

Evaluation of coagulation factors and serum ferritin in preeclamptic Pakistani women

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Abstract

Preeclampsia (PE) is a pregnancy-related disorder involving multiple organ systems and characterised by an increase in hypertension and proteinuria after 20 weeks of gestation. The study aimed to determine the role of coagulation factors and ferritin in relation to PE susceptibility in Pakistani women. Blood samples of 100 normotensive and 100 preeclamptic women, including 73 with mild PE and 27 with severe PE were taken for the study to evaluate activated partial thromboplastin time (aPTT), prothrombin time (PT), international normalising ratio (INR), fibrinogen levels, platelet count (PLT) and ferritin levels. Prolonged aPTT, PT and INR were recorded in both PE groups with a decrease in platelets and fibrinogen levels, compared to the control groups. Ferritin levels were not significantly ($p=0.23$) different in any of the groups. In conclusion, coagulopathic disorder should be clinically suspected and the coagulating factors in PE patients should be examined for early detection, effective antenatal care and for the proper management of this disorder to decrease maternofetal mortality, morbidity and perinatal mortality.

Keywords: Pregnancy, Preeclampsia, Coagulation factors, Ferritin

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Introduction

Preeclampsia (PE) is a pregnancy-related disorder involving multiple organ systems, characterised by an increase in hypertension and proteinuria after 20 weeks of gestation.¹ It is a multi-factorial and multi-systemic disorder that causes complications in 5-7% pregnancies and is the leading cause of maternal and foetal morbidity and mortality worldwide.¹ Annually 63,000 maternal and 50,000 infant deaths are predictably associated with preeclampsia.² Maternal mortality due to PE is 15-20% in developing countries.³ According to one study, the incidence of preeclampsia is around 19% in Pakistan.⁴

Studies have shown various factors involved in the susceptibility of preeclampsia, but the etiological details

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are still being debated. PE may also result in a variety of haematological aberrations.⁵ Profound changes in the coagulation and fibrinolytic systems occur during normal pregnancy causing a hypercoagulable state. During PE, the distinct accentuation of hypercoagulable or prothrombotic state could lead to changes in the kidney and placenta. Other coagulation abnormalities such as aPTT, PT with INR are more sensitive.⁶ Alteration in coagulation factors increases the risk of bleeding complications in preeclampsia.⁷ Haemorrhages are a major problem and the main cause of maternal mortality, which usually occurs during operative delivery or regional anaesthesia procedure.⁸ The iron released from red blood cell destruction can cause oxidative stress, both in the vascular system and the placenta, and may lead to the etiologic factor of preeclampsia through endothelial cell damage. A body iron status can be reliably indicated by serum ferritin levels in healthy individuals. Low levels of ferritin predicts iron deficiency, while high levels does not always indicate an excess of iron.⁸ Ferritin is a chief iron storage protein found in various organs including placenta, bone marrow, kidney and in plasma.⁹ Bone marrow iron stores are correlated with its concentration. During pregnancy, serum ferritin concentration falls with advancing gestation period.¹⁰ Early assessment of PE severity is essential to prevent complications during pregnancy, therefore, the present study aimed to compare coagulation factors and ferritin levels in PE patients with normotensive pregnant women.

Methods and Results

This study was conducted in the Pakistan Institute of Medical Sciences (PIMS) Islamabad, Quaid-e-Azam International Hospital, Islamabad and Quaid-i-Azam University, Islamabad after receiving approval from the ethical committees of all three institutes. Two hundred blood samples of pregnant women of ages less than 35 years and in their third trimester were included for the study which was conducted from September 2015 to July 2017. The individuals for the study comprised 100 pregnant women with PE including 73 with mild and 27 with severe PE as per the PE diagnostic criteria, and 100 normotensive pregnant women as the control group. Informed consent was taken and detailed performas were filled out before

sample collection after which all the subjects were measured for PT, aPTT, INR and ferritin levels.

Patients diagnosed with PE, defined as a new onset of elevated blood pressure of $>140/90$ mmHg along with proteinuria $\geq 1+$ on dipstick test on two occasions at least 6 hours apart, or >300 mg per day on two occasions were selected for this study.¹¹ Patients with blood pressure of $>140/90$ mmHg but $<160/110$ were categorised as having mild PE, while patients with $\geq 160/110$ mmHg blood pressure and proteinuria $\geq 3+$ on dipstick test were included in the severe preeclampsia category. The normotensive control group included women with uncomplicated gestation and blood pressure of $<125/85$ mmHg and no proteinuria. Subjects were excluded if they had one or more of the following: diabetes, asthma, kidney disease, haematological disorder, autoimmune disease, urinary tract infection, current or past history of smoking, anticoagulation therapy, placental abruption and heavy vaginal bleeding.

aPTT, PT, INR, fibrinogen levels and PLT were checked by automated coagulation analyser (pochH-100i, Japan). Ferritin levels were determined by ferritin ELISA kit (cat# 1601-16, California, USA).

All statistical data was expressed as mean \pm S.E.M (standard error of mean). Statistical analysis was carried out by using lme4 and eayanova package of R 3.5.1 (R Development Core Team, 2018). The comparison of groups with the control group was analysed by ANOVA ea1 command.

Individuals in the study hailed from different areas of Punjab, Khyber Pakhtunkhwa and Kashmir in Pakistan. The characteristics of patients and the control group at diagnosis are shown in Table 1. Significant difference was noted between the control and preeclamptic groups with regard to age ($p=0.002$), systolic and diastolic blood pressure ($p\leq 0.001$) with non-significant change in body mass index (BMI) ($p=0.126$). Furthermore, the gestational age of patients with mild and severe PE was significantly lower ($p\leq 0.001$) compared to the control group, while a

Table-1: Clinical characteristics of controls and Preeclamptic patients.

Parameters	Controls	Preeclampsia		p value
		Mild	Severe	
Age (Years)	27.017 \pm 0.32b	28.14 \pm 0.42ab	29.17 \pm 0.59a	P=0.002
BMI (kg/m ²)	27.67 \pm 0.28a	28.72 \pm 0.47a	28.39 \pm 0.54a	P=0.126
GA (weeks)	36.45 \pm 0.46a	34.07 \pm 0.54b	31.67 \pm 0.96b	$p\leq 0.001$
Systolic blood pressure (mmHg)	114.71 \pm 0.51c	40.39 \pm 0.93b	174.94 \pm 2.02a	$p\leq 0.001$
Diastolic blood pressure (mmHg)	73.88 \pm 0.45c	93.10 \pm 0.86b	112.51 \pm 1.86a	$p\leq 0.001$

Mean with different superscript represents p value (significant difference at $p<0.05$) in the columns comparing PE groups with controls. Body mass index (BMI), Gestational age (GA)

Table-2: Coagulation profile of control and preeclamptic groups.

Parameters	Controls	Preeclampsia		p value
		Mild	Severe	
PLT ($10^9/L$) (150-400)	260.18 \pm 5.26a	224.5 \pm 9.26b	209.18 \pm 11.89b	$p<0.001$
aPTT (s) (25-31.5)	31.54 \pm 0.52b	34.31 \pm 0.82a	35.28 \pm 1.00a	$p<0.001$
PT (s) (9-12)	12.10 \pm 0.23b	12.88 \pm 0.37ab	13.91 \pm 0.43a	$p=0.001$
INR (s) (0.1-0.8)	0.81 \pm 0.01b	0.86 \pm 0.01a	0.93 \pm 0.02a	$p<0.001$
Fibrinogen (mg/dl) (175-400)	279.40 \pm 5.04a	264.56 \pm 4.82ab	253 \pm 5.86b	$p=0.004$
Ferritin (ng/ml) (13-150)	56.24 \pm 3.23a	54.68 \pm 2.91a	54.4 \pm 6.25a	$p=0.23$

Mean with different superscript represents p value (significant difference at $p<0.05$) in the columns comparing PE groups with controls. Platelet count (PLT), Activated partial thromboplastin time (aPTT), Prothrombin time (PT), International normalising ratio (INR).

family history of preeclampsia was more prominent in the PE groups compared to the group of normotensive females.

Mean and statistical significance of coagulation parameters was observed and tabulated in Table 2. Prolonged aPTT, PT and INR were observed in both PE groups especially in the one with severe PE with a decrease in PLT and fibrinogen. Non-significant ($p=0.23$) decrease was observed in ferritin levels in PE groups compared to the control group. Statistical significance was checked for each parameter in both mild and severe preeclamptic groups against the control group (Table 2).

Conclusion

As PE is disease of theories, it is a poorly understood pregnancy complication that can prove fatal for expectant mothers. There is a constant search for prognostic factors to predict the progression and severity of the disease. In the present study, prolonged aPTT, PT and INR was observed with a significant decrease in fibrinogen levels and PLT. According to previous reported literature, the absence of clotting abnormalities cannot be declared due to platelet count $>150,000/mm^3$.¹² However, for early detection of coagulation abnormalities, aPTT measurement is crucial in preeclamptic patients who have normal platelet counts. Our results are supported by the findings of Jahromi, and Rafiee⁶ and in contradiction to the notion that all patients with PE and coagulation abnormality have platelet count $<100,000/mm^3$.¹³ Ferritin levels were not statistically different in all the study groups but routine investigation of serum ferritin levels in pregnant women with PE may help in establishing diagnosis before clinical manifestations and non-anaemic pregnant women should be stopped from taking iron supplements.

Hence, an evaluation of certain clinical risk factors helps in early detection, effective antenatal care and proper management of PE which could decrease maternal mortality, morbidity and perinatal mortality. Future studies

on preeclampsia on a larger population might provide valuable information in the understanding its pathophysiology and help in the development of preventive and therapeutic strategies. Most PE risk factors are not modifiable, which is why as an ultimate long-term goal in Pakistan, better prenatal care is required that ensures timely diagnosis and management of this complication to avoid possible maternal and perinatal deaths due to PE.

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Conflict of interest: None.

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References

1. Ukah UV, Magee L, Payne B, Hutcheon J, von Dadelszen P. 320. Pregnancy characteristics, management and outcomes according to different definitions of pre-eclampsia and other hypertensive disorders of pregnancy. *Pregnancy Hypertens* 2018; 13: S125.
2. Goulopoulou S, Davidge ST. Molecular mechanisms of maternal vascular dysfunction in preeclampsia. *Trends Mol Med* 2015; 21: 88-97.
3. Shamsi Mahmoudabadi F, Ziaei S, Firoozabadi M, Kazemnejad A. Exposure to extremely low frequency electromagnetic fields during pregnancy and the risk of spontaneous abortion: a case-control study. *J Res Health Sci* 2013; 13: 131-4.
4. Tariq M, Rehmani H, Tayyab M, Kamal F, Yasmeen N, Sultan F. Clinicopathological study of pre-eclampsia. *Biomedica* 2000; 16: 60-5.
5. Chen Y, Lin L. Potential value of coagulation parameters for suggesting preeclampsia during the third trimester of pregnancy. *Am J Med Sci* 2017; 354: 39-43.
6. Jahromi BN, Rafiee SH. Coagulation factors in severe preeclampsia. *IRCMJ* 2009; 11: 321-4.
7. Sharma UK, Kouli R, Sonowal R, Saikia P. Coagulation Parameters in Pre-eclamptic and Eclamptic Patients-A Comparative Study of 90 Cases. *J Contemp Med Res* 2016; 3: 2235-8.
8. Lakshmi CV. Comparative Study of Coagulation Profile in Mild Preeclampsia, Severe Pre-eclampsia, and Eclampsia. *Int J Sci Stud* 2016;4:180-3.
9. Milman N, Agger AO, Nielsen OJ. Iron status markers and serum erythropoietin in 120 mothers and newborn infants: effect of iron supplementation in normal pregnancy. *Acta Obstet Gyn Scan* 1994; 73: 200-4.
10. Fatima N, Islam F, Noor L, Das SR, Zeba D, Zesmin F. Serum ferritin in preeclampsia and eclampsia: a case control study. *Faridpur Med Coll J* 2013; 8: 18-21.
11. Kallela J, Jääskeläinen T, Kortelainen E, Heinonen S, Kajantie E, Kere J, et al. The diagnosis of pre-eclampsia using two revised classifications in the Finnish Pre-eclampsia Consortium (FINNPEC) cohort. *BMC Pregnancy Childbirth* 2016; 16: 221.
12. Metz J, Cincotta R, Francis M, DeRosa L, Balloch A. Screening for consumptive coagulopathy in preeclampsia. *Int J Gynecol Obstet* 1994; 46: 3-9.
13. Leduc L, Wheeler JM, Kirshon B, Mitchell P, Cotton DB. Coagulation profile in severe preeclampsia. *Obstet Gynecol* 1992; 79: 14-8.