

An association of renal profile with maternal complications in women with preeclampsia

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Abstract

Background: Preeclampsia is a multisystem disorder characterized by the development of hypertension to the extent of 140/90 mmHg or more with proteinuria after the 20th week in a previously normotensive and nonproteinuric woman. Renal parameters, if raised above the normal pregnant values, can help establish the severity of preeclampsia and its associated complications and can help in predicting maternal and perinatal outcomes. The aim of the article was to assess the renal profile in preeclampsia and its association with maternal complications. The main objectives were to assess the renal parameters (Blood urea, Serum creatinine, Uric acid, Urinary protein by dipstick) in patients with preeclampsia. **Materials and Methods:** This prospective observational study was conducted in a tertiary health center over two years, from October 2020 to October 2022. Informed written consent had been obtained from women as per the inclusion criteria. With pre-determined proforma, detailed history was obtained. All pregnant women who fulfilled the inclusion criteria after 20 weeks of gestation were included in the study. Apart from routine antenatal investigations in pregnancy, Renal Function Tests (RFTs) were also done in women with preeclampsia. The renal parameters used in the study were Blood urea, Serum creatinine, Serum uric acid, and Urinary protein. The patients with raised renal parameters were followed up repeatedly till delivery. The RFTs were repeated if needed. The maternal outcomes were noted. **Results:** In the present study, out of 167 women, 67% of preeclampsia patients had no complications, 22% had developed impending eclampsia, 6% had developed hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome, and only 3% of the patients had gone into eclampsia. Serum uric acid levels were more than 6.3 in 76% of patients with impending eclampsia, 50% of patients with eclampsia, and 36% of patients with HELLP syndrome. Almost 90% of the patients with HELLP syndrome had severe proteinuria of urinary protein as 3+, while 73% of impending eclampsia patients had urinary protein 3+. **Conclusion:** Due to severe impact of preeclampsia on pregnancy outcomes, prompt, and early identification of preeclampsia by using these renal function tests and timely initiation of treatment is essential.

Keywords: Preeclampsia, impending eclampsia, HELLP syndrome, maternal complications, renal function

Introduction

Hypertension during pregnancy is defined as a sustained systolic blood pressure of 140 mmHg or more and diastolic blood pressure of 90 mmHg or more. This is best confirmed when evidence is present on two occasions at least six hours apart but within seven days.

During normal pregnancy, renal blood flow and Glomerular Filtration Rate (GFR) are increased⁽¹⁾. With the development of preeclampsia, there may be a number of reversible anatomical and pathophysiological changes. Renal perfusion and glomerular filtration are reduced⁽²⁾. There is increased renal arteriolar resistance and glomerular endotheliosis⁽³⁾, which blocks the filtration barrier. Due to this, there is a decrease in filtration, which causes the renal parameters to rise above the normal values. Renal parameters, if raised above the normal pregnant values, can help establish the severity of preeclampsia and its associated complications and can help in predicting maternal and perinatal outcomes⁽⁴⁾.

Urea - In normal pregnancy, average plasma urea levels are 3.5, 3.3, 3.1 $\mu\text{mol/L}$ in 1st, 2nd, and 3rd trimesters, respectively⁽⁵⁾. The fall in urea level is due to reduced protein degradation and increased clearance of solute due to increased GFR. In preeclamptic women, the blood urea rises when there is a gross decline in kidney function and glomerular damage. The reduced intravascular volume, along with reduced GFR, plays a role in raised blood urea.

Creatinine - Creatinine levels also fall in normal pregnancy. The 1st, 2nd, and 3rd trimester creatinine levels are 0.4-0.7mg/dl, 0.4-0.8mg/dl, and 0.4-0.9mg/dl, respectively. In preeclamptic women, the serum creatinine rises with a significant reduction of glomerular filtration rate, GFR as creatinine is completely filtered by the glomerulus.

Uric Acid - Normal pregnancy induces relative hypouricemia. The plasma urate concentration is decreased by over 25% as early as the 8th week of pregnancy and is 2-4.2 mg/dl⁽⁶⁾. The uric acid levels increase again to non-pregnant levels by the third trimester as 3.1-6.3 mg/dl. In early

pregnancy, the renal handling of urate is such that 10% original filtered load appears in the urine. Later in pregnancy, there is a net increase in reabsorption of uric acid so that by the third trimester, the uric acid levels are near to non-pregnant levels.

A number of other changes also occur in normal pregnancy, including increased excretion of nutrients, calcium, and protein. This is due to an altered hemodynamic system and altered tubular function.

Proteinuria – It is defined as the excretion of more than 300 mg protein in a 24-hour urine sample, which correlates with more than 300 mg/dl or more than 1+ dipstick in a random sample after excluding urinary tract infection. Approximately 2/3rd of women with hypertension in pregnancy have preeclampsia or gestational hypertension, while 1/3rd have chronic hypertension.

Maternal complications include eclampsia, cerebrovascular accident - usually intracerebral hemorrhage, occasionally rupture intracranial aneurysm, or cerebral thrombosis. This may be fatal, or the woman may be left with a residual neurological deficit such as hemiplegia, dysphasia, or visual disturbances. Other maternal complications include abruption placenta, hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome, acute left ventricular failure with pulmonary edema, acute renal failure, disseminated intravascular coagulation.

Eclampsia is the highly prevalent maternal complication. In India, the incidence rate of eclampsia ranged from 0.18 to 3.7 percent, and the World Health Organization (WHO) estimates that eclampsia causes 50,000 maternal deaths annually⁽⁷⁻⁹⁾. From 1990 to 2019, incidence, prevalence, and death due to maternal hypertensive disorders were highest in populations aged 25–29 years, followed by populations aged 30–34 and 20–24 years, and lowest in those 10–14 and 55–59 years old⁽¹⁰⁾.

Materials and Methods

The study was conducted in the Department of Obstetrics and Gynaecology (OBGY) at a tertiary care hospital in Pune. It was a prospective observational study conducted, which included pregnant women after 20 weeks of gestation visiting the antenatal clinic of OBGY OPD during the period from October 2020 to October 2022.

The inclusion criteria of the study was singleton pregnancies, antenatal women with gestational age more than 20 weeks, and diagnosed with criteria of preeclampsia (i. e. women with systolic BP > 140 mmHg and diastolic BP > 90 mmHg associated with proteinuria). The exclusion criteria of the study were pregnancy with chronic hypertension, women with underlying renal disease, and pregnancy with medical disorders like Diabetes Mellitus (DM) and Coronary Heart Disease (CHD).

In this study, all pregnant women with preeclampsia after 20 weeks of gestation had undergone Renal Function Tests (RFTs) including blood urea, serum uric acid, serum creatinine, and urinary protein by dipstick. All the tests were done once at the time of enrolment. If the women were detected preeclamptic before 20 weeks of gestation or in case of any premonitory signs and symptoms with uncontrolled blood pressure, RFTs have been repeated for monitoring purposes. However, only the initial test reports were considered and analyzed for this study. The reference ranges used in the study were: Blood urea: 20mg/dl; Serum creatinine: 0.9 mg/dl; Serum uric acid: 6.3 mg/dl; Urinary protein: 1+ on dipstick.

Using pre-determined proforma, information was obtained. Detailed history and examination were done. Apart from routine antenatal, RFTs, were done and analyzed based on the above reference ranges. The patients with raised renal parameters were followed up repeatedly. All women were followed till delivery. The RFTs were repeated if needed. Maternal complications were noted, including impending eclampsia, eclampsia, and HELLP syndrome.

Protocol was submitted to Institutional Ethical Committee. Informed written consent from the participants was obtained after informing them that the participation would be voluntary and there would be no harm to the participants in the study. Confidentiality of the information obtained from the patient was maintained.

Results

A total of 167 pregnant women had preeclampsia. The mean age of the women was 23.55±3.7 years (Table 1). Out of these women, 48% of the women with preeclampsia were primigravida, and 52% were multigravida. In all, 44% of women who presented with preeclampsia were under the 25-29 years age group, while 22% of women were under the 30-34 years age group. Only 6% of the patients were more than 35 years of age.

Table 1: Characteristics of women participants included in study

Characteristics	Number (%) / mean ± SD
Age group	23.55±3.7
19-24	43 (25.7)
25-29	75 (44.9)
30-34	38 (22.8)
35-41	11 (6.6)
Gravida	
Primi	80 (47.9)
Multi	87 (52.1)
Gestational age/trimester of pregnancy outcome	
Full-term	57 (34.1)
Preterm	110 (65.9)

In all, 56% of the women with preeclampsia underwent a cesarean section, while 43% delivered vaginally. Out of 167

women, 66% had preterm delivery (less than 37 weeks), and 34% were delivered at term (more than 37 weeks).

Table 2: Association between maternal complications and renal function test parameters

Maternal complication	Sr. Urea n (%)		Chi sq; P value	Sr. Uric acid n (%)		Chi sq; P value	Sr. Creatinine n (%)		Chi sq; P value	Urinary protein n (%)		Chi sq; P value
	≤20	>20		≤6.3	>6.3		<1	≥1		≤2 +	≥3 +	
Eclampsia	3(50)	3(50)	4.553; 0.208	3 (50)	3 (50)	8.66; 0.03	5(83.3)	1(16.7)	8.170; 0.043	2(33.3)	4(66.7)	1.941; 0.585
HELLP, IE	3(27.3)	8(72.7)		7 (63.6)	4 (36.4)		6(54.5)	5(45.5)		1(9.1)	10(90.9)	
IE	6(15.8)	32(84.2)		9 (23.7)	29 (76.3)		11(28.9)	27(71.1)		10(26.3)	28(73.7)	
No	20(17.9)	92(82.1)		53 (47.3)	59 (52.7)		53(47.3)	59(52.7)		31(27.7)	81(72.3)	

Maternal complications and Renal Function Tests

Out of 167 women, 67% of preeclampsia patients had no complications, 22% had developed impending eclampsia, 6% had developed HELLP syndrome, while only 3% of the patients had gone into eclampsia. Blood urea levels of more than 20 mg/dl were seen in 82% of women without comorbidities, 84% with impending eclampsia, 72% with HELLP syndrome, and 50% with women with eclampsia. Serum creatinine levels are more than 1 in 71% of patients with impending eclampsia, 45% of patients with HELLP syndrome and 16% of patients with eclampsia. Serum uric acid levels are more than 6.3 in 76% of patients with impending eclampsia, 50% of patients with eclampsia, and 36% of patients with HELLP syndrome. Out of 167 women, 90% of the patients with HELLP syndrome had severe proteinuria of urinary protein as 3+. While 73% of impending eclampsia patients had urinary protein as 3+.

Discussion

The main finding of the present study was that preeclampsia was reported among nearly one-third women (29%) with age ≥ 30 years. Women of Advanced Maternal Age (AMA) were 1.5 times more likely to have preeclampsia compared to women under 35 years of age. Besides, women of AMA were significantly more likely to have preterm deliveries before 34 and 37 weeks and to have Small Gestational Age (SGA) infants, the risk increase being 70% in preterm delivery before 34 weeks and 40% in both preterm delivery before 37 weeks and SGA. Also, women of AMA had a two-fold increased risk of requiring cesarean deliveries. Finally, these obstetric risks have also led to approximately 50% higher frequencies of neonatal asphyxia and 40% of admission of the infant to the neonatal intensive care unit⁽¹¹⁾.

Maternal complications

Among complications, out of 167 women, 67% were classified as having preeclampsia without any complications, 22% had developed impending eclampsia, 6% had developed HELLP syndrome, while only 3% of the patients had gone

into eclampsia. The majority of patients with HELLP syndrome and impending eclampsia were reported to have severe proteinuria, i.e. 3+. On the other hand, more than half (55%) of patients with preeclampsia also had severe proteinuria (≥3+), and 23% and 18% had urine albumin of 2+ and 1+, respectively.

Comparison of renal function tests

In the present study, 71% of women with impending eclampsia had HELLP syndrome, and 16% of eclampsia patients had serum creatinine levels greater than 1 mg/dl. The proportion associated with higher creatinine was significantly higher in the impending eclampsia group and surprisingly lower in the eclampsia group. Another renal parameter evaluated was uric acid; the mean level was 6.57 ± 6.40 mg/dl, with higher (>6.3 mg/dl) concentrations in 76% of cases of impending eclampsia, 50% of patients with eclampsia, and 36% of patients with HELLP syndrome.

Compared to gestational hypertension and healthy pregnant women, the mean serum levels of uric acid and creatinine were significantly higher in preeclampsia, according to a study by Vyakaranam et al.⁽¹²⁾. The average values of renal function parameters were found to be within the normal range by Abdelrahman et al.⁽¹³⁾. However, there were significant mean differences in creatinine, urea, and uric acid between preeclamptic and normal pregnant women. MohammedJumaah⁽¹⁴⁾ reported similar outcomes. The results are in contrast to a study by Ambad et al., who found that preeclampsia and eclampsia had significantly elevated serum urea, creatinine, and uric acid levels⁽¹⁵⁾. These differences could be due to study settings and sample size.

Mode of Delivery

In the present study, 56% of the women with preeclampsia underwent a cesarean section, while 43% delivered vaginally. In the study by Yalamati et al., 29 out of 116 preeclampsia patients (25%) underwent a cesarean section⁽¹⁶⁾. This difference may be due to present study being conducted in hospital-based settings. Preeclampsia patients with Acute Kidney Failure (AKI) also had a higher rate of cesarean sections⁽¹⁷⁾.

Conclusion

The present study aimed to assess the renal profile, including blood urea, serum creatinine, and uric acid, in patients with pre-eclampsia and its association with maternal outcomes. The groups had no significant difference in the means of serum creatinine and uric acid. Although normal, blood urea was significantly higher in impending eclampsia and preeclampsia than patients with eclampsia. This suggests the need of regular monitoring of RFT of patients with preeclampsia.

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