Case-control Study

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Diagnostic and Prognostic Markers in Preeclampsia: Maternal Health Indicators A Case-Control Study

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Abstract

Preeclampsia is a pregnancy-related syndrome that is one of the frequent reasons for neonatal and maternal deaths and illness throughout the world. Preeclampsia affects roughly 2% to 8% of all pregnancies, resulting in more than 63,000 maternal fatalities per year around the world. Early detection of preeclampsia would allow for intervention and attentive monitoring, reducing the disorder's negative implications. The present study, aimed to evaluate the role of maternal serum uric acid and calcium versus Umbilical artery Doppler blood flow in preeclamptic patients at 28-30 weeks of gestation compared to Normotensive pregnant participants at El-Shatby Maternity University Hospital. There were significant negative correlations between serum calcium and UAPI across both preeclampsia groupings (mild and severe). Moreover, a significant positive correlations between serum uric acid and UAPI in both mild and severe preeclampsia groups. The preeclampsia group exhibited a significant decline in serum calcium levels, whereas serum uric acid levels and umbilical artery Doppler parameters showed a significant increase. These variations were more detectable in severe preeclampsia, suggesting their potential use as a predictive marker for preeclampsia severity.

Keywords: Preeclampsia; Serum calcium

1. Introduction

Preeclampsia is one of the most influential factors of maternal and neonatal deaths in the world affecting pregnant females with a prevalence of approximately 2-15% of all pregnancies [1]. Predictors of preeclampsia were identified through comparative studies of normal uncomplicated pregnancies against preeclampsia-complicated pregnancies [2]. Identifying predictors allows successful intervention that would reduce the negative consequences of the syndrome [3].

Hypertensive disorders of pregnancy (including pre-eclampsia) are the second most common cause of maternal deaths worldwide causing an estimated 62,000– 77,000 deaths per year [4]. Preeclampsia causing more than 63,000 maternal deaths per year around the world. It is deemed as a potentially fatal illness in high-income nations with a greater number of maternal deaths in low and middle-income countries [5].

The perinatal mortality rate expands fivefold due to Preeclampsia, with iatrogenic prematurity accounting for most death cases. Preterm birth is responsible for roughly congenital neurologic impairment and most of newborn mortality. Preeclampsia is responsible for 15% of premature deliveries in the United States [5]. In 2015, the World Health Organization (WHO) estimated that around 585,000 mothers died each year during pregnancy or childbirth, and 51.1% of these deaths occurred due to increased blood pressure in pregnant women, which is one of the problems faced by mothers pregnant all over the world [6].

According to the World Health Organization (WHO), Egypt's maternal mortality ratio (MMR) has seen a significant decline over the past few decades. In 2000, the MMR was estimated at 79 deaths per 100,000 live births. By 2020, this figure had decreased to approximately 17 deaths per

100,000 live births [7]. In the course of pregnancy; 4.2 percent of the women would have pregnancy-induced high blood pressure, 3.8 percent used to have preeclampsia, and 0.3 percent of the women suffered eclampsia [5].

Two types of Preeclampsia were recognized; "early onset" (a condition that develops before the 34th week of pregnancy) as well as "late onset" (identified as arising beyond the 34th week of pregnancy). For the mother and the fetus, the seriousness of early-onset preeclampsia is greater than that of late-onset preeclampsia. Early-onset preeclampsia had a stronger link to inadequate and incomplete spiral arterial remodeling than late-onset preeclampsia, which changes might be seen in uterine Doppler artery profiles. These findings back up the hypothesis that a placental impairment causes early-onset preeclampsia, whereas late-onset preeclampsia is caused by a maternal constitution that is susceptible to or suffers from microvasculature disorders [8]. Preterm and term disorder is another categorization of preeclampsia, denoting preeclampsia with a preterm (before the 37th week of pregnancy) or term birth (during or after 37th week of pregnancy) [9].

Preeclampsia's has also been linked to preterm birth, small for gestational age (SGA) infants, or maybe both, likely to have variable results, especially for the mother's ongoing cardiovascular wellness.

Many screening methods for predicting preeclampsia have been assessed as in research throughout decades and assessed by WHO [10,11]. The UK National Institute for Health Research has also produced a new overview of predictive testing, which includes an assessment of preventative interventions and financial modeling [12]. There has been a lack of agreement in the diagnosis of preeclampsia, and a definition of hypertension and preeclampsia is essential to compare different studies and outcomes. The aforementioned definitions have been proposed by the International Society for the Study of Hypertension in Pregnancy (ISSHP) for research reasons but have also taken into consideration a recommendation for clinical diagnosing criteria [13,14].

In the last 50 years, ultrasonography has revolutionized obstetrics by providing a view into the uterus through which the anatomic structures of the fetus may be assessed. Doppler flow investigations of the maternal and fetal vasculature, which were recently included, have supplied further helpful data that enables the fetal unit's development to be evaluated. Doppler investigations are noninvasively, patient-friendly, and may be performed simultaneous as a comprehensive abnormality scanning. As a result, their usefulness in screening for unfavorable fetal and maternal consequences has been widely researched [15].

The umbilical artery Doppler evaluation in the third trimester of pregnancy is performed to monitor fetal well-being. Umbilical artery abnormalities Doppler is a procedure that can detect placental impairment and, as a result, intrauterine growth restriction (IUGR) or preeclampsia [16].

Umbilical artery Doppler evaluation is demonstrated to lower neonatal death and illness in gestational potential hazard circumstances. The umbilical arterial pattern wave is typically "saw tooth" shaped, with flow continuously moving forward, towards to the placenta. Diastolic flow is absent or reversed in an irregular waveform.

Clinical Analysis showed that early-onset severe preeclampsia was accompanied by increased UA where perinatal death was considerably higher [17,18] therefore serum UA would promote fetus prognosis better than blood pressure testing. Babies performed much better when their blood pressure was only high without hyperuricemia, as opposed to patients with both raised blood pressure and hyperuricemia [18]. Even with mild hypertension and a high UA, the fetus' prognosis was poor. Accordingly, renal function changes that affect UA may be more important than hypertension in preeclampsia.

Uric acid affects the placental vasculature by inhibiting the generation of nitric oxide (NO) and can alter trophoblasts, leading to inaccurate invasion and arteriole remodeling [19]. In cytotrophoblastic cells, increased XO enzymatic activity has been found, resulting in an increase in UA levels in preeclampsia. Endothelial cells suffer oxidative damage as a result of the above. Reduced NO levels cause an increase in COX-2 and thromboxane activity, impairing placental perfusion and limiting fetal intrauterine growth [20]. Lowering UA may be useful in management of fetal growth restriction [21].

As a result, it can be evaluated if hyperuricemia can be utilized as a biomarker to identify females who are at risk of pregnancy problems and poor outcomes. (76) Monitoring serum uric acid levels in preeclampsia patients may aid in predicting who will undergo eclampsia [22].

Calcium is another significant modulator of preeclampsia whereby increasing the level of calcium stimulates the negative feedback of parathyroid hormone, resulting in lower calcium ion concentrations intracellularly, and smooth muscle relaxation, in addition to less susceptibility to tension or stimulus [23].

Moreover, calcium excretion is accompanied by

an ion exchange to magnesium, leading to greater serum magnesium concentrations, relaxing smooth muscle in blood vasculature, and hypertension regulation [24].

This research aimed to evaluate the significance of maternal serum uric acid and calcium versus Umbilical artery Doppler blood flow in preeclamptic patients at 28-30 weeks of gestation compared to Normotensive pregnant subjects at El-Shat by Maternity University Hospital.

2. Materials and Methods

2.1 Patients and Methods

This case-control study was conducted on 90 pregnant females with gestational age between 28-30 weeks. They were nominated from admitted patients to El-Shatby Maternity University Hospital after obtaining informed consent to join this studyThe study participants included 90 pregnant women divided into two groups: Group I (Control) consisted of 45 healthy pregnant women, while Group II (Cases) included 45 pregnant women diagnosed with preeclampsia. The cases were further categorized into two subcategories: 20 women with mild preeclampsia and 25 with severe preeclampsia. Participants who met the criteria were selected based on a gestational age of 28–30 weeks, and newly diagnosed preeclamptic cases were classified according to the American College of Obstetricians and Gynecologists (ACOG). Exclusion criteria involved gestational age outside the specified range, chronic hypertension, pre-existing renal, liver, cardiac diseases, diabetes, gout, and autoimmune disorders such as systemic lupus erythematosus (SLE).

2.2 All patients and controls included in the study were subjected to the following:

All patients and controls encountered extensive assessment involving, Medical history evaluation, clinical and obstetric examination, and laboratory investigations. The medical history covered the following: age, gravidity and parity, last menstrual period (LMP), medical and drug history, and previous preeclampsia incidents. Clinical examination evaluates the following: general appearance, edema, and vital signs such as blood pressure and pulse rate. A complete obstetric examination was also conducted. Blood samples were collected under aseptic conditions for the following analysis, complete blood count, liver function tests (serum ALT, AST, total bilirubin, and ALP), kidney function tests (serum urea and creatinine), and complete urine analysis using a urinary dipstick.

2.2.1 Serum total calcium

Serum total calcium concentration was determined by colorimetric test using Arsenazo – III (Sigma Aldrich, USA). Calcium with Arsenazo-III at neutral pH, yield a blue colored complex. The intensity of the color formed is proportional to the calcium concentration in the sample [25].

2.2.2 Serum uric acid

Serum uric acid level measurement was done by enzymatic color test using Uricase and Peroxidase enzymes. The study utilized the SIEMENS Dimension Clinical Chemistry System for biochemical analysis. Ultrasound imaging data were collected using the Mindray DC-30 machine. The ultrasound assessment measured fetal biometry parameters such as biparietal diameter (BPD), abdominal circumference (AC), femur length (FL), and estimated fetal weight (EFW). The amniotic fluid index (AFI) was used to evaluate the amount of amniotic fluid. Doppler analysis of the umbilical artery was conducted to determine key parameters, including the systolic/diastolic (S/D) ratio, resistive index (RI), and pulsatility index (PI).

The abdominal transducer is placed over anterior abdominal wall over the uterus and is carefully manipulated till a free loop of umbilical cord is seen by gray scale imaging, then Color Doppler was used to identify the umbilical artery blood flow. Then pulse Doppler waveform was obtained by putting the sample gate on the umbilical artery with 0° angle of insonation. It was done in fetal apnea as breathing alters the Doppler shifts.

When 3 or 4 waves of equal height were seen the image was frozen and measurements were taken. Indices are obtained directly from machine.

When umbilical artery S/D, RI, PI exceeds 95th centile and if there is absent and reverse end diastolic flow in velocity in umbilical artery; this is considered abnormal.

2.3 Statistical analysis of the data

Data were fed to the computer using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp).

Qualitative data were described using number and percent. Comparison between different groups regarding categorical variables was tested using Chi-square test. Quantitative data were described using mean and standard deviation for normally distributed data while abnormally distributed data was expressed using median, minimum and maximum. Significance test results are quoted as two-tailed probabilities. Significance of the obtained results was judged at the 5% level.

The used tests were:

2.3.1 Chi-Square test:

It tests the association between qualitative nominal variables; it is performed mainly on

frequencies.

2.3.2 F- test (ANOVA):

It was performed for comparison between more than two groups.

2.3.3 Kruskal Wallis test:

For abnormally distributed quantitative variables, to compare between more than two studied groups and Post Hoc (Dunn's multiple comparisons test) for pairwise comparisons

2.3.4 Pearson coefficient:

To correlate between two normally distributed quantitative variables

2.3.5 Receiver operating characteristic curve (ROC):

It is generated by plotting sensitivity (TP) on Y axis versus 1-specificity (FP) on X axis at different cut off values. The area under the ROC curve denotes the diagnostic performance of the test. Area more than 50% gives acceptable performance and area about 100% is the best performance for the test. The ROC curve allows also a comparison of performance between two tests.

- Sensitivity

The capacity of the test to correctly identify diseased individuals in a population "TRUE POSITIVES". The greater the sensitivity, the smaller the number of unidentified case "false negatives".

- Specificity:

The capacity of the test to correctly exclude individuals who are free of the disease "TRUE NEGATIVES". The greater the specificity, the fewer "false positives" will be included.

- Positive Predictive value (PPV):

The probability of the disease being present, among those with positive diagnostic test results.

– Negative Predictive value (NPV):

The probability that the disease was absent, among those whose diagnostic test results were negative.

3. Results

This study included a total of 90 pregnant women who attended to El-Shat by Maternity University Hospital; 45 normotensive pregnant females as control and 45 patients with preeclampsia which were subdivided into 20 females having mild preeclampsia and 25 females having severe preeclampsia.

3.1 Socio-demographic Parameters of the Population under Study

The age of the studied groups was not significantly different among groups (F=0.203, p=0.816). BMI increased significantly in dual mild and severe preeclampsia groupings compared to the healthy controls (F= 48.912, p<0.001). Gravidity and parity variation in the three studied groups was not significant (p=0.136). There has been no significant difference between the three studied groups concerning gestational age (P= 0.844) (fig 1).

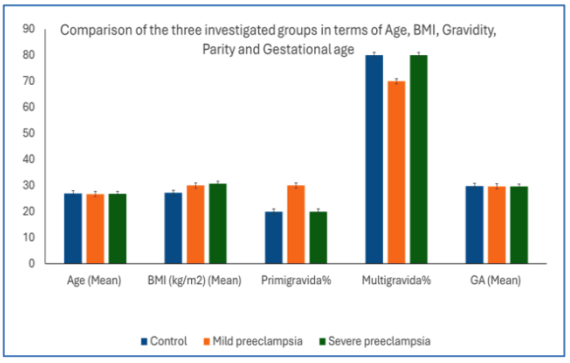

Figure 1. Comparison of history and demographic data of the investigated groups**.**

3.2 Comparison between the three studied groups functions for liver and kidney functions

Our data revealed that the mean values of ALT and AST were significantly higher in both mild and severe preeclampsia groups as compared to the control group.

Moreover, ALT and AST were significantly increased in the severe preeclampsia group compared to the mild preeclampsia group (P<0.001).

On the other hand, there were no statistically significant differences as regard total bilirubin and ALP among the three studied groups (P=0.942, 0.834 respectively (fig. 2).

It was found that there were insignificant differences between study groups as regarding urea and creatinine levels (P= 0.426, 0.417 respectively) (fig. 2).

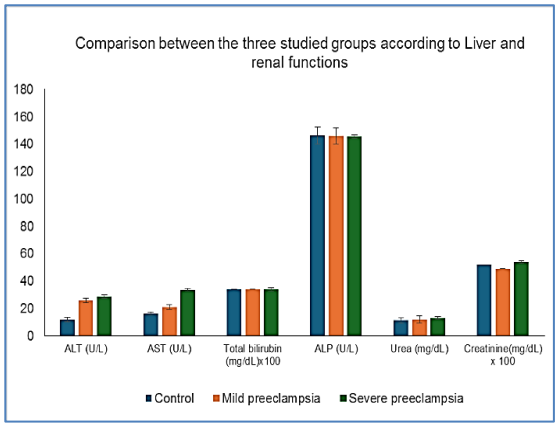

Figure 2. Comparison of liver and Renal functions in the studied groups.

3.3 Comparative Analysis of CBC and Serum Biomarkers across

The Studied Groups

It was found that there were insignificant differences between study groups as regard hemoglobin level and albumin.

Regarding platelet level, there was significant decrease among both preeclampsia groups compared to the control group and more significant decrease in severe preeclampsia group compared to mild preeclampsia group (F=47.757, P1 & p2<0.001, p3= 0.015) (Figure 3).

There was statistically significant difference between the three studied groups as regard serum calcium and uric acid (F= 179.73, 104.77 respectively and over all p value <0.001).

a) Serum calcium:

There was a significant decrease in serum calcium level in both preeclampsia groups compared to the control group.

Moreover serum calcium level was significantly decreased in severe preeclampsia group compared to mild preeclampsia group.

b) Serum uric acid:

On the other hand, serum uric acid level was significantly increased in both preeclampsia groups compared to the control group.

As well, serum uric acid level was significantly higher in severe preeclampsia group compared to mild preeclampsia group (fig. 3).

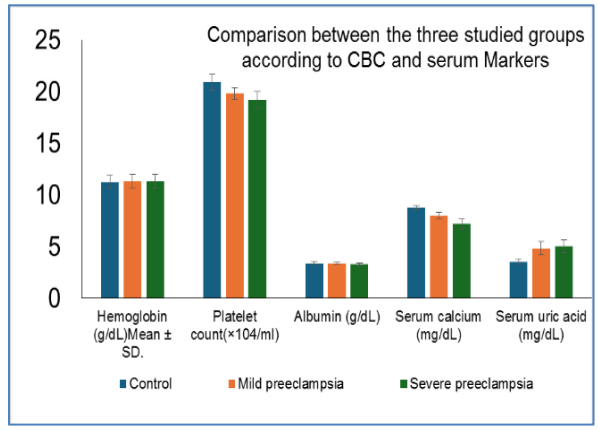

Figure 3. Comparative analysis of CBC and serum markers among the studied groups

3.4 Comparison between the three studied groups regarding estimated fetal weight:

It was found that there was a significant decrease in estimated fetal weight among both preeclampsia groups compared to the control group (F= 18.41, P<0.001) (Table 1).

Table 1: Comparison between the three studied groups according to EFW.

EFW	**Control (n = 45)**	**Mild preeclampsia (n = 20)**	**Severe preeclampsia (n = 25)**
Min. -Max. **Mean ± SD.**	2060.0-3250.0 2754.0 359.83	1610-2850 2348.5 429.40	1610-2660 2259.6 289.10
Sig. bet. Grps	F; 18.41 $p_1<0.001^*, p_2<0.001^*, p_3=0.163$		

IQR: Inter quartile range, SD: Standard deviation
F: F for ANOVA test, Pairwise comparison bet. each 2 groups was done using Post Hoc Test (Tukey)

3.5 Comparison between the three studied groups regarding amount of liquor

It was found that there was significant decrease in liquor among preclampsia groups especially in severe preeclampsia (Table 2).

Table 2: Comparison between the three studied groups according to amount of liquor

Amount of liquor	Control (n = 45)		Mild preeclampsia (n = 20)		Severe preeclampsia (n = 25)	
	No.	**%**	**No.**	**%**	**No.**	**%**
Normal	45	100.0	16	80.0	13	52.0
Decreased	0	0.0	4	20.0	12	48.0
χ2=26.565*, P<0.001*						

X^2: **Chi square test**
p: p value for comparing between the studied groups
*: Statistically significant at $p \leq 0.05$

3.5 Comparison between the three studied groups regarding umbilical artery Doppler parameters. Our data demonstrated that UARI, UAPI and UASD were significantly higher in both preeclampsia groups compared to the control group.

As well, the Doppler findings were significantly higher among severe preeclampsia group compared to mild preeclampsia group (F= 44.294, 100.933and 55.361 respectively, P <0.001) (fig. 4).

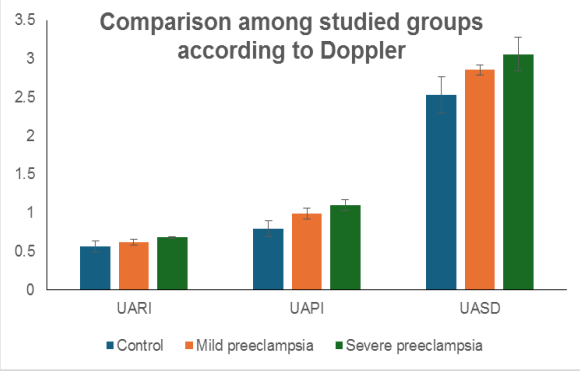

Figure 4. Comparison of the studied groups by Doppler

3.6 Diagnostic ability of serum calcium and serum uric acid in detecting severity of preeclampsia

Regarding serum calcium, at the cut-off value of ≤7.2; its sensitivity and specificity in predicting severe from mild preeclampsia has been estimated to be 95% and 90% respectively (AUC= 0.92, 95%CI= 0.66-0.93)(Table 3, fig. 5).

Concerning serum uric acid, at the cut-off value >5.6 the sensitivity was 82% and the specificity was 70% (AUC= 0.8, 95%CI= 0.32-0.9) in predicting severe from mild preeclampsia (Table 3, fig. 6).

Table 3: sensitivity, specificity and accuracy of serum calcium and uric acid to predict severe preeclampsia from mild preeclampsia.

	AUC	P	95% C.I	Cut off	Sensitivity	Specificity	PPV	NPV
Serum calcium (mg/dL)	0.92	0.001*	0.66 – 0.93	≤7.2	95.0	90.0	92.0	93.0
Serum uric acid (mg/dL)	0.80	0.008*	0.320 – 0.9	>5.6	82.0	70.0	82.6	81.0

AUC: Area Under a Curve p value: Probability value CI:Confidence Intervals, NPV: Negative predictive value , PPV: Positive predictive value
*: Statistically significant at $p \leq 0.05$

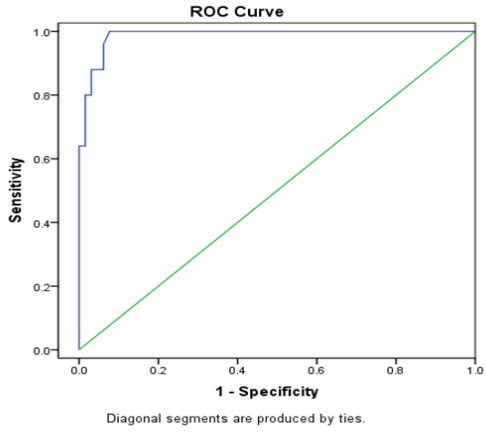

Figure 5: Sensitivity, specificity and accuracy of serum calcium to predict severe preeclampsia from mild preeclampsia.

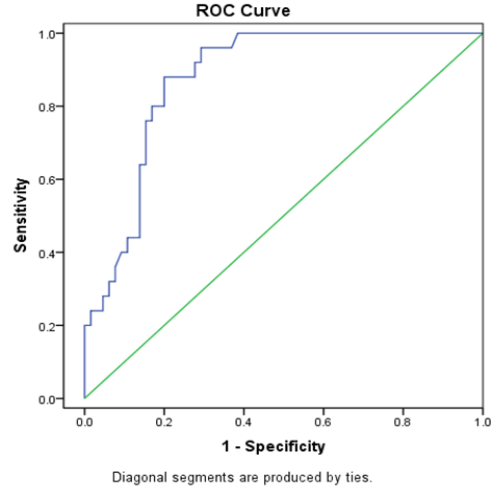

Figure 6: sensitivity, specificity and accuracy of uric acid to predict severe preeclampsia from mild preeclampsia.

3.7 Diagnostic ability of umbilical artery Doppler parameters in detecting severity of preeclampsia

Table (4) and figure (7) illustrate diagnostic ability of umbilical artery parameters in detecting severity of preeclampsia. AUC, cut-off, sensitivity and specificity of UARI to predict severe preeclampsia from mild preeclampsia was 0.91, >0.66, 82.0%, 91.0% respectively. AUC, cut- off, sensitivity and specificity of UAPI to predict severe preeclampsia from mild preeclampsia was 0.90, >1.13, 83.0%, 88.0% respectively. AUC, cut-off, sensitivity and specificity of UASD to predict severe preeclampsia from mild preeclampsia was 0.80, >2.98, 78.0%, 80.0% respectively.

Table 4: sensitivity, specificity and accuracy of Doppler to predict severe preeclampsia from mild preeclampsia.

Doppler	AUC	p	95% C.I	Cut off	Sensitivity	Specificity	PPV	NPV
UARI	0.91	<0.001*	0.910 – 1.0	>0.66	82.0	91.0	88.1	79.1
UAPI	0.90	<0.001*	0.929 – 1.0	>1.13	83.0	88.0	80.6	81.0
UASD	0.80	<0.001*	0.750 – 0.974	>2.98	78.0	80.0	75.9	77.0

AUC: Area Under a Curve p value: Probability value CI:Confidence Intervals NPV: Negative predictive value PPV: Positive predictive value *: Statistically significant at $p \leq 0.05$

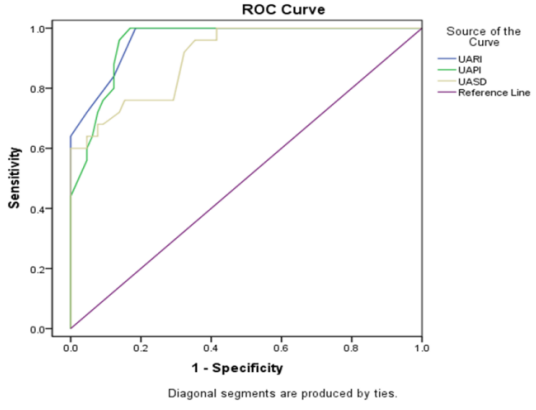

Figure 7: ROC curve for different umbilical artery Doppler parameters to predict severe preeclampsia (n = 25) from mild preeclampsia (n = 20).

4. Discussion

Preeclampsia can lead to complications during pregnancy, such as oligohydramnios, premature delivery, reduced weight at delivery, serious asphyxia at delivery, miscarriage, as well as intrapartum mortality [26]. It's a placental disorder caused by a lack of trophoblast invasion, which causes oxidative stress, inflammatory processes and endothelial impairment [27].

Due to the obvious serious consequences of these disorders, predicting its occurrences is necessary, and it may assist evaluate whether terminating the pregnancy is a better alternative than expecting to be monitored [28].

The goal of the following study was to determine the significance of maternal serum uric acid and calcium versus umbilical artery Doppler blood flow in preeclamptic patients at 28-30 weeks of gestation compared to normotensive pregnant participants at El-Shatby Maternity University Hospital.

The findings of this study revealed that there were no significant differences in age between study groups; however, BMI was significantly greater in the severe preeclampsia group.

Odegard et al., were in agreement with our results, who compared patients with preeclampsia to those who were healthy, found that the patients with preeclampsia had higher body mass indices and blood pressure [28,29].

In the present research, we discovered that preeclampsia patients had a significant reduction in serum calcium values, as well as a significant rise in serum uric acid values. Williams et al., who agreed with our findings, found that serum uric acid levels in those having gestational high blood pressure as well as preeclampsia ensure significantly greater blood pressure levels than those who have normal blood pressure [30].

Other investigation reveals similar results; that elevated uric acid concentration and low calcium level had been significantly related to severe preeclampsia and eclampsia, and that their values correlate to the severity of the condition in comparison to females with normal blood pressure [31]. Ryu A et al., also discovered that uric acid levels were significantly greater in preeclampsia patients [32].

In rat models, Mazzali et al., observed a crystal independent process caused a rise of serum uric acid level, which has been followed with high blood pressure [33]. Throughout modulation of together renin-angiotensin besides nitric oxide pathways, reduced serum uric acid level was correlated to reducing blood pressure [34].

In terms of serum calcium, Changes of arterial blood pressure in preeclampsia can be attributed

with variations of concentrations of serum calcium, that are perfectly described with calcium level intracellularly. According to Mohieldein et al., muscular contractions of smooth muscle in blood vessels are caused by a rising of calcium level intracellularly or drop in serum calcium concentrations, which results of this risen vascular resistance [35]. Because ionized calcium would be required to the biosynthesis of NO as well as prostacyclin, its shortage exacerbates oxidative stress.

An influence of calcitrophic hormone upon intracellular calcium explains the protective effect of calcium on blood pressure. Calcium influx is stimulated by 1, 25-dihydroxyvitamin D in a number of different cells, particularly smooth muscles cell in vessels [36]. Like such result, 1, 25-dihydroxyvitamin D acts as repressive factor, causing contraction and a rise in peripheral vascular resistance. As a result, low calcium regimens that cause a 1, 25-dihydroxyvitamin D action are likely to raise blood pressure [35].

In the current study, we discovered that preeclampsia patients had a significant decrease in estimated fetal weight. This is in agreement with previous study that found preeclampsia patients having lower weight at delivery, premature birth, besides neonates that were small for their gestational ages [35].

In this context, compared to the control group, our study found statistically significant differences in UARI, UAPI, and UASD in preeclampsia. When compared to both preeclampsia groups, these values were significantly lower in the healthy controls. Additionally, they have been significantly lower in females with mild preeclampsia in comparison to females with severe preeclampsia, demonstrating their validity in predicting preeclampsia severity.

Adekanmi et al., confirmed similar findings, reporting a significant reduction in umbilical artery Doppler values among healthy controls compared with females having preeclampsia [37].

In the current study, we observed that serum calcium and UAPI had significant negative correlations in both mild and severe preeclampsia groups, while serum uric acid and UAPI had significant positive correlations within together mild as well as severe preeclampsia groupings.

As in current study we found that AUC, cut-off, sensitivity, specificity, PPV and NPV of serum calcium in predicting mild preeclampsia was 0.92, ≤7.2, 95%, 90%, 92%, 93% respectively. AUC, cut-off, sensitivity, specificity, PPV and NPV of serum uric acid to predict severe preeclampsia from mild preeclampsia was 0.8, >5.6, 82%, 70%, 82.6%, 81.0% respectively.

According to Williams et al., positive predictive validity serum uric acid concentrations within the context of gestational hypertension to differentiate HELLP syndrome from non-HELLP syndrome have been 35 percent as well as relative risk, with a 95% confidence interval around 1.93 (0.81-4.6) [30].

According to our findings, a maternal serum uric acid concentration of >5.6 mg/dL is the strongest predictor of preeclampsia. A comparable study showed that uric acid values more than 5.9 mg/dL have been correlated by poor neonatal consequences [38].

When the identification of preeclampsia was in doubt, Redman and colleagues revealed that serum uric acid levels were correlated to significant neonatal mortality and maternal morbidity, including severe hypertension. The serum uric acid concentration at 28 to 32 weeks of gestation was proven to be a strong predictor of perinatal mortality in Redman's study [39].

When the Doppler S/D ratio of the umbilical artery appeared aberrant, 40% women suffered preeclampsia, 20% participants expressed PIH, and 40% of them had IUGR. End diastolic flow was absent in five individuals, which was correlated to preeclampsia, IUGR as well as deaths in utero. Data suggests absent end diastolic outflow has been correlated to adverse gestational consequences.

Uric acid concentrations have been significantly greater in females having HELLP syndrome, but it was insufficient to identify HELLP disorder group, therefore combined parameters, which is used in our study, may be more valuable [40].

5. Conclusion

Serum calcium, uric acid, and umbilical artery Doppler parameters can be used as predictive markers to identify and categorize the severity of preeclampsia in pregnant women. Even the serum calcium level showed the highest sensitivity and specificity compared to other parameters.

Furthermore, the best indicator for predicting the severity of preeclampsia is a combination of serum calcium, uric acid, and umbilical artery Doppler indices.

Finally, it would be more convincing to take on that no unique biomarker will accomplish 100 percent sensitivity and specificity, however, a combination of biomarkers, as well as umbilical artery Doppler indices combined with clinical information, will be more likely to be utilized in clinical management.

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