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Procalcitonin- A Biomarker for Severity of Preeclampsia

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Abstract

Introduction: Hypertensive disorders of pregnancy, affecting approximately 10% of pregnancies, include chronic hypertension, gestational hypertension, and preeclampsia. Preeclampsia poses significant risks, including maternal and fetal morbidity and mortality. Elevated levels of pro-inflammatory cytokines, such as procalcitonin (PCT), have been observed in preeclampsia, indicating its potential as a biomarker.

Aim: The study aimed to evaluate the levels of procalcitonin (PCT) in preeclamptic patients compared to normotensive pregnant women, to explore its potential as a biomarker for preeclampsia.

Methods: This prospective study included antenatal women between 30-34 weeks gestation, divided into two groups: Group A (preeclamptic) and Group B (normotensive). Clinical assessments, including blood pressure measurements, were conducted. Serum procalcitonin was measured using the VITROS B.R.A.H.M.S test. Statistical analysis compared mean PCT levels between groups and evaluated correlations with clinical parameters.

Results: Group A (preeclampsia) had significantly higher systolic (155.56±3.26 mmHg) and diastolic (94.76±3.02 mmHg) blood pressure compared to Group B (120.32±6.24 mmHg and 84.63±3.44 mmHg, respectively; $p<0.0001$). Mean procalcitonin levels were also significantly higher in Group A (0.55±0.26) versus Group B (0.04±0.02; $p<0.0001$). Positive correlations were found between PCT levels and systolic ($r=0.39$) and diastolic blood pressure ($r=0.41$) and corelation of procalcitonin with severity of preeclampsia.

Conclusion: Pregnant women with preeclampsia exhibit elevated procalcitonin levels compared to those with normal pregnancies, suggesting that PCT may reflect the heightened inflammatory response associated with preeclampsia. These findings indicate PCT's potential as a biomarker for early diagnosis and severity differentiation in preeclampsia.

Keywords: Hypertensive disorders, preeclampsia, procalcitonin, biomarkers, inflammation.

Introduction

Hypertensive disorders of pregnancy affect about 10% of pregnancies, characterized by new-onset hypertension (≥140 mmHg systolic or ≥90 mmHg diastolic) after 20 weeks' gestation, according to the International Society for the Study of Hypertension in Pregnancy (ISSHP). This includes chronic hypertension, gestational hypertension, and preeclampsia. The American College of Obstetricians and Gynecologists (ACOG) defines preeclampsia by a systolic blood pressure of 140 mmHg or more or diastolic blood pressure of 90 mmHg or more on two occasions at least four hours apart, along with proteinuria.[1]

In normal pregnancies, the innate immune system activates a maternal inflammatory response; however, in preeclampsia, an excessive systemic inflammatory response results in endothelial dysfunction and clinical symptoms.[2] Elevated levels of pro-inflammatory cytokines, including procalcitonin, have been observed in preeclampsia patients compared to normotensive pregnant women. Procalcitonin, traditionally used as a marker for systemic inflammation,10 shows potential as a biomarker for preeclampsia due to its quick response to inflammatory changes. Despite some studies reporting higher procalcitonin levels in preeclampsia patients,[3] conflicting findings exist,[4] highlighting the need for further research on procalcitonin's role as a biomarker for preeclampsia.

Early diagnosis of preeclampsia is crucial to prevent associated morbidities and mortalities. Identifying preeclampsia early using appropriate inflammatory biomarkers can help mitigate risks. Additionally, considering genetic and ethnic variations in inflammatory factor levels may enhance the accuracy of these biomarkers in early detection.

This study aims to investigate procalcitonin level variations between patients with preeclampsia and those with normotensive pregnancies, seeking to identify significant differences that could establish procalcitonin as a potential biomarker for preeclampsia, thereby contributing to improved clinical practices and outcomes.

Material and Method

Approval was obtained from the Institutional Research Review Board and Ethical Committee prior to the study. Antenatal cases between 30-34 weeks of gestation were recruited after obtaining informed consent.

Participants were divided into two groups:

[1]. Group A (Cases): Pregnant women with preeclampsia.

[2]. Group B (Controls): Pregnant women with normal blood pressure.

Both groups underwent general and obstetric examinations, along with routine blood investigations, including CBC, blood typing, blood sugar, RFT, LFT, VDRL, HBsAg, HIV, anti-HCV, thyroid profile, rubella IgG and IgM, USG and urine analysis. Fasting venous blood (3 ml) was collected under aseptic conditions, allowed to clot, and centrifuged at 3000 rpm for 5 minutes. Serum samples were stored at -20˚C until serum procalcitonin (PCT) levels were assessed using the VITROS B.R.A.H.M.S test. Data were compiled to analyze the association of PCT levels between the two groups.

Statistical analysis

Statistical analysis involved expressing quantitative data as mean and standard deviation, while qualitative data were represented in percentages and proportions. A t-test was employed for quantitative data analysis, and the chi-square test was used for qualitative data. A p-value of less than 0.05 was considered statistically significant and

for some parameters pearson correlation (r) found positive with procalcitonin level.

Selection Criteria

Inclusion Criteria

- All Pregnant women (30-34 weeks) with singleton live pregnancy and willing to provide consent were included.

Exclusion Criteria

- Chronic hypertension.
- Chronic medical conditions (e.g., diabetes, heart disease, kidney disease, malignancies, autoimmune disorders) were excluded.

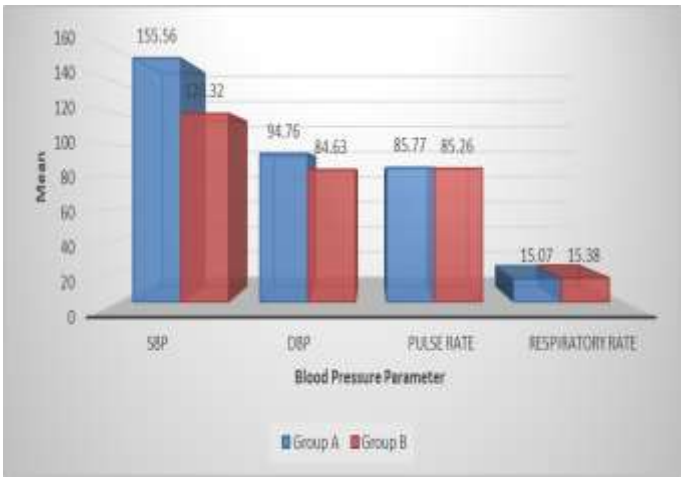
Results and Observation

Group A's mean age was 28.06±5.86 years, while Group B was 28.58±5.48 years. Ethnically, Group A included 103 Hindus (68.67%), 44 Muslims (29.33%), and 3 Christians (2.00%), compared to Group B with 109 Hindus (72.67%), 40 Muslims (26.67%), and 1 Christian (0.67%). Education levels in Group A were 24.00% primary, 24.67% high school, 27.33% secondary, and 24.00% graduate or higher, while Group B had 30.67% primary, 24.67% high school, 21.33% secondary, and 23.33% graduate or higher.

In terms of occupation, Group A comprised 42.00% homemakers, 44.00% in private jobs, and 14.00% in government jobs. Group B had 40.00% homemakers, 46.67% in private jobs, and 13.33% in government jobs. Urban residents made up 72.67% of Group A and 66.67% of Group B. Hemoglobin levels showed that 50.67% of Group A had Hb ≥9 g/dL, while 55.33% of Group B did. Edema was present in 54.00% of Group A and 20.00% of Group B. The mean gestational age was 32.02±1.48 weeks for Group A and 31.88±1.40 weeks for Group B.

The demographic profile of two groups were similar.

Graph 1: Distribution of study population according to Vitals.



Group A had a mean systolic blood pressure (SBP) of 155.56±3.26 mmHg, significantly higher than Group B's 120.32±6.24 mmHg ($p<0.0001$). Diastolic blood pressure (DBP) also showed a significant difference, with Group A at 94.76±3.02 mmHg and Group B at 84.63±3.44 mmHg ($p<0.0001$). The pulse rate was similar between groups: Group A at 85.77±9.36 beats per minute and Group B at 85.26±8.89 beats per minute ($p=0.62$). The respiratory rates were 15.07±2.63 breaths per minute for Group A and 15.38±2.61 for Group B. In terms of Amniotic Fluid Index (AFI), 142 cases (94.67%) in Group A and 149 cases (99.33%) in Group B had an AFI of 7 or greater. In Group A, 142 cases (94.67%) had an Amniotic Fluid Index (AFI) of 7 or greater, while 8 cases (5.33%) had an AFI below 7. In Group B, 149 cases (99.33%) had an AFI of 7 or greater, and 1 case (0.67%) had an AFI below 7.

Table 1: Distribution of study population according to Laboratory parameters

Laboratory parameters		Serum Procalcitonin				P values
		Group A		Group B		
		Mean	SD	Mean	SD	
SGOT	<40	0.6	0.25	0.05	0.02	<0.0001
	≥40	0.53	0.27	0.04	0.02	
SGPT	<40	0.57	0.25	0.05	0.028	<0.0001
	≥40	0.56	0.26	0.045	0.027	
Uric Acid	<40	0.56	0.26	0.046	0.027	<0.0001
	≥40	0.53	0.27	0.049	0.032	
Creatinine	<0.7	0.63	0.26	0.04	0.03	<0.0001
	0.7-1.3	0.51	0.27	0.047	0.028	
	>1.3	0.59	0.24	0.05	0.026	

In patients with SGOT levels <40 U/L, Group A had a mean serum procalcitonin level of 0.60±0.25, compared to 0.05±0.02 in Group B (p<0.0001). For SGOT ≥40 U/L, Group A's mean was 0.53±0.27 vs. 0.04±0.02 in Group B (p<0.0001). For SGPT <40 U/L, Group A had 0.57±0.25, while Group B had 0.05±0.028 (p<0.0001). For SGPT ≥40 U/L, Group A's mean was 0.56±0.26 compared to 0.045±0.027 in Group B (p<0.0001). In terms of uric acid, levels <7.5 mg/dL in Group A showed a mean procalcitonin level of 0.56 vs. 0.046 in Group B (p<0.0001), while levels ≥7.5 mg/dL had Group A at 0.53 and Group B at 0.049 (p<0.0001). For creatinine <0.7 mg/dL, Group A's mean CA-125 was 0.63±0.26 vs. 0.04±0.03 in Group B (p<0.0001). For creatinine 0.7-1.3 mg/dL, Group A had 0.51±0.27 compared to 0.047±0.028 in Group B (p<0.0001). For creatinine >1.3 mg/dL, Group A's mean was 0.59±0.24 vs. 0.05±0.026 in Group B (p<0.0001).

Graph 2: Correlation of study population according to S. Procalcitonin

In Group A, 0.67% had levels <0.1, 20.67% had 0.1-0.3, 30.67% had 0.4-0.6, 38.00% had 0.7-0.9, and 10.00% had >0.9. In Group B, 10.67% had levels <0.1, 25.33% had 0.1-0.3, 28.00% had 0.4-0.6, 31.33% had 0.7-0.9, and 4.67% had >0.9. The mean procalcitonin level was significantly higher in Group A (0.55±0.26) than in Group B (0.04±0.02), with a p-value of <0.0001.

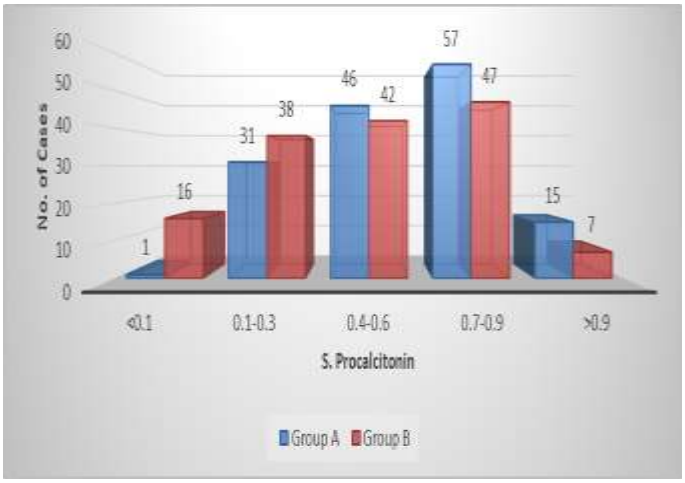


Table 2: Correlation severity of study population according to S. Procalcitonin

S. Procalcitonin	Mild Pre-eclampsia		Severe Pre-eclampsia	
	No. of Cases	Percentage	No. of Cases	Percentage
<0.1	27	20.93	0	0.00
0.1-0.3	49	37.98	2	9.52
0.4-0.6	43	33.33	3	14.28
0.7-0.9	7	5.42	7	33.33
>0.9	3	2.32	9	42.85
Total	129	99.98	21	
Mean±SD	0.56±0.26		0.76±0.29	
p-value	0.001			

In the mild pre-eclampsia group, 20.93% had levels <0.1, 37.98% had levels 0.1-0.3, 33.3% had levels 0.4-0.6, 5.42% had levels 0.7-0.9, and 2.32% had levels >0.9. In contrast, the severe pre-eclampsia group had no cases with levels <0.1, 9.52% with levels 0.1-0.3, 14.28% with levels 0.4-0.6, 33.3% with levels 0.7-0.9, and 42.85% with levels >0.9. The mean serum procalcitonin level was 0.56±0.26 for mild pre-eclampsia and 0.76±0.29 for severe pre-eclampsia, with a p-value of 0.001, indicating statistically significant difference between the two groups.

Table 3: Pearson correlation of Procalcitonin with SGOT/SGPT, Creatinine/Uric acid, SBP/DBP

Parameter	SGOT	SGPT	Creatinine	Uric Acid	SBP	DBP
r-value	0.27	0.26	0.3	0.32	0.39	0.41
p-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

The correlation coefficients indicate statistically significant positive correlations: SGOT and SGPT have an r-value of 0.27 ($p < 0.001$); SGPT alone has an r-value of 0.26 ($p < 0.001$). For creatinine, the r-value is 0.30 ($p < 0.001$), and for uric acid, it is 0.32 ($p < 0.001$). Additionally, systolic blood pressure (SBP) shows a moderate positive correlation with an r-value of 0.39 ($p < 0.001$), while diastolic blood pressure (DBP) has an r-value of 0.41 ($p < 0.001$).

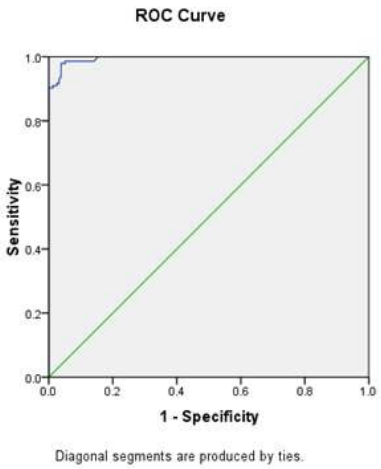
Table 4: ROC Analysis for estimating the optimal threshold score of procalcitonin and its sensitivity and specificity

AUC	**0.995**
P-Value	<0.0001
95 CI	0.991-0.999
Cutoff	0.119
Sensitivity	97.9
Specificity	96.2

The area under the receiver operating characteristic curve (AUC) is 0.995 ($p < 0.0001$), demonstrating excellent diagnostic performance and statistical significance, with a 95% confidence interval of 0.991 to 0.999. The optimal cutoff value is 0.119, yielding a sensitivity of 97.9%

(accurately identifying 97.9% of true positive cases) and a specificity of 96.2% (correctly identifying 96.2% of true negative cases).

Graph 3:



Discussion

Procalcitonin (PCT) is a prohormone that acts as a biomarker for bacterial infections. It is produced rapidly in response to infection, with levels detectable in plasma within 2 hours and peaking at around 6 hours, remaining stable for 20-72 hours. This characteristic makes PCT valuable for early detection, severity assessment, and prognosis of bacterial infections, as well as for guiding antibiotic selection.[8]

In the context of preeclampsia (PE), which is linked to an exaggerated inflammatory response during pregnancy, PCT is being investigated as a potential predictive marker. While research is limited, studies indicate that PCT may serve as a useful predictor for PE.[9]

Table No. 1 shows that Group A had significantly higher systolic (155.56±3.26 mmHg, $p < 0.0001$) and diastolic blood pressure (94.76±3.02 mmHg, $p < 0.0001$) than Group B, with no significant differences in pulse ($p = 0.62$) and respiratory rates ($p = 0.60$). Jannesari R et al.[10] found systolic blood pressure of 112.7 ± 16.5 mmHg in normal pregnant women vs. 159.1 ± 24.8 mmHg in those with preeclampsia ($p < 0.05$), and diastolic pressures of 69.3 ± 11.6 mmHg vs. 100.7 ± 14.4 mmHg ($p < 0.05$). Rao R S et al.[11] reported systolic blood pressures of 109.76 mmHg in controls vs. 150.00 mmHg in preeclamptic women, with diastolic pressures of 74.29 mmHg vs. 100.00 mmHg.

In Group A, 0.67% had levels <0.1, 20.67% had levels 0.1-0.3, 30.67% had levels 0.4-0.6, 38.00% had levels 0.7-0.9, and 10.00% had levels >0.9. In Group B, the distribution was 10.67% <0.1, 25.33% 0.1-0.3, 28.00% 0.4-0.6, 31.33% 0.7-0.9, and 4.67% >0.9. The mean PCT level was significantly higher in Group A at 0.55±0.26 compared to 0.04±0.02 in Group B ($p < 0.0001$). A similar study by Jannesari R et al.[10] reported a mean PCT of 0.04 ng/mL (±0.01) in normal pregnant women and 0.05 ng/mL (±0.03) in those with preeclampsia ($p = 0.001$). Fatimah N I et al.[12] found a median PCT level of 241.34 pg/mL in pregnant women with preeclampsia (n=40) versus 227.78 pg/mL in those without (n=25), with a significant difference ($p = 0.005$).

The area under the receiver operating characteristic curve (AUC) is 0.995 ($p < 0.0001$), indicating excellent diagnostic accuracy. The 95% confidence interval for the AUC is 0.991 to 0.999, with an optimal cutoff value of 0.119. At this cutoff, the sensitivity is 97.9%, correctly identifying 97.9% of true positives, while the specificity is 96.2%, accurately identifying 96.2% of true negatives. Similarly, Aydin S M et al.[13] found a statistically significant AUC for procalcitonin and NLR, with a p-value < 0.05 at the 95% confidence interval. Setiawan G W et al.[14] reported an optimal cutoff for procalcitonin at 0.095 ng/mL, with sensitivity at 68% and specificity at 100%.

Conclusion

This study finds that pregnant women with preeclampsia (PE) have higher procalcitonin (PCT) levels than those

with normal pregnancies, indicating PCT may reflect the heightened inflammatory response in PE. Additionally, PCT levels are significantly elevated in severe preeclampsia compared to mild cases, suggesting it could effectively differentiate between the severities of the condition. While these findings are promising, the study notes limitations and calls for future research to address them, including exploring a wider range of inflammatory factors to enhance the understanding of inflammatory mechanisms in preeclampsia and improve PCT's clinical utility as a biomarker.

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