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Analysis of CRP, PCT, D - Dimer in Preeclampsia Patients

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Abstract: ***Background: Preeclampsia (PE) remains one of the most common medical complication of pregnancy, it is the leading cause of maternal morbidity and mortality. No single test can predict preeclampsia so there has been growing interest in the combination of markers for PE screening. Material and Methods: The study was carried out on 100 cases divided into two groups viz 50 cases of preeclamptic women served as study group while 50 normotensive healthy pregnant women were served as control group. Demographic and clinical risk factors were noted. Pearson's correlation test was used to analyze the inter - correlation between CRP, PCT and D - dimer. Results: 78.0% cases of preeclampsia was found to be in age group of 20 - 30 yrs with mean of 25.4±5.3 years. hsCRP level in study group >7mg/L was found in 86.0% cases while in control group only in 4 (8.0%) cases it was >7mg/L. Both severe pre - eclampsia and mild preeclampsia groups showed significantly higher PCT values and D - dimer values when compared with healthy control group (p<0.001). Conclusion: Procalcitonin level and D - dimer level are good predictors for preeclampsia among pregnant women. and could be used as screening tests for detection and severity of pre - eclampsia.***

Keywords: Preeclampsia, C - reactive protein, Precalcitonin, D - dimer

1. Introduction

Hypertensive disorders are among the commonest medical disorders during pregnancy and continue to be a major cause of maternal and perinatal morbidity and mortality worldwide. In developing countries they rank second only to anemia, with approximately 7 - 10% of all pregnancies being complicated by some form of hypertensive disease.

It is a complicated, multi - organ disease occurring in up to 6 - 8% of pregnancies, typically after 20 weeks of gestation in previously normotensive women [(1, 2).]

As the most common medical complication of pregnancy, it is the leading cause of maternal morbidity and mortality. [(3)] The severe form of PE is associated with higher risk of different adverse maternal and fetal outcomes. [(4)] Epidemiological studies are indicating that the incidence rate of PE is increasing worldwide, and it is accounting for about 50, 000 deaths worldwide annually. [(5)]

The hs - CRP is a sensitive marker of tissue damage and inflammation. It is useful in differentiating acute inflammation as well as assessment of severity of inflammation. PCT has been widely used as a marker of bacterial infection. [(6)] Recently, it has been used as indicators of systemic inflammations mainly induced by bacterial infection. The half - life of PCT is 25–30 h and rises and decreases more quickly during and after alleviation of infection than other inflammatory factors such as erythrocyte sedimentation rate and CRP. [(7)]

In PE, there is a deterioration of maternal renal function with the possibility of a rise in serum creatinine to more than 0.9 g/L, liver involvement with elevated liver enzymes, pulmonary edema, hematological disorders including thrombocytopenia, hemolysis and disseminated intravascular coagulation, neurological involvement with visual disturbances, severe headaches and hyperreflexia, and intrauterine growth restriction. [(8, 9)]

Women with preeclampsia in the 3rd trimester showed significantly higher levels of serum procalcitonin, C - reactive protein (CRP), and plasma D - dimer levels, and these hematological indices were significantly higher in patients with severe as compared to mild preeclampsia. [(10)]

In his study, we compare the levels of hsCRP, PCT and D - dimer in pregnant women with mild and severe PE and women with normal pregnancy.

2. Material and Methods

The prospective case - control study was carried out in the Department of Obstetrics and Gynecology, MLB Medical College, Jhansi, UP, after approval of institutional ethical committee. An informed consent was taken from all participants. One hundred cases were taken in this study, which were divided into two groups viz 50 cases of preeclamptic women served as study group while 50 normotensive healthy pregnant women were served as control group.

Preeclampsia was defined as gestational hypertension with proteinuria, specifically, blood pressure of 140 mmHg systolic or higher or 90 mmHg diastolic or higher; and 24 - hour urinary protein greater than or equal to 300 mg or proteinuria greater than or equal to 1+ by dipstick testing, after the 20th week of pregnancy in a previously normotensive and nonproteinuric woman.

Women without a history of convulsion and/or neurologic deficit, who will be diagnosed as eclamptic constituted the

eclampsia group (E). Normotensive, healthy third trimester women will be chosen as the controls (C).

The cases of chronic renal disease, chronic hypertension, diabetes mellitus, gestational diabetes, cardiovascular disease, premature rupture of membranes, urinary tract infection, autoimmune disease, malignancy were excluded from the study.
Blood pressure was taken after resting for 5 min, with both arms, and a series of recordings was made at 5 - min intervals for three times.

Blood sample was collected when the patients first presented for the evaluation and before initiation of any treatment. Estimation of serum CRP concentration was done by liquid phase immuneprecipitation assay and turbulometry. Cut off value for CRP was 5 mg/l. Serum procalcitonin level was measured by ELISA kit according to the manufacturer's instructions. Plasma D - Dimer was measured using D - Di test a rapid latex agglutination slide test. .

Statistical analysis
Data was presented as mean, standard deviation. Pearson's correlation test was used to analyze the inter - correlation between CRP, PCT and D - dimer.

3. Results

The present study was conducted on 100 antenatal women with gestational age after 20 wks who were presented in the department, out of them 50 cases who developed Pre - eclampsia were described as Study Group and 50 normotensive cases were taken as control group. Maximum no. of patients 34 (78.0%) who developed preeclampsia and those who remained normotensive 24 (48.0%) were young in the age group of 20 - 30 years. Majority of cases were lower class in both the groups and maximum cases were belongs to rural area in both the groups because the study area surrounded by rural area and serving the medical facilities to very vast area. Maximum cases were having BMI between 18.5 - 25.

Table 1: Demographic Profile of Cases

	Study Group		Control Group	
	No.	%	No.	%
Age (yrs)				
<20	6	12.0	6	12.0
20 - 30	34	78.0	24	48.0
>30	10	20.0	20	40.0
Gravida				
Primiparity	20	40.0	12	24.0
Multiparity	30	60.0	38	76.0
Socioeconomic status				
Upper	2	4.0	3	6.0
Middle	15	30.0	20	40.0
Lower	33	66.0	27	54.0
Residential area				
Rural	36	72.0	32	64.0
Urban	14	28.0	18	36.0
BMI				
<18.5	0	0	0	0
18.5 - 25	38	76.0	30	60.0
>25	12	24.0	20	40.0

Maximum no. of patients 34 (78.0%) who developed preeclampsia and those who remained normotensive 24 (48.0%) were young in the age group of 20 - 30 years. Majority of cases were lower class in both the groups and maximum cases were belongs to rural area in both the groups because the study area surrounded by rural area and serving the medical facilities to very vast area. Maximum cases were having BMI between 18.5 - 25.

Table 2: Blood Pressure

BP (mm Hg) Mean Value	Study Group	Control Group	P Value
Systolic BP	155.4±6.02	115.0±5.6	<0.05
Diastolic BP	110.4±3.2	80.4±2.4	<0.05

Mean systolic blood pressure was 155.4±6.02 and mean diastolic blood pressure was 110.4±3.2 in the study group, at the time of delivery, whereas in control group mean systolic blood pressure was 115.0±5.6 and mean blood pressure was 80.4±2.4. Both systolic and diastolic blood pressure were significantly elevated in pre - eclampsia cases.

Table 3: Signs and Symptoms in Pre - Eclampsia Cases

Symptoms/ Signs	No.	%
Blurring of vision	2	4.0
Convulsions	3	6.0
Headache	10	20.0
Oliguria	-	-
Pedal Edema	36	100
Proteinuria	50	100
Asymptomatic	12	24.0
Vulval edema/abdominal edema	24	48.0
Epigastric pain	2	4.0

Proteinuria and pedal edema were found to be most common sign, which was present in all 50 (100%) and 75.0% cases in study group followed by abdominal edema 48.0%. All patients in control group were asymptomatic.

Table 4: hsCRP LEVEL, D - dimer and PCT level in study and control group

Biomarker	Study Group		Control Group	
	No.	%	No.	%
hsCRP Level (mg/L)				
<7	7	14.0	46	92.0
>7	43	86.0	4	8.0
d - dimer Level (mg/l)				
<4.0	0	0	44	88.0
>4.0	50	100	6	12.0
PCT Level (ng/ml)				
<0.25	2	4.0	46	92.0
>0.25	48	96.0	4	8.0

hsCRP level in study group was >7mg/L was found in 43 (86.0%) cases while in 7 (14.0%) cases it was <7mg/L while in control group only in 4 (8.0%) cases it was >7mg/L.

All 50 cases the d - dimer level in study group was >4mg/L was found while in control group, only 6 (12.0%) cases were d - dimer level of>4mg/l.

In 48 (96.0%) cases PCT level was found >2.5ng/ml while in control group it was found in 4 (8.0%) cases.

Table 5: Comparison of HSCRP, PCT and D - dimer among study and control group

Parameter	Study group		Control group (n=50)	P value
Parameter	Mild preeclampsia (n=30)	Severe preeclampsia (n=20)		
hsCRP (mg/L)	10.6±2.5	15.55±5.25	5.44±3.94	<0.001
d - dimer (mg/l)	4.6±0.5	6.9±0.7	1.6±0.9	<0.001
PCT (ng/ml)	0.33±0.054	0.77±0.1	0.14±0.07	<0.001

Both severe pre - eclampsia and mild preeclampsia groups showed significantly higher PCT values when compared with healthy control group (p<0.001). Higher d - dimer levels were found in pre - eclampsia and mild preeclampsia groups compared to control group. Also, severe pre - eclampsia group showed significantly higher PCT values when compared with mild pre - eclampsia group (P=0.012).

4. Discussion

Preeclampsia (PE) remains one of the most serious complications of pregnancy. It still remains the enigma of theories. The underlying cause of pathophysiological mechanism responsible for disease process, initiates 10 - 12 weeks of pregnancy. Various clinical, biophysical and biochemical tests have been recommended to predict the development of pre - eclampsia during early pregnancy but none of these have been proved as an ideal test for prediction. There were many studies regarding the role of CRP in PE and its association with disease severity, but there were few studies for PCT. [11 - 18]

Despite great research efforts, in 2004, the World Health Organization concluded that no single test was yet available to provide accurate screening for PE. Since then, there has been growing interest in the combination of markers for PE screening.

Rebelo *et al*. have indicated the association between CRP and late PE in a systematic review and meta - analysis [19], many studies have confirmed the association [11 - 15, 20] and many did not. [21 - 23]

In this study maximum cases 34 (78.0%) of preeclampsia was found to be in age group of 20 - 30 yrs with mean of 25.4±5.3 years which is close to results of Bilir F, et al [24] study which reports mean age of 26.9±4.6 years.

Maximum cases in study group belonged to lower and middle class, (66.0% and 30.0% cases) and 72% cases were from rural area because of study area which is surrounded by rural area.

In our study 24.0% cases were found to be BMI > 25 however in control group it was 40% cases who have BMI > 25. Direkv and - Moghadam A, et al [25] study also reported no significant association between BMI and preeclampsia. Reys LM, et al [26] study concluded that high BMI is a significant risk factor for development and severity of preeclampsia among pregnant women.

Blood pressure (systolic and diastolic) of women in this study was (155.4±6.02) significantly higher among preeclampsia than controls (115.0±5.6). This finding in agreement with results of Hakim J, et al [27] study that reported significant association between gestational hypertension with preeclampsia development and severity.

The study found significant higher means of serum procalcitonin among preeclampsia patients 48 (96.0% cases in comparison to controls in which only 4 (8.0%)) cases were higher Precalcitonin level (p<0.001). Serum procalcitonin is a new marker in pregnant women population. Montagnana et al [28] showed that serum procalcitonin was associated with preeclampsia. Following this study, Can et al [29] found that there was a significant correlation between severe preeclampsia and procalcitonin levels.

In all cases of study group, D - Dimer levels were higher in comparison to control group where only 6 (12.0%) cases had raised d - dimer levels. Our result supported by the study of Kucukgoz GU, et al [30] which shows d - dimer and procalcitonin significantly higher among PE and can be used to predict severity of PE. Women with preeclampsia in the 3rd trimester showed significantly higher levels of serum procalcitonin, C - reactive protein (CRP), and plasma D - dimer levels, and these hematological indices were significantly higher in patients with severe as compared to mild preeclampsia [30].

Procalcitonin and D - dimer were correlated significantly to each others in all study participants. This finding is consistent with results of Kaya B, et al [31] study. A significant correlation was observed in present study between mean arterial blood pressure and both procalcitonin and D - dimer (p<0.001). This finding is in accordance with results of Jaimes F, et al [32] study and Kucukgoz GU, et al [30] study.

Despite great research efforts, in 2004, the World Health Organization concluded that no single test was yet available to provide accurate screening for PE. Since then, there has been growing interest in the combination of markers for PE screening.

5. Limitations of study

1) Restriction of study duration and cases of lower socioeconomic status, additionally, unavailability and high cost of these tests, PCT and D - dimer, in our country lead restriction in the sample size.
2) This study conducted at a tertiary center, so that findings of the study supported large sample size of Indian population.
3) No follow - up done.

6. Conclusion

Procalcitonin level and D - dimer level are good predictors for preeclampsia among pregnant women and could be used as screening tests for detection and severity of pre - eclampsia.

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