IOSR Journal Of Pharmacy www.iosrphr.org
(e)-ISSN: 2250-3013, (p)-ISSN: 2319-4219
Volume 8, Issue 8 Version. I (August 2018), PP. 75-83

Relationship among Pregnancy Associated Plasma Protein-A(PAPP-A) Gene Expression, Serum PAPP-A and Insulin levels in Patients with Preeclampsia in Egyptian Women

Amal K. Seleem[1], A. A. Abdel Aziz[2], Hosam Abdelfatah[2],
M. S. A.El-Gharib[3], Faeza El-Dahtory[4] and Eatimad A. Basha[5]
[1](Department of Biochemistry, Faculty of Medicine / Mansoura University, Mansoura, Egypt)
[2](Department of Gynocology, Faculty of Medicine/ Mansoura University, Mansoura, Egypt)
[3](Department of Chemistry, Faculty of Science/ Port Said University, Port Said, Egypt)
[4](Genetic Unit, Children Hospital / Mansoura University, Mansoura, Egypt)
[5](Department of Chemistry, central laboratories, Ministry of Health-Damietta, Egypt)
Corresponding author: Eatimad A. Basha

ABSTRACT: *to assess PAPP-A gene expression, serum PAPP-A and insulin levels in maternal blood of preeclamptics and to compare them with normotensive pregnant women. Control 60 women with Preeclampsia and 30Nonpreeclampsianormotensive women as control. Three groups were chosen; mild preeclampsia group 30 women, severe preeclampsia group 30and control group 30 women. Maternal blood samples for PAPP-A and Insulin were collected from the patients at second trimester and compared. Term placentas were collected from Egyptian women delivering at University Hospital from the gynecological and Obstetrics Department, Mansoura University, two hours of delivery. Expression of the PAPPA gene was assayed by quantitative real time PCR. Serum PAPPA levels were lowered in maternal blood of preeclamptic as compared to normotensive mothers (P < 0.001). Insulin levels were significantly increased in preeclamptic mothers as compared to normotensive mothers (P < 0.001). Insulin had a positive correlation with PAPPA gene expression in MPE group and it is highly statistically significant in preeclamptic mothers. PAPPA levels had a positive correlation with PAPPA gene expression in SPE group with highly statistically significant in sever preeclamptic mothers. Measurement of insulin, serum PAPPA and PAPPA gene expression may be useful in predicting the risk of preeclampsia.*

Keywords: Insulin; PAPPA, Gene Expression, Preeclampsia

Date of Submission: 07-08-2018 Date of acceptance: 23-08-2018

I. INTRODUCTION

The placenta acts as the interface between fetus and mother during gestation. Abnormal placental development leads to serious consequences for both fetal and maternal health, such as intrauterine growth restriction and preeclampsia[1].Pregnancy-associated plasma protein-A (PAPP-A) is a large highly glycosylated protein complex which has been shown to be responsible for the cleavage of insulin-like growth factor (IGF) binding proteins, which are inhibitors of IGF action in several biological fluids. Since IGFBPs have a key role in the modulating IGF activity, PAPP-A could be important in regulating fetal growth and development and in trophoblastic invasion of the deciduae[2]. PAPP-A is a well-known first trimester serum marker of pathological pregnancies. Since serum PAPP-A is reduced in the first trimester of pregnancies with fetal trisomies, PAPP-A in combination with other markers has been used for noninvasive early detection of trisomies. It is also reported that maternal serum PAPP-A is reduced in various complicated pregnancies such as fetal growth restriction and preeclampsia [3]. Insulin is a hormone that facilitates the transport of glucose from the bloodstream into cells. In response to increased blood sugar after a meal, pancreas secretes insulin into the bloodstream. When insulin resistance occurs, the normal amount of secreted insulin is not sufficient in order to deliver glucose into the cells. Pancreas subsequently increases its production of insulin to deliver blood sugar into the cells. Obesity and pregnancy are among the factors which can create insulin resistance. For these conditions there are theories that can explain etiology. Obesity is a cause of insulin resistance in modern societies. Obesity is often accompanied by an increase in fat cell size. This causes changes in adipokines, including a reduction in adiponectin and an increase in tumor necrosis factor alpha and free fatty acids which increase insulin resistance [4].Preeclampsia, which is characterized by pregnancy-induced hypertension and proteinuria, complicates3–4% of pregnancies and thus is a leading cause of maternal and fetal morbidity and mortality [5].There are no early gestation

screening tests available to predict the occurrence of preeclampsia, and the only effective therapy for established preeclampsia is delivery. Prophylactic strategies, including calcium supplementation and aspirin therapy, have been mostly unsuccessful [6, 7]. Novel therapeutic targets, identified preferably during early gestation when there is time for therapeutic modification, are needed for future clinical trials aimed at preventing preeclampsia. Mild preeclampsia is associated with the lowest maternal and neonatal mortality and morbidity rate, while severe preeclampsia before 35 weeks into pregnancy is associated with significant maternal and prenatal complications. Severe preeclampsia occurs when blood pressure reaches over 160/110 and proteinuria is above 5 g in 24-hour urine collection[8]. Many metabolic changes during pregnancy increase adipose tissue and subsequently insulin resistance. Various placental hormones, in addition, alter maternal physiology to supply embryonic requirements. There is also a 30-fold increase inhuman placental lactogen [hPL]that leads to the secretion of insulin from pancreas [9]. Studies show that hPL plays a role in insulin resistance [10]. 6-fold increase in human chorionic growth hormone is another factor causing insulin resistance [11]. Blood glucose and insulin levels were measured 2hours after a 75 g oral glucose use in pregnant women; results showed that people with high blood insulin levels have higher risk for preeclampsia [12]. However, other studies found no relationship between elevated insulin and risk of preeclampsia[13, 14].Hence, the present study was planned to assess PAPPA gene expression, maternal insulin and PAPPA levels in blood of preeclamptics and to compare them with normotensive pregnant women.

II. MATERIALS AND METHODS

2.1 Study participants

Sixty patients with Preeclampsia were collected from the gynaecological and Obsteric department, Mansoura University, Egypt (mean age: 30.7.±4.3 years) between August 2015 and September 2016. Three strictly, gestational age matched groups were constructed. The first group consisted of 30women who were diagnosed as mild preeclampsia (MPE) during routine prenatal visits at second trimester. The second group consisted of 30 women who were diagnosed as severe preeclampsia(SPE)and the third group consisted of30 healthy control pregnant whose blood samples were taken during prenatal visits at second trimester of the gestational week that matches the other two groups and these women were followed up to delivery. Ages of women, gravidity, pregnancy outcomes, blood pressure values, maternal weights and height were recorded. Body-mass indexes were calculated. Participants were excluded if they had a pregnancy termination, a major anomaly, a twin pregnancy, or if the pregnancy outcome was unknown (i.e. if they did not deliver at our hospital). Thirty other pregnant women were put in the control group .Controls were women who entered University Hospital, Mansoura University, Mansoura, Egypt Obstetric Maternal Study cohort within 2wk of each case and who remained normotensive and non proteinuric throughout pregnancy. Women with a history of diabetes; thyroid, liver, or chronic renal disease; or preexisting chronic hypertension (defined as blood pressure >140/90 or need for antihypertensive medications before pregnancy or before 20 wk gestation) were excluded.

Ethical approval: All study participants have provided a written informed consent, and the study protocols have been approved by the Coordinating Ethics Committee of the Internal Medicine University Hospital, Mansoura University, Mansoura, Egypt Obstetric Maternal Study cohort. All experiments were performed in accordance with the approved guidelines.

The 30 women were assigned to the control group who were matched according to Weight, BMI, maternal age, and gestational age after assessing their files in the center and choosing most similar women to form healthy group to preeclamptic groups(Table 1).

2.2 Methods

Insulin levels were measured by radioimmunoassay from samples taken from mothers in the second trimester of pregnancy.. Insulin was measured by ELISA (Linco, St. Charles, Missouri) with intra-assay CV 6.0, inter-assay CV 10.3, and sensitivity was 2 μU/ml. The quantitative determination of PAPP-A in the maternal serum was performed with an Immulite/ Immulite1000 device using solid phase, chemiluminescenceimmunometric sandwich method. Blood samples were centrifugated as soon as they were taken; they were not stored in deep freezer and studied as soon as possible.

Fresh samples of 30 human placentas were obtained within 30 min after placental delivery in gynaecological and Obsteric department, Mansoura University, Egypt. After a rinse of the samples with normal saline, the amniotic membranes and the maternal decidua were removed, then the samples were snap frozen in liquid nitrogen and stored at -27^0C until RNA isolation by *using miRNeasy mini kit (Qiagen, cat no. 217004,* Germany). TaqMan real-time PCR ((provided by Thermo Scientific, U.S.A, cat No. #K1641)Was used to quantify the expression of PAPPA gene in placenta. iScript One-Step RT-PCR Kit for Probes (Bio-Rad) was used to reverse-transcribe and amplify the RNA template for 40 cycles, and the cycle at which the signal rose above a fixed threshold (Ct) was determined. The quantitative PCR amplification was performed using 25 ml reaction volumes containing reaction mix (Bio-Rad), Protector RNase Inhibitor (Roche Applied Sciences), 0.5

U iScriptRTase, 8.5 ml RNA template (i.e. 425 ng), 0.25 mM each primer, and 175 nM probe. The quantitative PCR program consisted of an initial reverse transcription of 30 min at 50 8C, an initial PCR activation step of 15 min at 95 8C followed by 40 cycles of 1 min at 94 8C, 1 min at 55 8C, and 1 min at 72 8C.The antisense probe was generated from a partial human PAPP-A cDNA (572bp corresponding to GenBank™ accession number :NM 002581;nucleotides1599-2151),The following primers were used. PAPPA: forward 5\ - CGGTTCAACTTTGATGGTGGAGAG -3\, reverse 5\ - ATTCTGGCGACTTGATTGGGCGTG -3\.

2.3 Statistical analysis

Data analysis was done by Statistical package for social science (SPSS) version 16. The data were collected and entered to the computer. Statistical analysis was done using Statistical Package of Social Science (SPSS) Version 16 (Chicago, USA), IL 60606-6307. The quantitative data was presented in the form of mean and standard deviation. One way Annova f test was used for quantitative data of the three groups followed by benferroni test to compare between each two groups. Pearson correlation coeffient was used to study relation between groups. Significance was considered at p value less than 0.05.

III. RESULTS

The maternal characteristics of each of the outcome groups are compared in Table 1.The patients with preeclampsia were not significantly different from the control group in terms of average age, BMI, and gestational age "Table1, 2and Figure1, 2". Levels of fasting insulin ,serum PAPPA ,PAPPA gene expression were studied among the case and control groups after the development of preeclampsia. Significant difference was found among fasting insulin among the two groups of preeclampsia and control group[$P< 0.001$] "Table 3 and Figure 3". The average fasting insulin increased for both case and control groups. Mean score for the level of fasting insulin among people with preeclampsia was higher than that of control group [$P< 0.001$] "Table 3". According to results of f-test, changes in insulin level were significant for both groups during pregnancy [$P< 0.001$] but there was no significant difference between group of mild preeclampsia and control group [$P=0.294$] "Table 4"; therefore, insulin rate increased in both groups. Mean PAPP-A levels were significantly lower in preeclampsia compared to their matched control. PAPP-A levels were not different when group with MPE compared with SPE group "Figure 4". PAPP-A was only minimally expressed in control group. PAPP-A was significantly lower in control group (0.65±0.39 percent) than in Severe preeclampsia group (P<0.001) or mild preeclampsia group (P=0.001).There was statistically significant difference between the groups of preeclampsia (P=0.001) "Figure 5".There was significant direct (positive correlation) between fasting insulin and PAPPA expression(r= 0.386)in MPE group**.** There was significant positive correlation between PAPPA expression and Serum PAPPA (r = 0.400) in SPE group "Table 4".

IV. DISCUSSION

Several studies have reported an association between preeclampsia and insulin resistance as characterized by higher glucose and/or insulin levels when compared with normotensive women, but an association between direct measurements of insulin resistance and preeclampsia has not been demonstrated [15-17].

Metabolic studies in women with GDM, a subgroup that has been associated with an increased preeclampsia risk, did not find any correlation between multiple measures of insulin resistance And β-cell function with the subsequent development of preeclampsia during pregnancy[18].Metabolic origins are implicated by differences in preeclampsia compared to normal pregnancy. Maternal hyper insulinemia and insulin resistance which support the growing conceptus in normal pregnancy are accentuated in preeclampsia. Preeclamptic pregnancies demonstrated 37% lower insulin sensitivity and 70% higher free fatty acid concentration at 29 to 39 weeks gestation than was present in control women .Moreover, women entering pregnancy with metabolic syndrome are more likely to develop preeclampsia. Obesity triples the risk of preeclampsia, yet 90% of obese pregnant women do not develop the disease. Insulin resistance also occurs in non-obese metabolic syndrome. Although inflammation and insulin resistance commonly are associated, lack of correlation between these processes has been found in studies of hypertensive disorders of pregnancy [19, 20].

Maternal serum levels of PAPP-A have long been known to be depressed in the first trimester of Down's syndrome pregnancies[21], which is widely used in prenatal diagnosis. Other chromosomal abnormalities and adverse pregnancy outcomes, e.g., intrauterine growth retardation and preeclampsia, are also associated with depressed levels of PAPP-A, as is low weight at birth[22].Our study is consistent with Bersinger's and Deveci's studies that PAPP-A at the early second trimester (17 weeks) significantly decreases in preeclampsia even in mild form .It was found that, in pregnancies with subsequent preeclampsia PAPP-A, SP1, HPL and PLGF were reduced at 17 weeks of gestation whereas at 25 and 33 weeks only PLGF remained below the controls. In growth-restricted pregnancies PAPP-A, SP1 and HPL were reduced at 17 weeks, and only HPL continued to be strongly affected thereafter [23]. Deveci et al. also found positive correlation between PAPP-A

level and mean blood pressure of the preeclamptic women and concluded that level of PAPP-A is related with severity of the disease [24]. There is also some evidence that serum PAPP-A is reduced in the second trimester in pregnancies that develop PE, but the levels are increased in cases with established disease [25-27].

PAPP-A is expressed in a variety of tissues and cell types, and is potently up-regulated by proinflammatory cytokines, such as tumor necrosis factor (TNF)-α and interleukin (IL)-1β). PAPPA is highly expressed in human placenta [28, 29]. The mean ±SD of the PAPP-A expression in control, mild preeclampsia and severe preeclampsia (0.5±0.39, 1.44±0.47and2.04± 0.37) respectively. PAPP-A expression significantly increased in both groups of MPE and SPE, when compared with control group (P = 0.001).We found PAPP-A no expression significantly between the group of severe preeclampsia and group of mild preeclampsia (P = 1.000). Findings in these studies have been inconsistent, probably reflecting lack of power in each individual study in combination with the complexity of the disease. Transcriptional comparisons of gene expression in sample from women with PE and women with normal pregnancies are therefore often hampered by relatively large differences body mass index(BMI), with significant difference between studied groups regard to BMI (P=0.021).

In the present study, there was a statistically significant difference between the groups of women with preeclampsia compared to the control group. The mean ± SD of maternal insulin level in control, mild preeclampsia and severe preeclampsia were 3.96±1.32, 5.39±1.99 and 9.40±5.19; respectively. Maternal insulin level significantly increased in both groups of MPE and SPE, when compared with control group (P = < 0.001).We found significantly between the group of MPE and group of SPE preeclampsia (P = <1.000).Control group was carefully selected among pregnant women who remained normotensive and non proteinuric throughout pregnancy. The results may refer to there is a relation between insulin, serum PAPPA levels and PAPPA gene expression and the mechanism and severity of the disease. It is important to keep in mind that the study was performed in a special group of patients. These findings dictate further mechanistic studies of insulin resistance and the metabolic syndrome in the pathophysiology of preeclampsia and indicate confirmatory tests for the predictive value of insulin resistance in other populations.

V. CONCLUSION

It is possible that the relation between maternal insulin level, serum PAPPA level and PAPPA gene expression, we detected, in cases may have been present at baseline, predating pregnancy. This point has important therapeutic implications. It is tempting to consider that improving insulin sensitivity in high risk women before and during early pregnancy may reduce the risk of preeclampsia taking into consideration other metabolic syndromes; however, the power calculation of the sample was low, suggesting that a larger sample is needed.

ACKNOWLEDGEMENT

The authors are indebted to all the women who have contributed to this study and their families by answering the questionnaire and donating biological samples. The authors would like to acknowledge and sincerely thank the all people for their help and support**.**

REFERENCES

[1] J. Wang, Q. Qiu, M. Haider, M. Bell, A. Gruslin, and J.K. Christians, Expression of pregnancy-associated plasma protein A2 during pregnancy in human and mouse.*J Endocrinol,202(3),*2009,337-345.

[2] L.S. Laursen, M.T. Overgaard, R. Soe, H.B. Boldt, L. Sottrup-Jensen, L.C. Giudice, C.A. Conover, and C. Oxvig, Pregnancy-associated plasma protein-A (PAPP-A) cleaves insulin-like growth factor binding protein (IGFBP)-5 independent of IGF: implications for the mechanism of IGFBP-4 proteolysis by PAPP-A.*FEBS Lett,504(1-2),*2001,36-40.

[3] S. Shiefa, M. Amargandhi, J. Bhupendra, S. Moulali, and T. Kristine, First Trimester Maternal Serum Screening Using Biochemical Markers PAPP-A and Free β-hCG for Down Syndrome, Patau Syndrome and Edward Syndrome.*Indian Journal of Clinical Biochemistry,28(1),*2013,3-12.

[4] N. Furukawa and E. Araki, [Type 2 diabetes and impaired glucose tolerance].*Nihon Rinsho,71(2),*2013,270-274.

[5] Report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy.*Am J Obstet Gynecol,183(1),*2000,S1-s22.

[6] W. Khaing, S.A. Vallibhakara, V. Tantrakul, O. Vallibhakara, S. Rattanasiri, M. McEvoy, J. Attia, and A. Thakkinstian, Calcium and Vitamin D Supplementation for Prevention of Preeclampsia: A Systematic Review and Network Meta-Analysis.*Nutrients,9(10),*2017.

[7] F.A. English, L.C. Kenny, and F.P. McCarthy, Risk factors and effective management of preeclampsia.*Integr Blood Press Control,8,*2015,7-12.

[8] B.M. Sibai, Diagnosis and management of gestational hypertension and preeclampsia.*Obstet Gynecol,102(1)*,2003,181-192.
[9] L. Goyvaerts, K. Lemaire, I. Arijs, J. Auffret, M. Granvik, L. Van Lommel, N. Binart, P. in't Veld, F. Schuit, and A. Schraenen, Prolactin receptors and placental lactogen drive male mouse pancreatic islets to pregnancy-related mRNA changes.*PLoS One,10(3)*,2015,e0121868.
[10] N. O'Gorman, D. Wright, D.L. Rolnik, K.H. Nicolaides, and L.C. Poon, Study protocol for the randomised controlled trial: combined multimarker screening and randomised patient treatment with ASpirin for evidence-based PREeclampsia prevention (ASPRE).*BMJ Open,6(6)*,2016,e011801.
[11] S. Handwerger and M. Freemark, The roles of placental growth hormone and placental lactogen in the regulation of human fetal growth and development.*J Pediatr Endocrinol Metab,13(4)*,2000,343-356.
[12] J. Romero and E. Spinedi, Two-hour insulinemia after oral glucose overload and women at risk of pregnancy-induced hypertensive disorders.*Hypertens Pregnancy,32(4)*,2013,355-366.
[13] S.I. Sherwani, H.A. Khan, A. Ekhzaimy, A. Masood, and M.K. Sakharkar, Significance of HbA1c Test in Diagnosis and Prognosis of Diabetic Patients.*Biomark Insights,11*,2016,95-104.
[14] H. Yu, X. Qi, and X. Wang, Application of glycated hemoglobin in the perinatal period.*Int J Clin Exp Med,7(12)*,2014,4653-4659.
[15] M. Phang and M.R. Skilton, Marine Omega-3 Fatty Acids, Complications of Pregnancy and Maternal Risk Factors for Offspring Cardio-Metabolic Disease.*16(5)*,2018.
[16] L.J. Li, I.M. Aris, L.L. Su, Y.S. Chong, T.Y. Wong, K.H. Tan, and J.J. Wang, Effect of gestational diabetes and hypertensive disorders of pregnancy on postpartum cardiometabolic risk.*Endocr Connect,7(3)*,2018,433-442.
[17] J. Lee, Y.T. Ouh, K.H. Ahn, S.C. Hong, M.J. Oh, H.J. Kim, and G.J. Cho, Preeclampsia: A risk factor for gestational diabetes mellitus in subsequent pregnancy.*PLoS One,12(5)*,2017,e0178150.
[18] J.C. Hauth, R.G. Clifton, J.M. Roberts, L. Myatt, C.Y. Spong, K.J. Leveno, M.W. Varner, R.J. Wapner, J.M. Thorp, B.M. Mercer, A.M. Peaceman, S.M. Ramin, M.W. Carpenter, P. Samuels, A. Sciscione, J.E. Tolosa, G. Saade, Y. Sorokin, and G.D. Anderson, Maternal Insulin Resistance and Preeclampsia.*American journal of obstetrics and gynecology,204(4)*,2011,327.e321-327.e326.
[19] J.V. Ilekis, U.M. Reddy, and J.M. Roberts, Preeclampsia--a pressing problem: an executive summary of a National Institute of Child Health and Human Development workshop.*Reprod Sci,14(6)*,2007,508-523.
[20] S.A. Founds, J.M. Catov, M.J. Gallaher, G.F. Harger, N. Markovic, and J.M. Roberts, Is there evidence of separate inflammatory or metabolic forms of preeclampsia? *Hypertens Pregnancy,30(1)*,2011,1-10.
[21] I. Ghoshal, B.S. Varashree, V.S. Belle, and K. Prabhu, Correlation of Pregnancy Associated Plasma Protein A and Zinc with Calculated Risk Ratio of Dual Test.*J Clin Diagn Res,11(9)*,2017,Bc24-bc26.
[22] C.Y. Ong, A.W. Liao, K. Spencer, S. Munim, and K.H. Nicolaides, First trimester maternal serum free beta human chorionic gonadotrophin and pregnancy associated plasma protein A as predictors of pregnancy complications.*Bjog,107(10)*,2000,1265-1270.
[23] N.A. Bersinger and R.A. Odegard, Second- and third-trimester serum levels of placental proteins in preeclampsia and small-for-gestational age pregnancies.*Acta Obstet Gynecol Scand,83(1)*,2004,37-45.
[24] K. Deveci, E. Sogut, O. Evliyaoglu, and N. Duras, Pregnancy-associated plasma protein-A and C-reactive protein levels in pre-eclamptic and normotensive pregnant women at third trimester.*J Obstet Gynaecol Res,35(1)*,2009,94-98.
[25] I. Kirkegaard, N. Uldbjerg, and C. Oxvig, Biology of pregnancy-associated plasma protein-A in relation to prenatal diagnostics: an overview.*Acta Obstet Gynecol Scand,89(9)*,2010,1118-1125.
[26] N.A. Bersinger, A.K. Smarason, S. Muttukrishna, N.P. Groome, and C.W. Redman, Women with preeclampsia have increased serum levels of pregnancy-associated plasma protein A (PAPP-A), inhibin A, activin A and soluble E-selectin.*Hypertens Pregnancy,22(1)*,2003,45-55.
[27] A. Atis, Y. Aydin, E. Basol, S. Kaleli, F. Turgay, and N. Goker, PAPP-A levels of late pregnancy in preeclampsia and HELLP syndrome.*Arch Gynecol Obstet,285(1)*,2012,45-49.
[28] D. Tornehave, J. Chemnitz, B. Teisner, J. Folkersen, and J.G. Westergaard, Immunohistochemical demonstration of pregnancy-associated plasma protein A (PAPP-A) in the syncytiotrophoblast of the normal placenta at different gestational ages.*Placenta,5(5)*,1984,427-431.
[29] C.A. Conover, Role of PAPP-A in aging and age-related disease.*Exp Gerontol,48(7)*,2013,612-613.

Table 1: Case and control matching

	Control (n = 30)	Mild Preeclampsia (n = 30)	Severe Preeclampsia (n = 30)
Age (year)	29.53± 4.36	30.03± 5.5	31.83± 3.69
Weight(Kg)	81.1± 12.73	81.4 ± 12.11	86.53 ± 12.98
Gestational age(Week)	20.72± 4.66	21.2± 3.57	19.83± 3.93
Body mass index (kg/m^2)	25.95 ± 3.56	27.30 ± 4.03	28.57 ± 2.92
Diastolic blood pressure (mmHg)	76.26 ± 3.37	94.33 ± 3.27	105.6 ± 3.23
Systolic blood pressure (mmHg)	114.30± 6.2	149.13± 5.5	167.2± 6.3

Table 2: Characteristics of subjects

	Control (n = 30)	Mild Preeclampsia (n = 30)	Severe Preeclampsia (n = 30)	Control (n = 30)
Age (year)	29.53	30.03	31.83	NS
Weight (Kg)	81.1	81.4	86.53	NS
Gestational age (wk)	20.72	21.2	19.83	NS
Body mass index (kg/m2)	25.95	27.30	28.57	0.021
Diastolic blood pressure (mmHg)	76.26	94.33	94.9	<0.001
Systolic blood pressure (mmHg)	114.30	149.13	149.25	<0.001

NS: Not statistically significant

Table 3: Insulin, serum PAPPA and The PAPPA gene expression

	Control (n = 30)	Mild Preeclampsia (n = 30)	Severe Preeclampsia (n = 30)	Control (n = 30)
Insulin(µIU/mL)	3.96±1.32	5.39±1.99	9.40±5.19	<0.001
PAPP-A (ng/ml)	104± 33.15	80.09± 21.74	75.77± 27.03	<0.001
PAPPA gene expression	0.65±0.39	1.44±0.47	2.04±0.37	< 0.0001

Table 4: Post hoc test between each two group

	Insulin (µIU/mL)	PAPP-A (ng/ml)	PAPPA Gene Expression
(*P* value)Group I versus II	0.294	0.004	< 0.001
Group I versua III	<0.001	0.001	< 0.001
Group II versus III	<0.001	1.000	< 0.001

Table 5: Correlation between PAPPA expression, insulin and serum PAPPA in the studied groups

PAPPA Gene Expression	control		Mild Preeclampsia		Severe Preeclampsia	
	r	p	r	p	r	p
Serum PAPPA	0.236	0.209	0.257	0.171	0.400*	0.029
Insulin	0.021	0.911	0.386*	0.035	-0.054	0.778

Pearson Correlation (r)

Statistical Significance at *P*-value <0.05

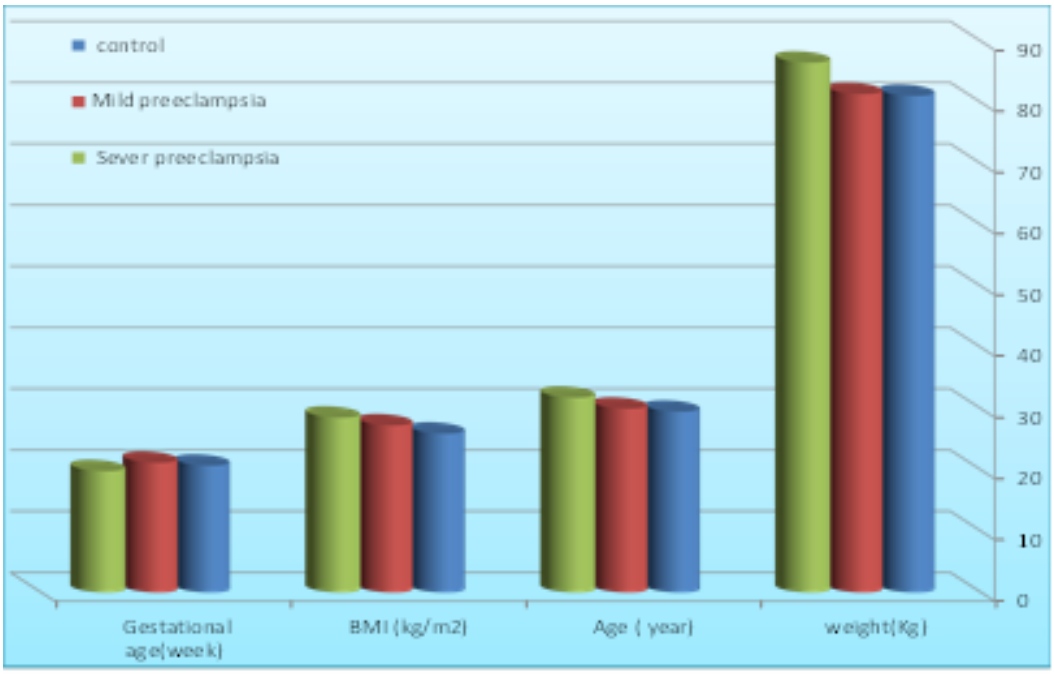

Fig. 1: Bar chart illustrates mean of age, weight, gestational age and MBI among studied groups

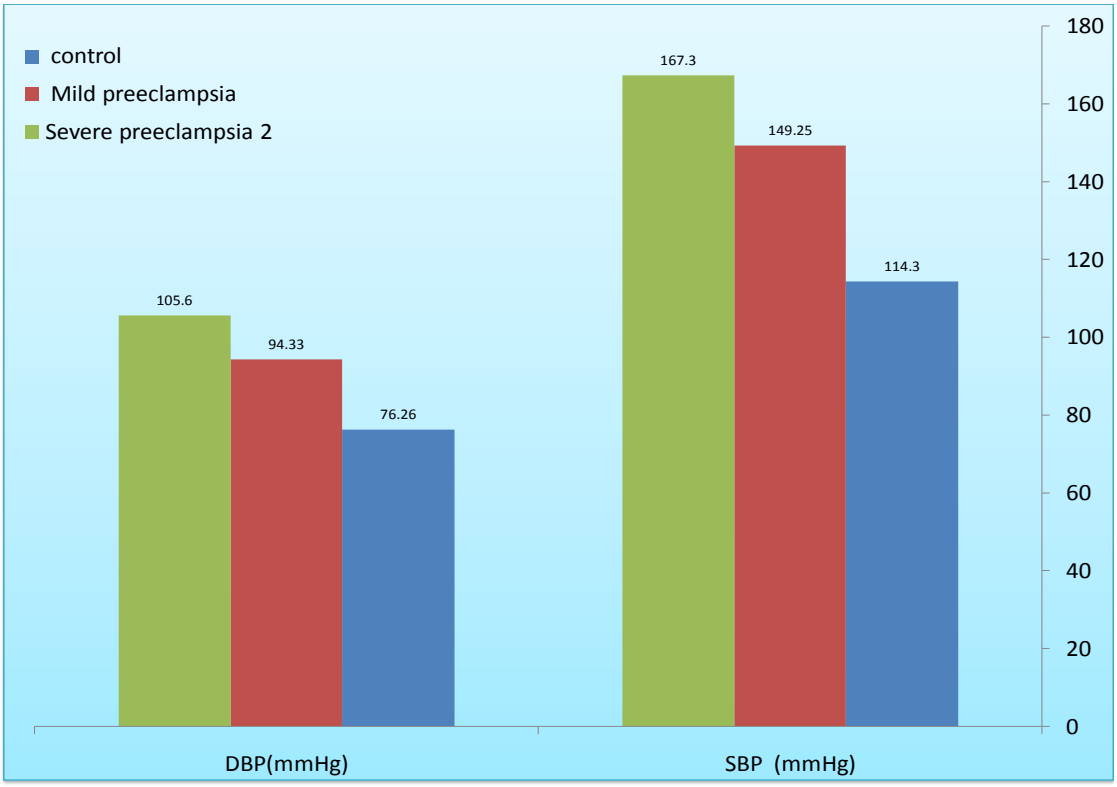

Fig. 2: Bar chart illustrates mean of SBP and DB among studied groups

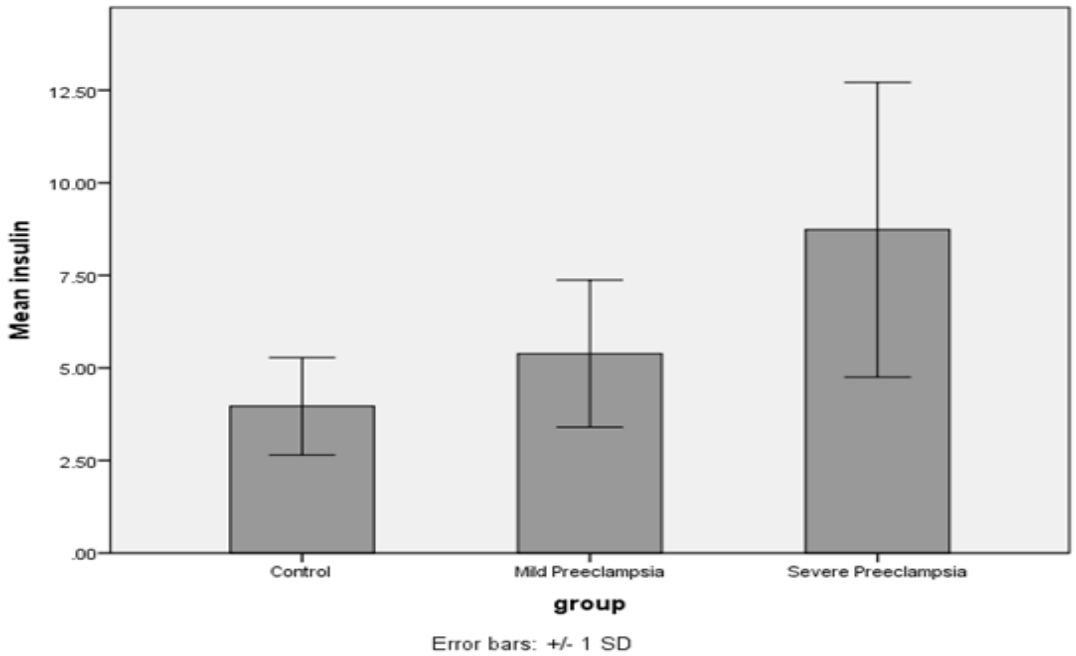

Fig.3:The average fasting insulin level in control and groups with preeclampsia

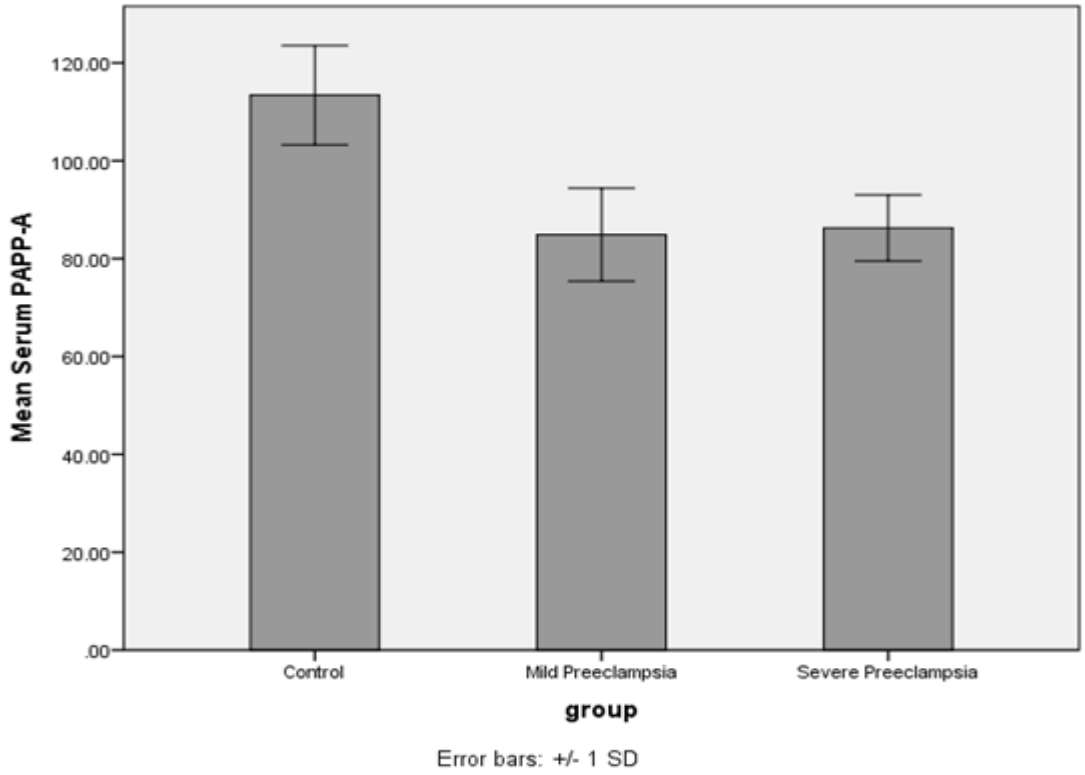

Fig. 4: Serum PAPPA Level in control and groups with preeclampsia

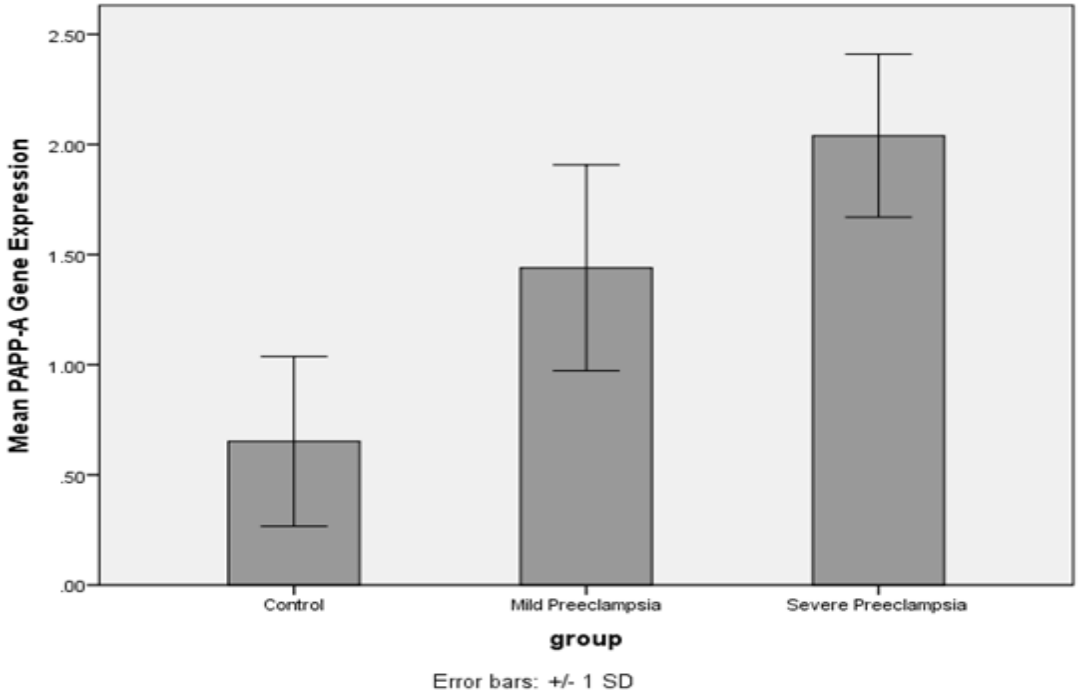

Fig. 5: Bar chart illustrates mean (± SD) of PAPPA expression of the studied groups among studied groups

Eatimad A. Basha", Relationship among pregnancy Associated Plasma Protein-A(PAPP-A) Gene Expression, Serum PAPP-A and Insulin levels in Patients with Preeclampsia in Egyptian Women." IOSR Journal of Pharmacy (IOSRPHR), vol. 8, no. 8, 2018, pp. 75-83.