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Maternal Serum Soluble Urokinase Plasminogen Activator Receptor And C-Reactive Protein Levels in Pre-Eclampsia: A Case-Control Study

Divya[1], Rachna Agarwal[2], Mohit Mehndiratta[3], Sandhya Jain[4], Vinita Rathi[5]

[1]Resident, Department of Obstetrics & Gynaecology, University College of Medical Sciences, New Delhi, India,
[2]Director Professor & Head, Department of Obstetrics & Gynaecology, University College of Medical Sciences, New Delhi, India,
[3]Director Professor and Head, Department of Biochemistry UCMS & GTB Hospital, Delhi,
[4]Director Professor, Department of Obstetrics & Gynaecology, University College of Medical Sciences, New Delhi, India,
[5]Director Professor, Department of Radiodiagnosis, UCMS & GTB Hospital, Delhi

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Corresponding Author:

Dr. Divya
Resident, Department of Obstetrics & Gynaecology, University College of Medical Sciences, New Delhi, India,

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ABSTRACT

Background & Objectives: Soluble urokinase plasminogen activator receptor (suPAR) is a biomarker increasingly used for monitoring systemic inflammation. We therefore aim to investigate the potential role of suPAR as a possible inflammatory marker in comparison to C-reactive protein (CRP, already known inflammatory marker) in preeclampsia (PE) and normotensive pregnancy as a prognostic marker.
Methods: This observational case-control study included 40 cases and 40 controls. Cases were defined as women diagnosed with pre-eclampsia for termination of pregnancy at ≥28 weeks of gestation while controls were normotensive healthy pregnant women. Maternal serum samples were taken in plain vials, centrifuged, stored at -20°C and further analysed for serum suPAR and CRP levels.
Results: The mean value of serum suPAR levels was higher in preeclamptic cases (5.08 ± 1.2 ng/mL) than in the control group (2.81 ± 0.52 ng/ml) and was statistically significant ($p<0.05$). The mean value of serum CRP levels was higher in preeclamptic cases 21.65 ± 9.18 mg/L than in the control group 15.62 ± 3.35 mg/L and was statistically significant ($p<0.05$) (Table 1). No significant difference was found on comparing serum suPAR levels between HELLP vs non-HELLP and non-severe vs severe pre-eclampsia.
Conclusion: Our study investigated suPAR and CRP levels in preeclampsia patients compared to controls. suPAR levels were significantly elevated in preeclamptic patients versus controls. Similarly, CRP levels were higher in preeclampsia cases than controls, suggesting their potential as biomarkers for the condition.

Keywords*: Soluble urokinase plasminogen activator receptor (suPAR), C-reactive protein (CRP), pre-eclampsia, biomarker.*

INTRODUCTION

Pre-eclampsia (PE) is one of the leading causes of perinatal morbidity and mortality, affecting 5-11% of all pregnancies. [1,2] PE is multisystem disorder characterized by new onset of hypertension and proteinuria or the new onset of hypertension plus significant end organ dysfunction with or without proteinuria. Systemic inflammation and the impairment of maternal immune tolerance cause cytokine mediated release of inflammatory markers like CRP, IL-6 etc. Soluble urokinase plasminogen activator receptor (suPAR) is one such marker of systemic inflammation and immune activation. Its expression is upregulated in many human diseases and high concentrations in blood are associated with increased mortality in both patients and apparently healthy individuals. [3,4,5] The aim of our study is to assess the levels of suPAR and also to evaluate CRP, which is a known marker of inflammation in PE cases and healthy pregnancy and to use suPAR as a prognostic marker.

OBJECTIVES

Our primary objective was to determine and compare maternal serum suPAR levels and CRP levels between pre-eclampsia cases and controls. Our secondary objectives were to determine and compare maternal serum suPAR and CRP levels between early-onset and late-onset pre-eclampsia, HELLP and non HELLP, also between PE without severe features and PE with severe features as a prognostic marker and to assess the presence of B lines in lung USG in preeclampsia and its correlation with suPAR.

MATERIALS AND METHODS

It was an observational case-control study including 40 subjects in each group conducted from May 2023 to November 2024. This study was undertaken in the Department of Obstetrics and Gynaecology, Department of Biochemistry and Department of Radiodiagnosis, University College of Medical Sciences and Guru Teg Bahadur Hospital, Dilshad Garden, Delhi after taking approval from the Institutional Ethics Committee-Human Research (IEC-HR) (Ethics approval number- IECHR-2023-59-94). Written informed consent was taken from all the cases and controls.

Sample size: This study is being conducted on evaluation of maternal serum suPAR and CRP levels. In a study conducted by Toldi et al considering the suPAR levels as 2.02 (1.8-2.4) in normal pregnancy and 3.18 (2.3-4.71) in preeclampsia pregnancy cases and CRP levels as 3.9 (2.1-7.25) in normal pregnancy and 6.60 (3.55-15.40) in preeclampsia pregnancy cases.[1]
To estimate this difference in median values at □=5% and power=90%, a sample of 15 and 28 cases is required in each group respectively. But due to availability of time resources we propose to take 40-40 cases in each group i.e. total of 80 subjects

Inclusion criteria for subjects: Singleton pregnancy with diagnosis of pre-eclampsia (PE) for termination of pregnancy (28 weeks and above period of gestation).

Exclusion criteria for subjects:
Pregnant women with the following conditions were excluded: Any febrile illness, known case of chronic hypertension, chronic renal disease, Diabetes mellitus, PROM/PPROM, multifetal gestation, conceived via ART, fetal congenital anomalies, known case of chronic inflammatory disease such as TB, autoimmune disease etc. APLA, patient on aspirin.

Women diagnosed with pre-eclampsia for termination of pregnancy at 28 weeks of gestation and above meeting the inclusion and exclusion criteria were taken as cases while normotensive healthy pregnant women (age and gestational age-matched) were taken as controls.

Methodology: After taking written informed consent, detailed history and examination of all the subjects were performed. All cases were investigated for pre-eclampsia. All subjects were classified as non-severe pre-eclampsia and severe pre-eclampsia, early-onset and late-onset pre-eclampsia. Maternal serum samples were taken in plain vials just prior to delivery, centrifuged and stored at -20◦C. Delivery details and neonatal outcomes were noted. Stored samples were analysed for suPAR and CRP using commercially available kits.

Statistical analysis:
For qualitative parameters both the groups will be compared by chi-square test / Fisher's exact test and quantitative parameters by unpaired t-test or Mann-Whitney U-test depending upon nature of data. $p<0.05$ will be considered as significant.

RESULTS

The cases and controls were comparable in age, gestational age, and socio-demographic characteristics. Among the preeclampsia (PE) group, 22 (55%) had non-severe and 18 (45%) had severe disease. Early-onset PE (<34 weeks) occurred in 20% of cases, more often in the severe group. HELLP syndrome was seen in 8 (44.4%) severe PE cases, and FGR occurred more frequently in severe PE (80%) than non-severe cases (20%). There was no maternal mortality and two neonatal deaths among cases.

The mean BMI of cases (26.37 ± 3.95 kg/m²) was significantly higher than controls (23.04 ± 1.49 kg/m²; $p < 0.05$). Caesarean delivery was more common in cases (30%) than controls (12.5%; $p < 0.05$). Mean birth weight was lower in cases (2.1 ± 0.4 kg) versus controls (2.85 ± 0.28 kg; $p < 0.05$), and NICU admission was higher among cases (45% vs 7.5%; $p < 0.05$).

Serum suPAR levels were significantly elevated in PE (5.08 ± 1.20 ng/mL) compared to controls (2.81 ± 0.52 ng/mL; $p < 0.05$). CRP levels were also higher in cases (21.65 ± 9.18 mg/L) than controls (15.62 ± 3.35 mg/L; $p < 0.05$) (Table 1, Fig 1 & 2).

Table 1: Comparison between cases and controls

Parameters	Cases	Controls	p-value
Serum suPAR	5.08±1.2	2.81±0.52	<0.05
Serum CRP	21.65±9.18	15.62±3.35	<0.05

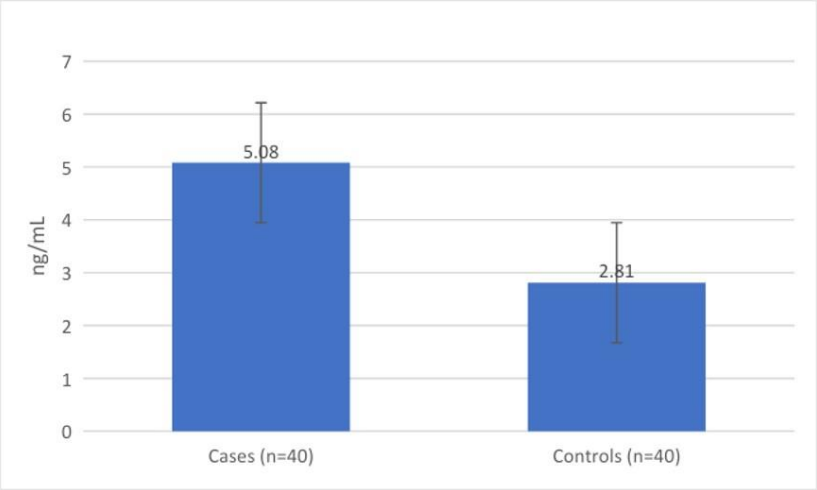

Fig 1: Comparison of serum suPAR levels between cases and controls

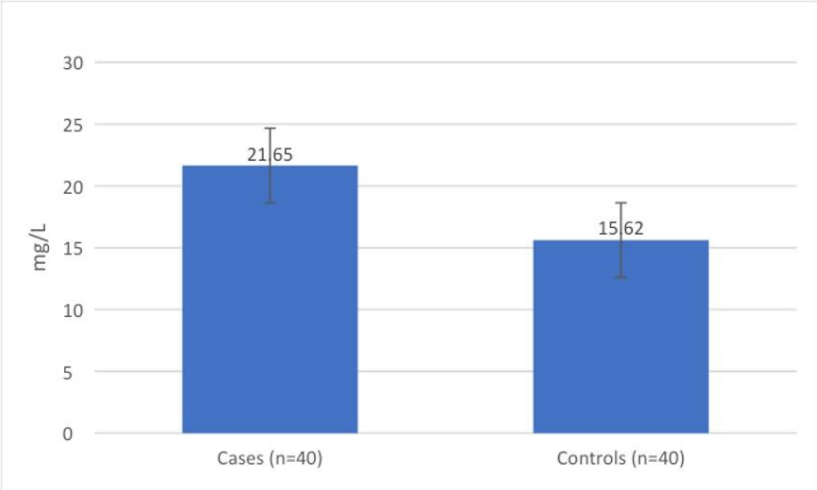

Fig 2: Comparison of serum CRP levels between cases and control

suPAR levels showed no significant difference between severe and non-severe PE (Table 2) or between HELLP and non-HELLP cases (Table 3). CRP was significantly higher in severe PE (24.04 ± 7.57 mg/L) and in early-onset PE (26.65 ± 9.89 mg/L) compared to late-onset PE (20.40 ± 8.56 mg/L; p = 0.003) (Table 4).

Table 2: Comparison between non-severe and severe PE

Parameters	Non-severe PE	Severe PE	p-value
Serum suPAR	5.15±1.36	4.99±0.95	0.54
Serum CRP	19.7±9.91	24.04±7.57	0.03

Table 3: Comparison between HELLP and non-HELLP groups

Parameters	HELLP	Non-HELLP	p-value
Serum suPAR	5.03±1.21	4.92±1.07	0.66
Serum CRP	21.9±9.99	23.18±5.04	0.47

Table 4: Comparison between early-onset & late-onset PE

Parameters	Early-onset PE	Late-onset PE	p-value
Serum suPAR	5.28±0.72	5.03±1.29	0.28
Serum CRP	26.65±9.89	20.4±8.56	0.003

DISCUSSION

In the present study, mean serum soluble urokinase plasminogen activator receptor (suPAR) levels were significantly higher in preeclamptic women compared to normotensive controls, indicating an inflammatory and endothelial activation component in preeclampsia (PE). Serum C-reactive protein (CRP) levels were also significantly elevated among cases, consistent with its established role as a marker of systemic inflammation.

No significant difference in suPAR levels was observed between severe and non-severe PE or between HELLP and non-HELLP groups, findings that align with previous studies suggesting that suPAR, though elevated in PE, may not reliably distinguish disease severity. In contrast, CRP levels showed significant elevation in severe and early-onset PE, reaffirming its sensitivity to disease activity.

The elevation of suPAR among preeclamptic women supports its potential as an adjunct biomarker reflecting chronic inflammation rather than acute disease severity. Variations in its levels may be influenced by sample timing, disease heterogeneity, or inter-individual differences. Nevertheless, its consistent rise in PE highlights its possible role alongside established markers such as CRP for a more comprehensive assessment of the inflammatory and endothelial components of the disorder.

The present study was limited by a modest sample size and single-point biomarker assessment. Serial measurements and larger, multicentric studies are needed to validate these findings and better define the prognostic role of suPAR in preeclampsia.

CONCLUSION

In this study, serum suPAR and CRP levels were significantly higher in preeclamptic women than in normotensive controls, indicating their role in systemic inflammation and endothelial dysfunction. While CRP correlated more strongly with disease severity, suPAR showed consistent elevation across all subgroups, reflecting its potential as a stable marker of the underlying chronic inflammatory process. suPAR may serve as a useful adjunct to traditional biomarkers for identifying women at risk and monitoring disease progression in preeclampsia.

ETHICS APPROVAL

Ethics approval was taken before conducting the study from the Institutional Ethics Committee-Human Research (IEC-HR) (Ethics approval number- IECHR-2023-59-94).

INFORMED CONSENT

A written informed consent was taken from all the subjects prior to the study.

CONFLICTS OF INTEREST

There were no conflicts of interest.

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