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Original Research Article

Serum human pregnancy specific glycoprotein 1 in pregnant women with preeclampsia in comparison with normal pregnancy

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ABSTRACT

Objectives: To compare the serum pregnancy specific glycoprotein 1 values of women with preeclampsia with the values of healthy pregnant women.

Materials and Methods: A total of 90 pregnant women, whom were recruited during their antenatal care visits to the obstetrical department in Hospital, were included. They were divided into two groups: 45 women with diagnosis of preeclampsia and 45 controls who were the women with healthy pregnancy. Blood samples were collected from both groups and the measurement of pregnancy specific glycoprotein 1 was done using an enzyme immunometric assay.

Results: The groups of preeclampsia pregnant women had markedly lower pregnancy specific glycoprotein 1 than the women with the uneventful pregnancies (9.8±3.8 vs 14.3±6.0 ng/ml; p value <0.001). Pregnancy specific glycoprotein 1 can significantly predict preeclampsia (P value <0.001) with an odds ratio of 0.839 and 95% confidence interval of 0.763 – 0.924. By application of receiver operating characteristic curve analysis, it was observed that the cut-off value of pregnancy specific glycoprotien1 for predicting preeclampsia was 10.4 ng/ml with 77% sensitivity and 60% specificity, the area under the curve 0.728 with 95% confidence interval between 0.622 and 0.835, P value < 0.001.

Conclusion: Pregnancies complicated by preeclampsia are associated with decreased maternal serum level of pregnancy specific glycoprotien. This abnormally decreased levels of might be a reflection of stressed or dysfunctional syncytiotrophoblasts, which is related to the pathogenesis of this placental disorder.

1. Introduction

Preeclampsia [PE] is a multiple system pathology of pregnancy defined previously as hypertension associated with proteinuria after 20 weeks of pregnancy.[1,2] Across years, the definition of Preeclampsia has been change,[3] and currently, definition of PE according to the International Society for the Study of Hypertension in Pregnancy (ISSHP) which embraces new onset hypertension associated with one features or more : proteinuria, maternal organ dysfunction (kidney, liver, nervous system organs), hematological disorder, and/or uteroplacental impairement.[4]

Pregnancy-specific glycoproteins (PSGs), known as Schwangerschafts Protein and pregnancy-specific beta 1 glycoproteins, are a family of soluble proteins released by the placental syncytiotrophoblasts during pregnancy.[5] Structurally PSG is a protein of more than 30 molecular forms, including precursors, glycoisoforms, and catabolic products.[6] Eleven glycoproteins can be referred to as PSG, the protein part of each consist of a single polypeptide chain of 37 to 49 kDa molecular weight. The carbohydrate

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part represent by 21 to 32% of the total protein molecular weight.[7]

PSGs have been detected as early as 3 days post-fertilization in the maternal serum, with the attachment of the blastocyst to the uterine wall,[8] and then the level increases gradually and reaches to the level of 200 400 μg/mL in the third trimester, while in the fetal serum, its level does not exceed 1-2 μg/L.[7]

PSGs can control the secretion of proangiogenic factors, TGF-β1 and VEGF A, by various types of cell included in placental development.[9] The provision of an immunomodulator environment and The stimulation of angiogenesis in the maternal–foetal interface indicate that PSGs are effective in progress of pregnancy and successful outcomes. Studies Previously have revealed that the level of PSG is abnormal in complicated pregnancies and illustrate the role of this protein for protect healthy pregnancies so, it is clear that the PSG level in serum diminished with complicatied pregnancy outcome abortion, ectopic pregnancy, fetal hypoxia and intrauterine growth retardation.[7,9] The study aim is to detect the relationship between PSG levels and preeclampsia by comparing serum PSG levels between pregnant with preeclampsia and normotensive healthy pregnants, and since the PSG1 mRNA is fairly expressed highly compared with other PSGs in the pregnancy first trimester and in the term placenta.[10]

2. Materials and Methods

A 90 pregnant women involved in a case –control study whom were recruited during their antenatal care visits to the obstetrical department in Hospital. The study performed from first of February 2022 to end of January 2023. The study was accepted by the scientific council of Obstetrics and Gynaecology of the Arab board for health specialization and the Health authority of the aforementioned hospital.

The participants were pregnant women in their third trimester whom were informed about the nature and purpose of the study and were consented to participate. These women were interviewed and underwent clinical and laboratory evaluation for diagnosis of PE and to ensure their eligibility to the study.

The participants (90 women) were divided into two groups:

The cases who were the pregnant women with diagnosis of PE.

The controls who were the pregnant women with healthy pregnancy.

Each group consisted from 45 women who were matched by gestational age.

The inclusion and exclusion criteria

Pregnant women aged more than 17 years and less than 40 years old, with single viable pregnancy and GA 28-36 weeks were included in the study.

The presence of diabetes, gestational diabetes, chronic hypertension, renal parenchymal disease (nephrotic syndrome, nephritis, renal failure,… etc.), liver disease (fatty liver disease, viral hepatitis, autoimmune hepatitis, cholestasis,… etc.), haemolytic anaemia (thalassemia, spherocytosis,.. etc.), thrombotic or thromboembolic disease and/or HELLP syndrome render the women ineligible for the study.

History, Physical examination with laboratory evaluation and Ultrasound (US) assessment done to all women included;

PE is diagnosed according to the criteria set by FIGO, ISSHP and USPTF[2,5,6] as the following:

The presence of gestational hypertension plus one or more of the following new onset conditions at or after 20 weeks of gestation:

1. Proteinuria: the presence of any of the following ≥ 30 mg/ml protein : creatinine ratio; ≥ 300 mg/24 hour; ≥ 2 + dipstick.
2. Maternal organ dysfunctions: which include:
   Acute kidney injury: elevated serum creatinine ≥ 90 μmol/L or ≥ 1 mg/dL.
   Liver involvement: elevated ALT and AST >40 IU/L, with or without right upper quadrant or epigastric abdominal pain;
   Neurological complications: e.g. blindness,persistent visual scotomata, altered mental status, clonus and severe headaches, iv. Hematological complications: hemolysis, thrombocytopenia (platelet count <150000/μL) and DIC.
3. Placental- Utero impairment: like Stillbirth, umbilical artery Doppler waveform analysis Abnormality, Fetal growth restriction.

2.1. PSG1 measurement

Venous blood was collected from participants whom were diagnosed with PE and from the gestation-matched controls. The blood was collected in plain tubes, let set for 30 minutes for clotting and then centrifuged for 10 minutes at 3000 rpm. The plasma was then kept at 20°C til the time of labrotary measurment. Serum PSG1 values were detected by using an enzyme immunometric assay kit (catalogue no.: MBS720765) from Mybiosource, Inc. The intra-assay CV ranged from intra-assay: CV <4.4% inter-assay: CV <5.6%. The lower limit of concentration detection was 1.0 ng/mL.

2.2. Statistical analysis

Statistical package version 24 (SPSS 24) was used for the data collection and statistical analysis. The data normal distribution was tested by Kolmogorov-Smirnov test. The data were represented as means and standard deviations (SD), and independent sample T test was used to test their statistical difference, and for the correlation analysis,

Pearson correlation was used. The data which didn't follow normal distribution were represented by medians, and Mann-Whitney U test was used to test the statistical difference, and for the correlation analysis Spearman correlation was used. The binary logistic regression model was used for the calculation of the odds ratio, and the receiver operating characteristic (ROC) curve used to measure the cutoff value for the prediction of PE. The level of significance (P value) was set to be of less than 0.05.

3. Results

The women in this study were divided into two groups: cases and controls, each group consisted of 45 women. Variables like age, GA, BMI, gravidity and parity didn't show significant statistical differences among the study groups where p values were more than 0.05 as shown in Table 1.

Women with PE (the cases) had lower PSG1 levels than the women with the uneventful pregnancies (the controls) as illustrated in Figure 1, by using independent sample T test, it was found that this difference was of statistical difference (p value < 0.001). The comparisons in the mean, SD, minimum and maximum PSG1 values among the study groups are shown on Table 2.

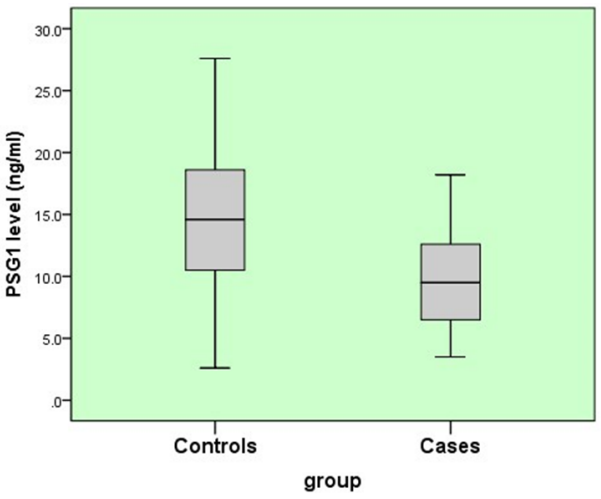

Figure 1: PSG1 levels in both groups of the study

PSG1 levels didn't have any significant correlations with neither the age, BMI, GA, nor the number of parities and gravidities of the women included in the study (P values > 0.05).

Table 3 shows the correlation coefficients and the P values between PSG1 and the other study variables.

From the results of this study, it was found that PE was associated with low levels of PSG1, by application of ROC curve analysis, it was observed that the cut-off value of PSG1 for predicting PE was 10.4 ng/ml with 77% sensitivity and 60% specificity, the area under the curve (AUC) = 0.728 with 95% CI between 0.622 and 0.835, P value < 0.001, as shown in Figure 2, Tables 4 and 5.

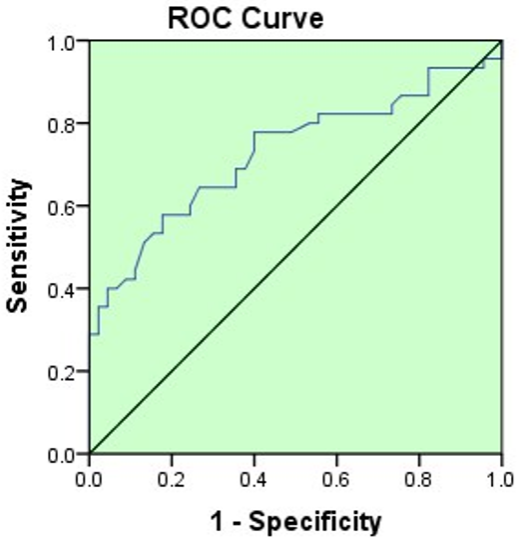

Figure 2: ROC curve of PSG1 for the prediction of PE

Table 1: Comparison between different sample's characteristics

Variable	Cases	Controls	P value
Age (mean ±SD)	25.8 ± 5.6	27.6 ± 5.7	0.154*
BMI (mean ±SD)	26.7 ± 3.0	27.7 ± 2.9	0.122*
Gravidity (median)	3	3	0.698**
Parity (median)	2	2	0.774**
GA at enrollment (median)	34	34	0.941**

*. By independent sample T test
**. By Mann-Whitney U test

Table 2: Comparison in the PSG1 level among study groups

Group	Mean (ng /ml)	SD	Minimum	Maximum	P value
Control	14.3	6.0	2.6	27.6	<0.001*
Case	9.8	3.8	3.5	18.2	

Table 3: The correlation analysis between PSG1 and the study variables

Variable	PSG 1
	Correlation coefficient / P value
Age	0.14* / 0.162
BMI	-0.07* / 0.507
GA at enrollment	-0.15** / 0.150
Parity	0.13** / 0.206
Gravidity	0.16** / 0.117

Table 4: Area under the curve (AUC)

Test Result Variable: PSG1				
Area	Standard Error	P value	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.728	0.054	< 0.001	0.622	0.835

Table 5: The cut-off value of PSG1 for predicting PE

Test Result Variable	Cut-off value (ng /ml)	Sensitivity	Specificity
PSG1	10.4	77%	60%

4. Discussion

This study had found that women with PE had significantly lower PSG1 levels than the women with the uneventful pregnancies (9.8 vs 14.3 ng/ml; p value < 0.001). This finding is similar to that reported by the authors Temur et al. where they reported that the PSG1 level in the maternal serum was significantly lower in patients with PE compared with that of the controls (11.60 vs. 17.58 ng/mL, p value = 0.003).[11] Also, the studies by Rattilla et al. and Tu et al. have also reported that maternal serum levels of PSG1 were lower in patients with PE.[12,13]

The abnormally decreased levels of PSG1 in pregnant women with PE might be a reflection of stressed or dysfunctional syncytiotrophoblasts, which is related to the pathogenesis of this placental disorder.[12]

Pihl et al. in their study had observed that the values of maternal serum PSG1 in the women who developed PE were of no significant difference than those who had uneventful pregnancies which didn't support the result of the current study.[14] The measurement of PSG1 in the study by Pihl et al. was done in the first trimester of pregnancy which could explain the dissimilarities in the results of both studies.

Regarding the correlation analysis, the current study found that PSG1 levels didn't have any significant correlations with neither the maternal age, BMI, GA, nor the number of parities and gravidities of the women included in the study, while in the study by Temur et al. a significant negative correlation was found between PSG1 and the maternal age, they also stated that gravidity of the women in the control group was significantly positively correlated with PSG1 level.[11]

For the prediction of PE, it was observed that PSG1 can significantly predict PE (P value < 0.001) with an odds ratio of 0.839 which mean that with the odds of developing PE is associated with decreased levels of PSG1. By application of ROC curve analysis, it was observed that the cut-off value of PSG1 for predicting PE was 10.4 ng/ml with 77% sensitivity and 60% specificity. In the study by Temur et al., it was also found that PSG1 can significantly predict PE with an odds ratio of 0.926, and the optimal cut-off value of PSG1 for detecting preeclampsia was 11.80 ng/ml with 66.7% sensitivity and 67.5% specificity, which is comparable to that of the present study.[11]

5. Conclusion

From the results of the present study, it could be concluded that pregnancies complicated by PE are associated with decreased serum maternal level of PSG1, and values <10.4 ng/ml can predict the development of PE with 77% sensitivity
and 60% specificity. The abnormally decreased levels of PSG1 in pregnant women with PE might be a reflection of stressed or dysfunctional syncytiotrophoblasts, which is related to the pathogenesis of this placental disorder.

6. Sources of Funding

None.

7. Conflict of Interest

None.

References

1. Burton GJ, Redman CW, Roberts JM, Moffett A. Pre-eclampsia: pathophysiology and clinical implications. *BMJ*. 2019;366:l2381.
2. Poon LC, Shennan A, Hyett JA, Kapur A, Hadar E, Divakar H, et al. The International Federation of Gynecology and Obstetrics (FIGO) initiative on pre-eclampsia: A pragmatic guide for first-trimester screening and prevention. *Int J Gynaecol Obstet*. 2019;145(Suppl 1):1–33.
3. Lowe SA, Bowyer L, Lust K, Mcmahon LP, Morton M, North RA, et al. SOMANZ guidelines for the management of hypertensive disorders of pregnancy 2014. *Aust N Z J Obstet Gynaecol*. 2015;55(5):1–29.
4. Brown MA, Magee LA, Kenny LC, Karumanchi SA, Mccarthy FP, Saito S, et al. Hypertensive disorders of pregnancy: ISSHP classification, diagnosis, and management recommendations for international practice. *Hypertension*. 2018;72(1):24–43.
5. Ballesteros A, Mentink-Kane MM, Warren J, Kaplan GG, Dveksler GS, et al. Induction and activation of latent transforming growth factor-β1 are carried out by two distinct domains of pregnancy-specific glycoprotein 1 (PSG1). *J Biol Chem*. 2015;290(7):4422–31.
6. Moore T, Dveksler GS. Pregnancy-specific glycoproteins: complex gene families regulating maternal-fetal interactions. *Int J Dev Biol*. 2014;58(2-4):273–80.
7. Timganova VP, Bochkova MS, Rayev MB, Khramtsov PV, Zamorina SA. Immunoregulatory potential of pregnancy-specific β1-glycoprotein. . *Med Immunol*. 2021;23(3):455–68.
8. Ha CT, Wu JA, Irmak S, Lisboa FA, Dizon AM, Warren JW, et al. Human pregnancy specific beta-1-glycoprotein 1 (PSG1) has a potential role in placental vascular morphogenesis. *Biol Reprod*.

2010;83(1):27–35.
9. Terentiev AA, Mokhosoev IM, Moldogasieva NT. Pregnancy-Specific Beta-1-Glycoproteins (PSGs): Structure, Functions and Biologically Active Peptides. In: Human Placenta: Structure & Development, Circulation & Functions. United States: Nova Science Publishers Inc; 2010. p. 125–43.
10. Bibbins-Domingo K, Grossman DC, Curry SJ, Barry MJ, Davidson KW, Doubeni CA, et al. Screening for Preeclampsia: US Preventive Services Task Force Recommendation Statement. *JAMA*. 2017;317(16):1661–7.
11. Temur M, Serpim G, Tuzluoğlu S, Taşgöz FN, Şahin E, Üstünyurt E. Comparison of serum human pregnancy-specific beta-1-glycoprotein 1 levels in pregnant women with or without preeclampsia. *J Obstet Gynaecol*. 2020;40(8):1074–8.
12. Rattila S, Dunk CE, Im M, Grichenko O, Zhou Y, Cohen M, et al. Interaction of Pregnancy-Specific Glycoprotein 1 With Integrin A5β1 Is a Modulator of Extravillous Trophoblast Functions. *Cells*. 2019;8(11):1369–9.
13. Tu C, Tao F, Qin Y, Wu M, Cheng J, Xie M, et al. Serum proteins differentially expressed in early- and late-onset preeclampsia assessed using iTRAQ proteomics and bioinformatics analyses. *Peer J*. 2020;8:e9753.
14. Pihl K, Larsen T, Laursen I, Krebs L, Christiansen M. First trimester maternal serum pregnancy-specific beta-1-glycoprotein (SP1) as a marker of adverse pregnancy outcome. *Prenat Diagn*. 2009;29(13):1256–61.

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