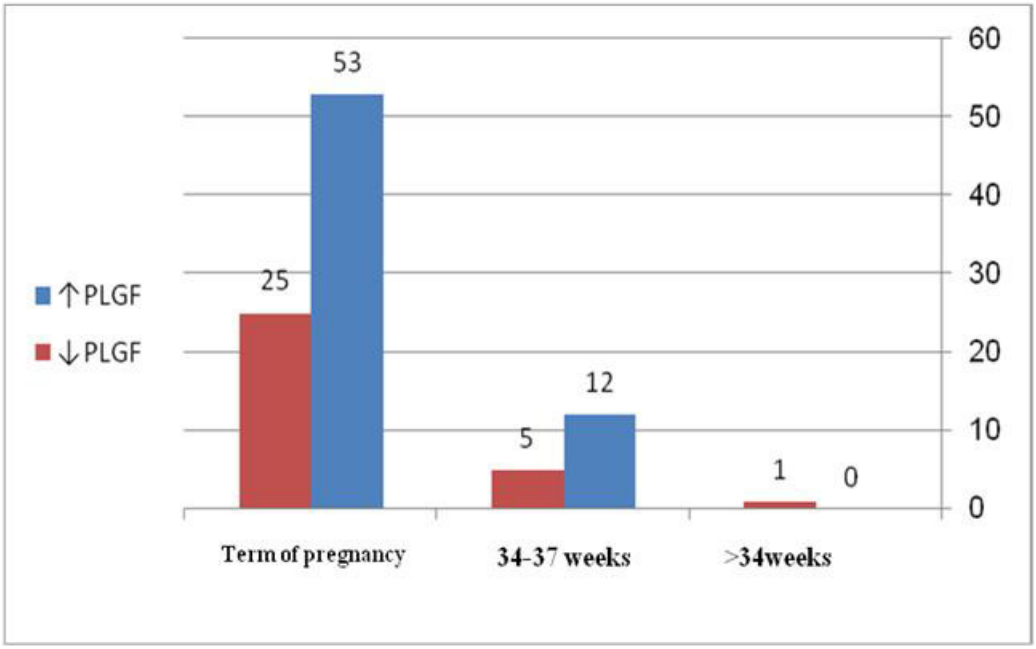

Figure 1. Relation between differences of serum PlGF levels with age of pregnancy. Variations had increased with development of pregnancy.

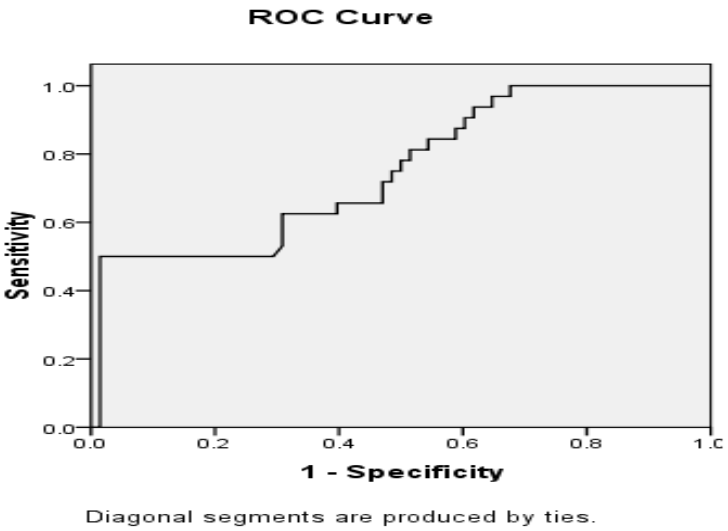

Figure 2. ROC curve for specificity and sensitivity of PlGF test.

DISCUSSIONS

Pre-eclampsia is considered as a dangerous position with or without chronic hypertension. Considering, PET is a major cause of prenatal morbidity and mortality all of the world, detection of pathophysiology and on time control of this disease is important. By now, there is not confident and inexpensive predictive test. Therefore, invention of early predictive test is important. In fact, this is major reason of do this study. As it was said, prevalence of PET in our study was 10%. This finding is agreed with other studies (3-10%) (Al-Jameil et al., 2013). E.g. in Tehran (2010) occurrence of disorder has been 4.6% (Rajaee et al., 2015). Although, similar study in Kerman showed 0.3% of pre-eclampsia prevalence in 2004 (Aali et al., 2004).

In our study, seven of ten patients had low levels of PlGF (≤100pg/mlit). Similar results were achieved with Rebeca Triosi. In this study, pre-eclampsia was associated with decreased levels of PlGF in second half of pregnancy. In another cohort study in India (2011) 110 of 218 pregnant women with PET had decreased

amounts of PlGF (P-value<0.001) (Nanjundan et al., 2011). In Harvard University, Rana studied 616 with suspected pre-eclampsia (2012). Finally, cases with lesser amounts of PlGF were associated with poor prognosis (P-value=0.0001) (Rana et al., 2012).

In some recent studies, antiangiogenic factors (such as SFLT-1) have checked in conjunction with PlGF. E.g. Widmer (2007) showed relation between increased levels of SFLT-1 and decreased amounts of PlGF and pre-eclampsia occurrence (Widmer et al., 2007). In a retrospective study by H.Stepan on German pregnant women, similar result has been achieved (Stepan and Faber, 2006). Judging from the maternal and neonatal serious consequences of PET, with any etiology, early detection of disorder will be effective on Primary Health Care (PHC).

In conclusion, our study result supports from a significant association with decreased levels of PlGF and pre-eclampsia happening (P-value=0.007). Despite of the limitation of our study which was the small sample size, this study shows high sensitivity of test. Therefore, this test may do as a powerful predictive test (96%), although specificity of this is low.

Considering similar results of different studies about low levels of PlGF and pre-eclampsia occurrence denote power of this item check as a predicative test. But, these results must be confirmed with further researches with larger sample sizes as well as meta-analysis studies. Also, study of PlGF linked with other angiogenic and anti angiogenic factors will be advantageous.

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