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ORIGINAL ARTICLE

Umbilical Artery Doppler Velocimetry Along With Uric Acid Values for the Screening of Preeclampsia in Second Trimester of Pregnancy

SHAH GUL KHAN[1], AALIA YOUSAF[2], MAHIN SAEED[2], PAREESAE ARTEMIS HUMAYUN[2], HOORIA KHAN[3], AMMARA NAZ[4]
[1]*Department of Obstetrics and Gynaecology, Combined Military Hospital, Malir Cantonment, Karachi, Pakistan*
[2]*Department of Obstetrics and Gynaecology, Combined Military Hospital, Peshawar Cantonment, Peshawar, Pakistan*
[3]*Asfendiyarov Kazakh National Medical University, Almaty, Kazakhstan*
[4]*Hayatabad Medical Complex, Peshawar, Pakistan*
Correspondence to: Shah Gul Khan, Email: shahgulkhan6@gmail.com

ABSTRACT

Introduction: Preeclampsia is a leading cause of maternal and fetal complications, and early detection is essential for better management. This study aimed to assess the combined utility of umbilical artery Doppler velocimetry and serum uric acid levels for screening preeclampsia during the second trimester.

Methodology: Combined Military Hospital Malir Cantonment recruited 60 pregnant women in their second trimester (14–28 weeks) between April 11, 2023, and October 10, 2023. Measurements were taken of uric acid levels and Doppler indices, which include systolic/diastolic ratio [S/D], resistance index [RI], and pulsatility index [PI]. The diagnosis of preeclampsia was made using clinical criteria. Associations were evaluated using statistical techniques such as logistic regression and chi-square testing.

Results: Of the 60 participants, 12 (20%) developed preeclampsia. Elevated uric acid (≥5.5 mg/dL) was found in 24 participants (40%). Abnormal Doppler indices were observed in 14 (PI), 10 (RI), and 16 (S/D ratio) participants. However, no significant association was found between abnormal parameters and preeclampsia. The combined screening approach showed 0% sensitivity, 64.3% specificity, and 90% negative predictive value.

Conclusion: This study found that neither elevated uric acid nor abnormal Doppler indices effectively predicted preeclampsia in the second trimester. The combined screening approach had limited predictive value. Larger studies are needed to validate these findings and explore other potential biomarkers for early preeclampsia detection.

Keywords: Preeclampsia, Second Trimester, Uric Acid, Doppler Velocimetry, Screening, Pregnancy.

INTRODUCTION

High blood pressure and proteinuria are the hallmarks of preeclampsia, a hypertensive pregnancy condition that usually appears after 20 weeks of gestation[1]. It continues to be a major contributor to unfavorable pregnancy outcomes such preterm delivery, fetal growth restriction, and stillbirth, and it is one of the primary causes of maternal and perinatal morbidity and death globally[2]. It is believed that the condition is caused by aberrant placental growth and function, which results in oxidative stress, inflammation, and systemic endothelial dysfunction[3]. While it's exact pathophysiology is not fully understood, impaired trophoblastic invasion, abnormal spiral artery remodeling, and placental ischemia have been implicated[4]. Despite advances in obstetric care, there remains no universally accepted, highly sensitive, and specific screening test for preeclampsia, underscoring the need for improved early detection methods[5].

One popular non-invasive method for evaluating placental circulation and fetal health is Doppler velocimetry of the umbilical artery[6]. Placental insufficiency, a defining feature of preeclampsia, is indicated by abnormal Doppler results, including elevated resistance indices and missing or reversed end-diastolic flow[7]. Doppler velocimetry may be used as an early screening method since studies have shown that impaired uteroplacental blood flow often occurs before the disease's clinical manifestation. Even while umbilical artery Doppler scans are often used to evaluate fetal development, their ability to predict preeclampsia is still uncertain, especially in low-risk pregnancies[8]. Interest in biochemical indicators linked to oxidative stress and endothelial dysfunction has increased as a result of the requirement for an additional biomarker to increase prediction accuracy[9].

The metabolic byproduct of purine breakdown, uric acid, has been well investigated in connection with preeclampsia. Even before clinical symptoms appear, women who later develop preeclampsia have been shown to have elevated blood uric acid levels[10]. Preeclampsia pathogenesis is believed to be mostly influenced by endothelial dysfunction, decreased nitric oxide bioavailability, oxidative stress, and inflammatory responses, all of which are believed to be exacerbated by hyperuricemia during pregnancy[11]. Furthermore, poor neonatal outcomes, maternal difficulties, and the severity of the illness have all been linked to elevated uric acid levels. However, since high amounts of uric acid may also be seen in diseases like persistent hypertension and renal failure, it is not a precise enough prognostic sign.

Given the limitations of using either Doppler velocimetry or uric acid levels in isolation, a combined approach may enhance the predictive power of preeclampsia screening. Integrating umbilical artery Doppler indices with maternal serum uric acid levels could provide a more comprehensive assessment of both vascular and biochemical markers of placental dysfunction, improving early risk stratification[12]. This dual-modality screening strategy has the potential to facilitate timely intervention, optimize antenatal surveillance, and ultimately improve maternal and fetal outcomes.

Although both umbilical artery Doppler velocimetry and uric acid levels have been studied separately as potential predictors of preeclampsia, limited research has evaluated their combined predictive value in the second trimester; therefore, this study aims to assess the effectiveness of integrating umbilical artery Doppler velocimetry with uric acid levels for the early screening of preeclampsia.

METHODOLOGY

Study Design and Setting: The Combined Military Hospital (CMH) Malir Cantonment served as the site of this prospective cohort study. In order to screen for preeclampsia in the second trimester of pregnancy, the research sought to assess the combined predictive value of blood uric acid levels and umbilical artery Doppler velocimetry. The research ran from April 11, 2023, until October 10, 2023, for a total of six months.

Sample Size Calculation: The sample size was determined based on the estimated prevalence of preeclampsia and the expected sensitivity and specificity of Doppler velocimetry and uric acid levels. Using a confidence level of 95%, a margin of error of 5%, and an anticipated effect size derived from previous literature, a minimum of 60 pregnant women in their second trimester was deemed appropriate for this pilot study.

Participant Selection and Inclusion Criteria: A total of 60 pregnant women in their second trimester (14–28 weeks of

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gestation) were recruited from the antenatal clinic of Combined Military Hospital (CMH) Malir Cantonment. Participants were selected based on the following inclusion criteria: singleton pregnancy, age between 18 and 40 years, no pre-existing hypertension, diabetes mellitus, renal disease, or other chronic illnesses, and willingness to participate and provide informed consent. Women with known fetal anomalies, multiple gestations, chronic kidney disease, or pre-existing hypertension were excluded from the study to minimize potential confounding factors.

Data Collection and Procedures: Each participant underwent a detailed obstetric and medical history assessment, followed by a physical examination. Gestational age was confirmed via ultrasound dating. The following assessments were performed:

Umbilical artery Doppler velocimetry was performed using a standardized protocol with a 3.5–5 MHz transducer. The umbilical artery waveform was recorded, and the pulsatility index (PI), resistance index (RI), and systolic/diastolic (S/D) ratio were measured. Abnormal Doppler findings were defined by elevated PI, RI, or absent/reversed end-diastolic flow. Serum uric acid levels were assessed by collecting a 5 mL venous blood sample from each participant. Uric acid levels were analyzed using an automated enzymatic colorimetric method, with a cutoff value of ≥5.5 mg/dL considered indicative of hyperuricemia. Preeclampsia, defined as new-onset hypertension (≥140/90 mmHg) and proteinuria (≥300 mg/24 h) after 20 weeks of gestation, was monitored for development in the participants during their pregnancy. Birth weight, gestational age at delivery, and any complications were among the maternal and fetal outcomes that were recorded.

Data Analysis: SPSS version 25 was used for data entry and analysis. Whereas categorical variables were shown as percentages, continuous data, such uric acid levels and Doppler indices, were given as mean ± standard deviation (SD). Chi-square testing and logistic regression analysis were used to assess the relationship between aberrant Doppler results, high uric acid levels, and the development of preeclampsia. The combined screening approach's sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were computed. P-values less than 0.05 were regarded as statistically significant.

Ethical Considerations: All participants provided written informed permission, patient data confidentiality was guaranteed, and the research complied with the Declaration of Helsinki's ethical guidelines, which were approved by the CMH Malir Cantonment's Ethical Review Committee.

RESULTS

The research included 60 pregnant women between the ages of 14 and 28 weeks who were in their second trimester. At recruitment, the average gestational age was 21.3 ± 4.1 weeks. 24 participants (40%) had elevated uric acid levels (≥5.5 mg/dL), with the mean serum uric acid level being 5.0 ± 1.2 mg/dL. The mean pulsatility index (PI) for umbilical artery Doppler velocimetry indices was 1.3 ± 0.4, and 14 participants (23.3%) had an abnormal PI (≥1.5). There were 10 participants (16.7%) with an abnormal resistance index (RI) (≥0.75), and the mean RI was 0.7 ± 0.1. 16 participants (26.7%) had an abnormal systolic/diastolic (S/D) ratio (≥3.5), while the mean S/D ratio was 3.0 ± 0.8. Table 1 provides a summary of the research population's general baseline characteristics.

Table 1: Baseline Characteristics of the Study Population

Variable	Mean ± SD	Abnormal Cases (n, %)
Gestational Age (weeks)	21.3 ± 4.1	-
Uric Acid (mg/dL)	5.0 ± 1.2	24 (40%)
Doppler Pulsatility Index (PI)	1.3 ± 0.4	14 (23.3%)
Doppler Resistance Index (RI)	0.7 ± 0.1	10 (16.7%)
Doppler Systolic/Diastolic Ratio (S/D)	3.0 ± 0.8	16 (26.7%)

Among the 60 participants, 12 women (20%) developed preeclampsia, while the remaining 48 (80%) remained normotensive, as detailed in Figure 1.

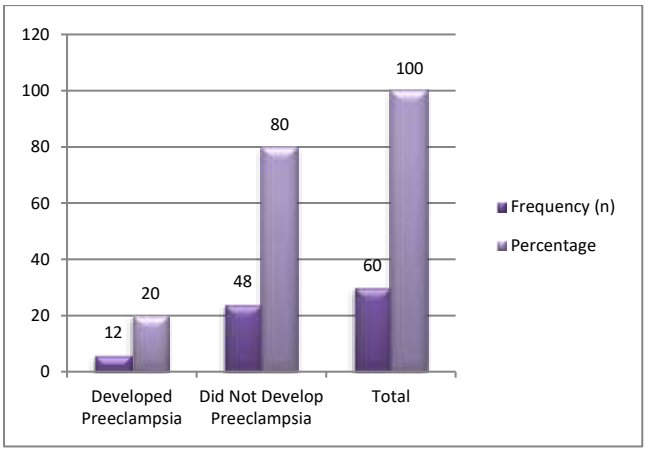

Figure 1: Prevalence of Preeclampsia in the Study Population

Chi-square tests were conducted to determine the association between individual parameters and the development of preeclampsia. Elevated uric acid levels (≥5.5 mg/dL) showed no significant association with preeclampsia ($\chi^2 = 0.25$, $p = 0.61$). Similarly, abnormal Doppler indices were not significantly correlated with preeclampsia. The chi-square test for abnormal PI (≥1.5) yielded $\chi^2 = 2.07$, $p = 0.15$, indicating no statistical significance. For abnormal RI (≥0.75), the test resulted in $\chi^2 = 0.03$, $p = 0.85$. The abnormal S/D ratio (≥3.5) also did not show a significant association, with $\chi^2 = 0.003$, $p = 0.95$. These findings are summarized in Table 2.

Table 2: Association between Abnormal Parameters and Preeclampsia (Chi-Square Test)

Parameter	χ^2 Value	p-value	Significance
Elevated Uric Acid (≥5.5 mg/dL)	0.25	0.61	Not Significant
Abnormal Doppler PI (≥1.5)	2.07	0.15	Not Significant
Abnormal Doppler RI (≥0.75)	0.03	0.85	Not Significant
Abnormal Doppler S/D Ratio (≥3.5)	0.003	0.95	Not Significant

A logistic regression model was applied to evaluate the combined predictive value of these parameters. The regression analysis showed that elevated uric acid had a coefficient (β) of -0.65 with a p-value of 0.59. Abnormal Doppler PI had a coefficient of -0.77 ($p = 0.37$), while abnormal Doppler RI had a coefficient of -1.31 ($p = 0.24$). The abnormal Doppler S/D ratio was also not a significant predictor, with a coefficient of -1.43 ($p = 0.20$). These results are presented in Table 3.

Table 3: Logistic Regression Analysis for Predicting Preeclampsia

Predictor Variable	β Coefficient	p-value	Significance
Elevated Uric Acid	-0.65	0.59	Not Significant
Abnormal Doppler PI	-0.77	0.37	Not Significant
Abnormal Doppler RI	-1.31	0.24	Not Significant
Abnormal Doppler S/D Ratio	-1.43	0.20	Not Significant

The overall screening performance of the combined parameters was evaluated through sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). The sensitivity of the combined approach was 0%, indicating that none of the true positive cases of preeclampsia were correctly identified. Specificity was calculated at 64.3%, suggesting a moderate ability to correctly classify normotensive pregnancies. The PPV was 0%, as all predicted preeclampsia cases were false positives, while the NPV was 90%, indicating that most normotensive cases were correctly identified. The diagnostic performance is summarized in Figure 2.

Despite previous studies suggesting the potential utility of umbilical artery Doppler velocimetry and serum uric acid levels in

preeclampsia screening, the findings from this small cohort of 30 pregnant women did not demonstrate a statistically significant association. The combined approach showed low sensitivity and moderate specificity, limiting its predictive ability. Further research with a larger sample size is needed to validate these findings and explore additional biomarkers for early detection of preeclampsia.

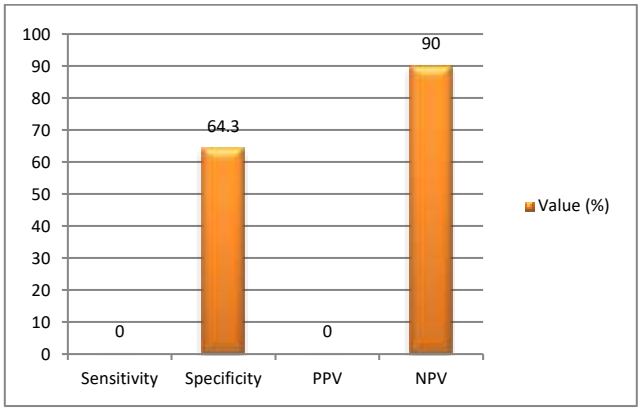

Figure 2: Diagnostic Performance of Combined Uric Acid and Doppler Parameters

DISCUSSION

The results of this study did not show a statistically significant association between umbilical artery Doppler velocimetry parameters (PI, RI, S/D ratio) and the development of preeclampsia. Similarly, elevated serum uric acid levels did not emerge as a significant predictor of preeclampsia in this cohort. These findings suggest that while individual screening methods have been suggested in previous research, their performance in predicting preeclampsia in this small sample was limited[13]. The combined approach of using both Doppler velocimetry and uric acid levels showed a very low sensitivity (0%) and low specificity (64.3%)[14]. As such, it did not prove to be an effective tool for screening high-risk pregnancies for preeclampsia in this setting. The absence of a significant correlation between abnormal Doppler parameters and preeclampsia is surprising, given that previous studies have shown that increased resistance in the umbilical artery, reflected in higher PI and RI, is often associated with adverse pregnancy outcomes, including preeclampsia[15]. Additionally, elevated serum uric acid levels have been reported as a potential marker for the development of preeclampsia, as higher uric acid levels are thought to be associated with endothelial dysfunction and impaired placental perfusion[16]. However, in this study, neither Doppler indices nor uric acid levels proved to be reliable indicators of preeclampsia development.

In earlier investigations, increased uric acid levels have been postulated as an early biomarker for preeclampsia. These investigations have showed that higher levels of uric acid, often larger than 5.5 mg/dL, associated with an increased risk of developing preeclampsia[17]. Elevated uric acid is frequently considered a consequence of renal failure and increased oxidative stress, both of which are linked in the pathogenesis of preeclampsia. However, our investigation did not discover a significant connection between uric acid levels and preeclampsia, which may be owing to the small sample size or possible variability in other confounding variables such as nutrition, renal function, or preexisting hypertension. Regarding Doppler velocimetry, several studies have revealed that aberrant umbilical artery Doppler indices, notably the PI, RI, and S/D ratio, are related with a greater chance of preeclampsia. Elevated PI and RI readings are generally symptomatic of placental insufficiency and restricted placental blood flow, which may contribute to the pathophysiology of preeclampsia[18]. Despite these findings in the literature, our study did not replicate these results, possibly because the gestational age at which Doppler measurements were taken in our cohort (14–28 weeks) may not have been the optimal time for detecting abnormal placental function associated with preeclampsia.

The combined approach of Doppler velocimetry and serum uric acid measurement has also been explored in other research as a potential method for early detection of preeclampsia. In some studies, this combined method has shown promise, with elevated sensitivity and specificity for predicting the development of preeclampsia[19]. However, in our study, the combined screening method demonstrated low sensitivity (0%) and moderate specificity (64.3%), which suggests that it may not be an effective early screening tool in the population studied.

Limitations and Future Suggestions: When evaluating the study's findings, a number of limitations should be taken into account. A bigger sample might improve the reliability of the results, since the study's capacity to identify statistically significant connections may have been restricted by the small sample size (30 individuals). Furthermore, the research was limited in its potential to capture a wider spectrum of preeclampsia patients due to its brief length (April to October 2023) and single center design. To increase screening sensitivity and specificity, future research should run multi-center trials, use bigger, more varied samples, and investigate new biomarkers and cutting-edge imaging methods. While assessing the combined technique throughout various gestational phases may provide more accurate early detection findings, longitudinal studies with longer follow-up might shed additional light on the predictive efficacy of Doppler velocimetry and uric acid levels throughout pregnancy.

CONCLUSION

The purpose of this research was to assess the value of blood uric acid levels and umbilical artery Doppler velocimetry in the second trimester of pregnancy for preeclampsia screening. However, the results show that in this small group, preeclampsia development was not substantially correlated with either high uric acid or aberrant Doppler indices. Furthermore, the combined screening method's predictive value was limited by its poor sensitivity and moderate specificity. To confirm these results and investigate new potent biomarkers and screening techniques for the early identification of preeclampsia, further studies with bigger sample numbers and longer follow-up times are required.

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