

Spot Urinary Albumin: Creatinine Ratio in Prediction of Pre- Eclampsia in Early Pregnancy

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Abstract:

Background: A multisystem condition known as pre-eclampsia has a two-stage disease pathophysiology, with aberrant placentation coming before endothelial failure and the subsequent onset of a systemic inflammatory response. One of the main causes of preeclampsia is endothelial dysfunction; microalbuminuria is a marker for this condition and can be used to predict pre-eclampsia in the early stages of pregnancy. Aims of this study to establish whether a spot urinary albumin: creatinine ratio measured between 17-20 week of gestation can predict subsequent preeclampsia.

Methods: This prospective observational study was done at Department of Obstetrics Gynaecology, Bokaro General Hospital, Bokaro Steel City, and Jharkhand from June 2018 to December 2019 (18 months). The study was performed on antenatal women (between 17-20 weeks of gestation) without hypertensive disorders of pregnancy at Obstetrics and Gynaecology Department who fulfils the inclusion criteria attending the OPD of Obstetrics and Gynaecology Department, Bokaro General Hospital. This was a Hospital based study, all Antenatal cases as per the inclusion and exclusion criteria attending the OPD of Obstetrics and Gynaecology Department, Bokaro General Hospital.

Results: Total 100 women were included who fulfilled inclusion and exclusion criteria. Normotensive patient 2(2.33%) were test positive (UACR \geq 35.5mg/mmol) and 84 (97.67%) were test negative (UACR \leq 36.5mg/mmol). In patient with pre-eclampsia 7(77.78%) were test positive and 2(22.2%) were test negative (p<0.0001). The sensitivity and specificity of the test was 77.78% and 97.67% respectively. The Positive predictive value was 77.78% and negative predictive value was 97.67%. Thus, spot urinary albumin: creatinine ratio can predict future preeclampsia with high sensitivity and specificity.

Conclusion: Preeclampsia is a major cause of perinatal and maternal mortality and morbidity. In order to prevent it we need to establish a test which can predict it in asymptomatic patients in early pregnancy.

Keywords: Pre-Eclampsia, Prediction, Early Pregnancy, Spot Urine Albumin-Creatinine Ratio.

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Introduction

Pregnancy is a physiological state associated with many alterations in the metabolic, biochemical, physiological, haematological and immunological process. If there are no complications, all these changes are reversible in few days to months after

delivery. Hypertensive disorders are among the commonest medical disorders during pregnancy and continue to be a major cause of maternal and perinatal morbidity and mortality worldwide. [1]In developing countries, they rank second only to

anaemia. Indeed, hypertensive disorders remain among the most significant and intriguing unsolved problem in obstetrics. These disorders complicate 5 to 10 % of all pregnancies and together they are one of the deadly triads– along with haemorrhage and infection. [2]

The American college of Obstetrics and Gynaecologists (2013) describes four types of hypertensive disease:

1. Preeclampsia and eclampsia syndrome.
2. Chronic hypertension of any etiology.
3. Preeclampsia superimposed on chronic hypertension.
4. Gestational hypertension.

Of hypertensive disorders the preeclampsia syndrome either alone or superimposed on chronic hypertension, is the most dangerous. It is a pregnancy specific syndrome of reduced organ perfusion secondary to vasospasm and endothelial dysfunction [3]. It is the second highest cause of maternal mortality constituting 12-18% of pregnancy related death. In developing countries, the incidence of disease reported to be 4-18% [4]. In India incidence of preeclampsia as recorded from hospital statistics vary widely from 5-15%. [5] It accounts for approximately a quarter of all antenatal admissions. Among the high-risk category, hypertensive disorders pre-eclampsia and eclampsia occur in about 6-8% of all pregnancies. [6] Pre-eclampsia and Eclampsia rank as one of major cause of maternal mortality and morbidity. [7] It occurs in 2 to 8 % of all pregnancies, 14-20% of primigravida, in 5.7-7.3% of multigravida and in 25% of chronic hypertensives. [8] It occurs most frequently in the last 6 weeks of pregnancy.

According to American College of Obstetrician and Gynaecologists, preeclampsia is defined as hypertension greater than 140/90 mm hg 4 hours apart associated with proteinuria greater than 0.3 gm/dL in a 24 hours urine collection or greater than 1 gm/l or +1 on urine dipstick examination. [9] Eclampsia is defined as the presence of new-onset grand mal seizures in a woman with preeclampsia. [9]

Preeclampsia is a syndrome, which affects virtually all maternal organ systems. [8] The dreadful complications associated with preeclampsia include eclampsia, HELLP (haemolysis, elevated liver enzymes and low platelets count) syndrome, pulmonary oedema, acute renal failure, abruption placenta and intracranial bleeding. [10]

The etiology of preeclampsia is unknown but thought to be related to hypoxia in the placenta and endothelial dysfunction [11]. The factors currently considered to be important include abnormal placental implantation, maternal immunological tolerance, cardiovascular, genetic, nutritional and

environmental factors. [12] The general consensus is that preeclampsia is an endothelial cell disorder resulting in mild to moderate microangiopathy of target organs such as brain, liver, kidney and placenta. [13] Several circulating markers of endothelial cell injury have been shown to be elevated in women who develop preeclampsia before they become symptomatic and these include endothelins, cellular fibronectin, plasminogen activator inhibitor-1 and altered prostacyclin/thromboxane profile. [14] There is increasing evidence that altered endothelial cell function plays an important role in the pathogenesis of preeclampsia. [15]

Aim and Objectives

Aim of the study

To establish whether a spot urinary albumin: creatinine ratio measured between 17-20 week of gestation can predict subsequent preeclampsia.

Objectives of the study

1. Prevention of preeclampsia by finding high risk patients with increased urinary albumin: creatinine ratio in early pregnancy.
2. To compare the level of urinary albumin: creatinine ratio with maternal outcome.
3. To study maternal and fetal outcome in study population.

Material and Methods

This prospective observational study was done at Department of Obstetrics Gynaecology, Bokaro General Hospital, Bokaro Steel City, and Jharkhand from June 2018 to December 2019 (18 months)

The study was performed on antenatal women (between 17-20 weeks of gestation) without hypertensive disorders of pregnancy at Obstetrics and Gynaecology Department who fulfils the inclusion criteria attending the OPD of Obstetrics and Gynaecology Department, Bokaro General Hospital. This was a Hospital based study, all Antenatal cases as per the inclusion and exclusion criteria attending the OPD of Obstetrics and Gynaecology Department, Bokaro General Hospital.

Sample Size Calculation:

The Sample Size for the proposed study was 100.

N (Total population) = 3196 (near about)

n =sample size for current study = 100

Z = Z Statistics for level of confidence (i.e. 1.96 for 95% confidence level)

Confidence level = 95%

P = Expected prevalence or proportion = 7% = 0.07

D = Precision = 5% = 0.05

$$n = \{z^2 p(1 - p)\} / d^2$$

Therefore,

$$n = [(1.96)^2 (0.07)(1 - 0.07)] / (0.05)^2 = 100.035 \sim 100$$

Hence, the required sample size

Inclusion Criteria

- All primigravida and multigravida patient with singleton pregnancy.
- Gestational age between 17-20 weeks.
- Normal renal function and no evident of proteinuria upon measurement with a dipstick.

Exclusion Criteria

- Women with multiple pregnancy.
- Women with hematuria, dip stick positive proteinuria.
- Ongoing urinary tract infection.
- Acute renal failure, chronic kidney disease.
- Women with chronic hypertension and diabetes.
- Poor obstetric history.
- Known major fetal anomaly or fetal demise.

Methodology

Clearance from the ethical and the scientific committees of BOKARO GENERAL HOSPITAL was duly taken prior to the start of study.

All primi and Multigravid patient with singleton pregnancies (between 17-20 weeks of gestation) attending the OPD or admitted under Obstetrics and Gynaecology Department at Bokaro General Hospital were recruited in the study. Written informed consent was obtained from all participating women. Information was collected through a pretested and structured proforma for each patient.

All women were clinically evaluated at the booking visit to rule out any risk factor for development of preeclampsia. Blood pressure was measured in sitting position with their right arm supported in horizontal position at the level of heart, after a 10 minutes or longer rest period. All women were given a sterile container without preservative and after instruction a midstream urinary sample was collected.

Urinary albumin was analysed on Olympus AU640 fully automated random access clinical chemistry analysed by immunoturbidimetry method. Creatinine was measured by modified Jaffe's Method. All these women were followed up till delivery. At each visit their blood pressure was measured and they were evaluated for the development of any signs and symptoms of preeclampsia such as edema, nausea, vomiting, epigastric pain, decreased urine output and visual disturbances.

Preeclampsia is defined as hypertension with blood pressure of more than 140/90mm oh Hg by using Korotkoff 5th sound of diastolic blood pressure associated with proteinuria. Based on these criteria the women studied were categorized as those who developed preeclampsia and those who remained normotensive.

Outcome:

Maternal:

1. Preeclampsia.
2. Gestational hypertension.

Fetal:

1. Live born.
2. Still born.
3. IUGR.
4. APGAR score.
5. NICU stay.
6. Perinatal mortality.
7. Birth weight.

Statistical analysis

All the data were selected randomly and tabulated, and then analyzed with appropriate statistical tools "MedCalc". Data were presented as mean with standard deviation or proportions as appropriate. Mean, median, standard deviation and variance were calculated and following statistical significance tests were applied.

1. Student's Unpaired T-test was used as the statistical tool to test for significance of observed mean differences.
2. Statistical analysis was done using "Chi – square Test".
3. Fisher's exact test used for categorical data.
4. |Z| PROPORTION TEST also used.
5. Analysis of variance "ANOVA" used for comparing three data at a time.

A "p-value" should be considered to be non-significant if > 0.05 and significant if <0.05.

Statistical methods were used to find the significance of homogeneity of study characteristics between the two groups of patients. Their inference were as follows- P>0.05 statistically insignificant.

Observation and Results

The study was performed on antenatal women (between 17-20 weeks of gestation) without hypertensive disorders of pregnancy at Obstetrics and Gynaecology Department who fulfils the inclusion criteria attending the OPD of Obstetrics and Gynaecology Department, Bokaro General Hospital.

Table 1: Measure of central tendency in different age distribution among the study population

Age (in year)	Normotensive (n=85)	Gestational HTN (n=6)	Preeclampsia (n=9)
Mean±SD	23.89±4.00years	26.83 ±3.31 years	21.56±2.55years

For test of significance here we use, “ANOVA(Analysis of variance)” The above result was significant with p value = 0.0040 {p<0.05}. Hence, there were statistically significant differences among the patients according to their age distribution with p value = 0.0040 {p<0.05}. In our study, mean maternal age in normotensive patients is 23.89±4.00years, in patients with gestational hypertension it was 26.83±3.31 years and, in patients with preeclampsia was 21.56±2.55 (p value =0.0040).

Table 2: Mean weight of mother among the study population

Weight of mother (in kg)	Normotensive (n=85)	Gestational HTN(n=6)	Preeclampsia (n=9)
Mean±S.D (μ±σ)	56.73 ±4.85 kg	64.83 ±4.99 kg	57.78 ±4.97 kg

For test of significance here we use, “ANOVA (Analysis of variance)” The above result was significant with p value = 0.0002 {p<0.05}. Hence, there were statistically significant differences among the patients according to their weight (in kg), with p-value=0.0002. In our study, mean maternal weight in normotensive patients is 56.73±4.85, in patients with gestational hypertension is 64.83±4.99 and in patients of preeclampsia is 57.78±4.97 (p value=0.00020).

Table 3: Mean BMI of mother among the study population

BMI of mother	Normotensive (n=85)	Gestational HTN (n=6)	Preeclampsia (n=9)
Mean ±SD(μ±σ)	22.4±1.81	27.17±1.83	23.98±1.58

For test of significance here we use, “ANOVA (Analysis of variance)” The above result was significant with p value = 0.0002 {p<0.05}. Hence, there were significant differences among the patients according to their BMI in normotensive, preeclampsia and gestational hypertensive patients. Mean BMI in normotensive patients was 22.4±1.81, in patients with gestational hypertension was 27.17 and in patients with preeclampsia was 23.98±1.58, ±1.83.

Table 4: Correlation between GRAVIDA with types of maternal output

Gravida	Types of maternal output			P value	Results
	Normotensive (n=85)	Gestation HTN (n=6)	Preeclampsia (n=9)		
G ₁	31(36.47%)	0(0%)	5(55.56%)	<0.0001	significant
G ₂	29(34.12%)	2(33.33%)	1(11.11%)	<0.0001	significant
G ₃	14(16.47%)	0(0%)	3(33.33%)	0.0153	significant
≥G ₄	11(12.94%)	4(66.67%)	0(0%)	0.0007	significant

For test of significance here we use, “Chi-square test” P-value=0.0039, significant. Hence, there were significant differences among the patients according to their association of gravida with p -value =0.0039. In normotensive patients 36.47 % patients were primigravida, 34.12 % were second gravida, 16.47% were third gravida and 12.94% were fourth

gravida. In patients with gestational hypertension 33.33% were second gravid and 66.67 % were fourth gravid.

In patients with preeclampsia 55.56% were primigravida, 11.11% were second gravida, 33.33% were third gravida. (P-value=0.0039).

Table 5: Mean Period of gestation among the study population

P.O.G (in weeks)	Normotensive (n=85)	Gestational HTN (n=6)	Preeclampsia(n=9)
Mean±S.D (μ±σ)	38.15±1.24 weeks	37.10±0.77 weeks	37.13±1.17weeks

In normotensive patients mean period of gestation was 38.15±1.24 weeks, in patients with gestational hypertension it was 37.10±0.77 weeks and in patients with preeclampsia 37.13±1.17 weeks.

Table 6: Mean S.B.P among the study population

S.B.P	Normotensive (n=85)	Gestational HTN (n=6)	Preeclampsia (n=9)
Mean ±S.D.(μ±σ)	110.47±9.02	127.33±6.56	149.33±6.56

For test of significance here we use, “ANOVA (Analysis of variance)” The above result was significant with p value {p<0.0001}. Hence, there were statistically significant differences among the patients according to their blood pressure, with p-value{p<0.0001}. In our study systolic blood pres-

sure were significantly higher in patients with preeclampsia. Mean SBP in patients with preeclampsia was 149.33±6.56 while in patients of gestational hypertension was 127.33±3.01 and in normotensive patients was 110.47±9.02 (p value is <0.0001).

Table 7: Mean D.B.P among the study population

D.B.P	Normotensive (n=85)	Gestational HTN (n=6)	Preeclampsia (n=9)
Mean±S.D.(μ±σ)	75.2±5.63	83.00±245	96.89±2.26

For test of significance here we use, “ANOVA (Analysis of variance)” The above result was significant with p value { $p < 0.0001$ }. Hence, there were significant differences among the patients according to their Diastolic blood pressure, with p value { $p < 0.0001$ }. In our study, Diastolic blood pressure was significantly higher in patients with preeclampsia. Mean DBP in patients with preeclampsia was 96.89±2.26, in patients with gestational hypertension was 83.00±2.45 and in normotensive patients it was 75.2±5.63. { $p < 0.0001$ }.

Table 8: Mean Platelet among study population

Platelet	Normotensive (n=85)	Gestational HTN (n=6)	Preeclampsia (n=9)
Mean±S.D.(μ±σ)	2.40±0.54	2.20±0.47	1.49±0.18

For test of significance here we use, “ANOVA (Analysis of variance)” The above result was significant with p value { $p < 0.0001$ }. Hence, there were statistically significant differences among the patients according to their mean platelets among study population with p-value { $p < 0.0001$ }. In normotensive patients mean platelets was 2.40±0.54, in patients with gestational hypertension it was 2.20±0.47 and in patients with preeclampsia it was 1.49±0.18 { $p < 0.0001$ }.

Table 9: Correlation between mode of delivery with types of maternal outcome

Mode of delivery	Types of maternal outcome			P value	Results
	Normotensive (n=85)	Gestational HTN (n=6)	Preeclampsia (n=9)		
LSCS	26(30.59%)	3(50%)	6(66.67%)	<0.0001	significant
NVD	59(69.41%)	3(50%)	3(33.33%)	<0.0001	significant

For test of significance here we use, “Chi-square test” P value = 0.0711, results were Not significant. Hence there were no statistically significant differences among patients according to mode of delivery with types of maternal outcome with p-value=0.0711. In normotensive patients, 30.59%

delivered by caesarean section and 66.67% vaginally. In patients with gestational hypertension 50% delivered by caesarean section and 50% vaginally. In patients with preeclampsia 66.67% delivered by caesarean section and 33.33% vaginally {p-value=0.0711}.

Table 10: Mean Birth weight among the neonates

Birth weight	Normotensive (n=85)	Gestational HTN (n=6)	Preeclampsia (n=9)
Mean±SD(μ±σ)	2.93±0.31kg	3.05±0.10	2.38±0.52kg
Minimum	1.9kg	2.90 kg	1.8kg
Maximum	3.6kg	3.20 kg	3.4kg
Median	3kg	3.05 kg	2.4kg

For test of significance here we use, “ANOVA (Analysis of variance)” The above result was significant with p value { $p < 0.0001$ }. In normotensive patients mean birth weight (mean±SD.) was 2.93±0.31. In patients with gestational hypertension it was 3.05±0.10 and in pre-eclampsia patients it was 2.38±0.52 { $p < 0.0001$ }.

Table 11: Correlation between NICU stay with types of maternal output

NICU stay	Types of maternal output			P value	Results
	Normotensive (n=85)	Gestational HTN(n=6)	Preeclampsia (n=9)		
1-7 days	10(11.76%)	2(33.33%)	2(22.22%)	<0.0001	significant
>7days	1(1.17%)	1(16.67%)	3(33.33%)		

For test of significance here we use, “Chi-square test”. All the above results were significant, with p value <0.0001.

Table 12: Correlation between perinatal complications with types of maternal outcome

Perinatal Complications	Types of maternal output			P value	Results
	Normotensive (n=85)	Gestational HTN (n=6)	Preeclampsia (n=9)		
IUGR	1(1.18%)	0(0%)	4(44.44%)	0.0004	Significant
MAS	5(5.88%)	0(0%)	2(22.22%)	0.4497	Ns
RDS	2(2.35%)	3(50%)	3(33.33%)	0.8825	Ns
Prematurity	7(8.24%)	2(33.33%)	3(33.33%)	0.1738	NS
Still Birth	2(2.35%)	0(0%)	0(0%)	--	
None	69(81.18%)	5(83.33%)	3(33.33%)	<0.0001	Significant

For test of significance here we use, “Chi-square test” Overall results were significant, with p value <0.0001. In our study, in normotensive patients 1(1.18%) babies were IUGR, 5(5.88%) were meconium aspiration syndrome, 2(2.35%) were premature, 2(2.35 %) were still born. In patients with gestational hypertension, 3(50%) babies had respira-

tory distress syndrome, 2(33.33%) babies were premature.

In patients with preeclampsia 4(44.44%) babies were IUGR, 2(22.22%) had meconium aspiration syndrome, 3(33.33% had respiratory distress syndrome, 3(33.33%) were premature.

Table 13: Distribution of women according to test positivity

Test used in study	Test positive	Test negative	Total
ACR (≥ 35.5 mg/mmol)	9(9%)	91(91%)	100

For test of significance here we use, “|Z|-PROPORTION test”. P value<0.0001, significant. In our study 9% patients were found test positive and 91% were found test negative with p value {p<0.0001}.

Table 14: Distribution of urinary UACR among the women with types of maternal outcome

Urinary ACR (mg/ mmol)	Types of maternal output			P value	Results
	Normotensive (n=85)	Gestational HTN (n=6)	Preeclampsia (n=9)		
Mean \pm SD	16.27 \pm 5.53	17.44 \pm 5.12	47.54 \pm 20.18	P<0.0001	Significant
Range	10 \pm 38.5	12.69 \pm 26.6	16 \pm 72.2		
Median	14.55	15.4	50.10		

For test of significance here we use, “ANOVA (Analysis of variance)”. Hence, there were statistically significant differences among the patients according to their mean Urinary ACR. In our study, mean UACR in normotensive patients was 16.27 \pm 5.53, in patients with gestational hypertension was 17.44 \pm 5.12, and in patients with preeclampsia 47.54 \pm 20.18 {p<0.0001}. Mean urinary ACR was higher in patients with preeclampsia.

Table 15: Correlation between UACR with types of maternal outcome

UACR (mg/ mmol)	Types of maternal outcome			P value	Results
	Normotensive (n=85)	Gestational HTN (n=6)	Preeclampsia (n=9)		
<35.5 (Normal)	83(97.65%)	6(100%)	2(22.22%)	<0.0001	Significant
≥ 35.5 (Abnormal)	2 (2.35%)	0(0%)	7(77.78)	<0.0001	Significant

For test of significance here we use, “Chi-square test” All the above results were significant, with pvalue <0.0001. In our study, in normotensive patients 83(97.65%) had UACR below 35.5mg/mmol which is normal, 2(2.35%) had UACR

≥ 35.5 mg/mmol which is abnormal. In patients with gestational hypertension all had UACR less than 35.5 mg/mmol. In patients with preeclampsia 7(77.78%) had UACR ≥ 35.5 mg/mmol, 2(22.22%) had UACR less than 35.5mg/mmol (p<0.0001).

Table 16: Association of UACR with pre-eclampsia

Test used in study	Preeclampsia		Normotensive	
UACR (≥ 35.5 mg/mmol)	No. of patients	Percentage	No. of patients	Percentage
Test positive (≥ 35.5)	7	77.78%	2	2.33%
Test Negative (<35.5)	2	22.22%	84	97.67%
Total	9	9%	86	86%

For test of significance here we use, “|Z|-PROPORTION test” P value <0.0001, significant

Sensitivity	Specificity	PPV	NPV	AUC	DP
77.78%	97.67%	77.78%	97.67%	0.88	9.47%

In our study, 2(2.33%) people of unaffected group were found test positive (UACR ≥ 35 mg/mmol) and 84(97.67%) were test negative (UACR<35mg/mmol). In patients with preeclampsia 7(77.78%) patients were found test positive and 2 (22.22%) were found test negative. Hence sensitivity of the test was 77.785, specificity was 97.67%, positive predictive value was 77.78%,

negative predictive value was 97.67 and area under curve was 0.88 (p<0.0001).

Discussion

Hypertensive disorders are among the commonest medical disorders during pregnancy and continue to be a major cause of maternal and perinatal morbidity and mortality worldwide [1].

These disorders complicate 5 to 10 % of all pregnancies and together they are one of the deadly triad— along with haemorrhage and infection [2]. Of hypertensive disorders the preeclampsia syndrome either alone or superimposed on chronic hypertension, is the most dangerous. In India incidence of preeclampsia as recorded from hospital statistics vary widely from 5-15% [5].

One of the early pathophysiological hallmarks is endothelial cell damage [15,16]. Endothelial dysfunction has been demonstrated as early as 22 weeks of gestation, and level of anti-angiogenic factors starts rising as early as 17 weeks of gestation. Microalbuminuria is a marker of endothelial cell dysfunction, might also be apparent by this time phase. Although 24-hour collection of urine is the gold standard for quantifying urinary albumin excretion, it is cumbersome, and results in a delay of at least 24 hour in diagnosing [17]. Therefore, the spot urinary albumin: creatinine ratio has been advanced as an alternative.

In present study a total of 100 patients studied and found that a spot UACR at 17-20 weeks of gestation was significantly higher in women who developed preeclampsia than those who did not. In this study, [15] women had adverse outcome. [9] Women developed preeclampsia and 6 developed gestational hypertensions. 85 women remained normotensive. In our study, 85% patients were normotensive, 6% patients developed gestational hypertension and 9% patients developed preeclampsia.

In study of Rajeshwari G et al. (2020) [18] 12.9% patients were found with pre-eclampsia. In study of Mishra et al. (2017) [19] 6% patients developed pre-eclampsia. In study of Gupta et al.(2016) [20] 2.25% patients were of preeclampsia and 2.27% patients developed gestational hypertension. The cause of variation is may be due to geographical variation, ethnicity, environmental, different food habit or sample size of the study.

In present study maximum number of patients was in age group of 21-30 years. In normotensive patients 22.35% were below 20 year and 8.24% were in 31- 40 year. In patients with gestational hypertension 83.3% were between 21-30 years and 16.67% was between 31-40 years of age. In patients with preeclampsia 44.44% were below 20 years and 55.56 % were above 31-40.

Mean age of patients in normotensive group was 23.89 years, in patients with gestational hypertension mean age was 26.83 years and in patients with preeclampsia 21.56 years (statistically significant) ($p = 0.0040$). Rajeshwari G et al. (2020) [18] showed mean age of healthy women was 19.02 years and in hypertensive was 30.2 years ($p > 0.05$) which statistically not significant.

In present study mean weight of normotensive pa-

tients is 56.73 kg, in patients of gestational hypertension mean weight is 64.83 kg in patients of preeclampsia, 57.78 kg, ($p = 0.0034$). Mean weight distribution in study population of our study is statistically significant. Gupta et al (2016) [20] study showed that mean maternal weight was 49kg. In our study mean B.M.I of the normotensive patients was 22.4, in patients with gestational hypertension it was 27.17 and in patients with preeclampsia 23.98. The result was statistically significant (p -value=0.0002). Mean B.M.I was higher in hypertensive patients.

Rajeshwari G et al. (2020) [18] showed mean B.M.I of unaffected patients 22.01 and preeclampsia patients 26.3 which was more than in unaffected patients (p - value=0.0001). Baweja et al. (2011) [21] showed that the mean B.M.I of unaffected patients was 26.8, in preeclampsia patients 30.3 and gestational hypertensive patients it was 27.8. Mean B.M.I was higher in preeclampsia patients (p -value=0.334).

Hence result of present study and other studies are comparable. The patients with preeclampsia in our study were with significantly low gravidity and parity. In normotensive patients 36.47 % patients were primigravida. In patients with preeclampsia 55.56% were primigravida. (P -value=0.0039). In Gupta et al.(2016) [20], in patients with preeclampsia 3 out of 6 patients were primigravida. Mishra et al.(2017) [19], also showed that 56.45% patients were primigravida. In Baweja et al. (2011) [21] study 66.67% of patients with preeclampsia were primigravida ($p = 0.98$). Thus present study and other studies are comparable. Preeclampsia is common in primigravida women.

In present study, in normotensive patients 7(8.24%) patients delivered before 36.6 weeks, 72(84.71%) between 37-39.6 weeks and 6(7.06%) delivered after 40 weeks, in gestational hypertensive 2(33.33%) delivered below 36.6 weeks and 4(66.67%) delivered between 37-39.6 weeks. In patients with preeclampsia 3(33.33%) delivered before 36.6 weeks and 6(66.67%) delivered after 40 weeks. Preterm deliveries occurred more in preeclampsia in comparison to normotensive patients. Baweja et al. (2011) [21] showed mean gestational age at delivery in unaffected group was 39.2 ± 1.9 , and in patients with preeclampsia it was 36.7 ± 2.4 ($p = 0.003$). Preterm deliveries were more in preeclampsia patients.

In our study, statistics reveal that in patients with preeclampsia 66.67% delivered by caesarean section and 33.33% were delivered vaginally. In patients with gestational hypertension 50% were delivered by caesarean section and 50% delivered vaginally. In normotensive patients 30.59% were delivered by caesarean section and 69.41% vaginally ($P = 0.0711$). The high rate of caesarean section in

preeclampsia could be because of early intervention to avoid serious sequelae.

In Gupta et al. (2016) [20] study, in unaffected group 21.4% patients delivered by caesarean section and 78.6% vaginally, in gestational hypertensive patients 20% by caesarean section and 80% vaginally and in patients with preeclampsia 66.7% by caesarean section and 33.3% vaginally ($p=0.001$).

In Baweja et al. (2011) [21] study, in unaffected group 27.8% patients delivered by caesarean section and 72.2% vaginally, in gestational hypertensive patients 27.3% delivered by caesarean section and 72.7% vaginally, in patients with preeclampsia 66.67% delivered by caesarean section and 33.3% vaginally ($p=0.115$).

There was high rate of caesarean delivery in preeclampsia in present study and other studies.

In present study mean birth weight babies of unaffected patients was 2.93 kg, in preeclampsia it was 2.38 and gestational hypertensive patients mean birth weight was 3.05 kg. Mean birth weight was significantly lower in babies of preeclampsia ($p<0.0001$). The result is comparable to some other studies. In Devi LT et al. (2018) [22] study mean birth weight was lower in preeclampsia. In mild preeclampsia 2.8kg in severe disease mean birth weight was 1.8 kg

In study of Gupta et al. (2016) [20], mean birth weight of babies was 2.9 kg in unaffected group, 3 kg in gestational hypertensive patients and 1.95kg in patients with preeclampsia ($P=0.001$).

In study of Baweja et al. (2011) [21], mean birth in unaffected group was 3.42kg, in gestational hypertensive patients 3kg and in preeclampsia it was 2kg ($p=0.02$).

In present study, in normotensive group 10(11.76%) babies required NICU stay <7 days and 1(1.1%) required >7 days, In babies of gestational hypertension 1(16.67%) required NICU stay >7 days and 2(33.33%) required <7 days. In babies of preeclampsia 3(33.33%) required NICU stay >7 days and 2(22.22%) % required <7 days ($p<0.0001$). In preeclampsia patients perinatal complication was more so NICU stay was more.

In our study, in normotensive patients 1(1.18%) babies were IUGR, 5(5.88%) were meconium aspiration syndrome, 2(2.35%) were premature, 2(2.35%) were still born. In patients with gestational hypertension, 3(50%) babies had respiratory distress syndrome, 2(33.33%) babies were premature. In patients with preeclampsia 4(44.44%) babies were IUGR, 2(22.22%) had meconium aspiration syndrome, 3(33.33%) had respiratory distress syndrome, 3(33.33%) were premature.

Overall perinatal complication was more in hyper-

tensive patients. IUGR and prematurity was more in preeclampsia. There was no perinatal death in present study. This may be due to early intervention and facility of NICU in our study. Other studies also showed that perinatal complication was more in preeclampsia. Devi LT et al. (2018) [22] study showed that FGR, oligohydramnios and intrauterine fetal death was more in preeclampsia and complications increased with severity of disease. Gupta et al. (2016) [20], study also showed more IUGR in preeclampsia. Baweja et al. (2011) [21] showed 3 out of 6 babies of preeclampsia was IUGR and 66.7% babies of preeclampsia were premature.

In present study, the sensitivity and specificity of test was 77.8% and 97.67% respectively. Positive predictive value, negative predictive value and accuracy were 77.8%, 97.6% and 88% respectively. The cut off for UACR was taken 35.5mg/mmol. The result was comparable to various studies.

Rajeshwari G et al. (2020) [18], Mishra et al. (2017) [19], Baweja et al. (2011) [21], and Modak R et al. (2020) [23] also taken the cut off 35.5mg/mmol and they showed that the spot UACR is a reliable predictor of preeclampsia with high sensitivity and specificity. Anupma Upadhyay et al. (2018) [24] showed that the Albumin to creatinine ratio is highly predictive to detect proteinuria and can be used as a rapid alternative test. Cut off for ratio was taken ≥ 0.2 .

Gupta et al. (2016) [20] study showed that spot UACR of more than 9.8mg/g of creatinine between 17 and 20 weeks of gestation can predict the development of preeclampsia in later pregnancy.

Conclusion

Preeclampsia is a major cause of perinatal and maternal mortality and morbidity. In order to prevent it we need to establish a test which can predict it in asymptomatic patients in early pregnancy. A spot urinary ACR value of more than equal to 35.5mg/mmol (measured by HPLC between 17-20 weeks of gestation) can predict Preeclampsia.

The sensitivity and specificity of the test is 77.78% and 97.67% respectively. So, it can be used as a good screening tool for predicting preeclampsia in early pregnancy.

References

1. Shah M R. Hypertensive disorders in pregnancy. 1st edn. Published by Jaypee. 2007:1-10.
2. Marlene M. Corton, Kenneth J. Leveno, Steven L. Bloom, Catherine Y. Spong, Jodi S. Dashe. Hypertensive disorders of pregnancy. Williams's obstetrics. 2014; 24:728-729
3. Kliman HJ. Uteroplacental blood flow the story of decidualization, menstruation and trophoblast invasion. Am J Pathol. 2011; 157:1759-68.

4. Kozar E, Costei AM, Boskovic R, Nulman I, Nikfar S, Koren G. Effects of aspirin consumption during pregnancy-on-pregnancy outcomes: meta-analysis. *Birth Defects Res Part B Dev Reprod Toxicol* 2003;68: 70–84.
5. Barrilleux PS, Martin JN. Hypertension Therapy during pregnancy. *Clin Obstet Gynecol* 2002; 45:22
6. Kamath S; Hypertension in pregnancy. *JAPI*,2006;54:269-270.
7. Park K; Preventative medicine in obstetrics, paediatrics & geriatrics. In: Park K. (Eds). *Park's textbook of preventive and social medicine*, 2.21st edn. M/s Banarasidas Bhanot publishers 2011; 514-517.
8. Branch DW, Porter TF. Hypertensive disorders of pregnancy, Scott JR, Sala PJD, Hammond CB, Spelacy WN, editors, in *Danforth's Obstetrics and Gynaecology*. Philadelphia USA: Lippincott Williams&Wilkins,1999,309-326.
9. American College of Obstetrician and Gynecologists. *Women's Health Care Physicians. Hypertension in Pregnancy. Chapter-2, Establishing the Diagnosis of Preeclampsia and Eclampsia*.2013; 19.
10. Fernando Arias, Shrish N. Daftary, Amarnath G. Bhide. Hypertensive disorder of pregnancy. *Practical guide to high-risk pregnancy and delivery*; 3rd edition: 421- 431.
11. H.H. Kay, S. Zhu, S. Tsoi. Hypoxia and lactate production in trophoblast cells. *Placenta* 2007;28(8-9):854-60.
12. Cunningham FG, Veno KJ, Bloom SL et al. *Pregnancy Hypertension*. In: *Williams Obstetrics*,23rd edition.2010.
13. Lam KY, Roberts JM. Contemporary concepts of the pathogenesis and management of preeclampsia. *JAMA* Jun 26,2002;287(24):3183-6 [Medicine].
14. Taylor RN, de Groot CJ, Cho YK et al. Circulating factors as markers and mediators of endothelial cell dysfunction in preeclampsia. *Semin Reprod Endocrinol* 1998;16(1):17-31
15. Vucic' N, Frleta M, Petrovic' D, Ostojic' V. Thrombophilia, preeclampsia and other pregnancy complications. *Acta Med Croatica* 2009;63: 297–305.
16. Young BC, Levine RJ, Karumanchi SA. Pathogenesis of preeclampsia. *Annu Rev Pathol* 2010; 5:173–92.
17. Hillege HL, Fidler V, Diercks GF, van Gilst WH, de Zeeuw D, van Veldhuisen DJ, et al. Urinary albumin excretion predicts cardiovascular and noncardiovascular mortality in general population. *Circulation* 2002; 106:1777–82.
18. Rajeshwari G, Akshaya Girish Dongare, G. L. Patil, Tejaswi Pujar. 'Evaluation of spot urinary albumin - creatinine ratio as a screening tool in the prediction of pre-eclampsia in early pregnancy: a pilot study', *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*, 2020;9(2):575-579.
19. Mishra et al., did a prospective observational study of 62 women with singleton pregnancies attending an antenatal clinic at a tertiary care hospital in Institute of Kidney Disease and Research Centre, Ahmedabad, between 20-28 weeks of gestation and concluded that single spot ACR values are higher in early pregnancy in asymptomatic women who developed preeclampsia later on. When measured early in the second trimester, an ACR more than equal to 35mg/mmol predicted preeclampsia well before the onset of clinical manifestation with high sensitivity of 87.5% and specificity of 96.3%. 2017.
20. Gupta et al.15 did a prospective study on 250 women with singleton pregnancies attending antenatal clinic at ESI hospital, Basaidarapur, New Delhi, concluded that a spot urinary albumin to creatinine ratio of more than 9.8mg/g of creatinine between 17 to 20weeks of gestation can predict the development of preeclampsia in later pregnancy with sensitivity and specificity of 67% and 76% respectively. 2016.
21. Baweja S, Kent A, Masterson R, et al. Prediction of pre-eclampsia in early pregnancy by estimating the spot urinary albumin: creatinine ratio using high performance liquid chromatography. *BJOG*. 2011; 118:1126–32.
22. L. Thulasi Devi, Anurag Ravi Nimonkar (2020) 'Spot urinary albumin creatinine ratio as a predictor of preeclampsia and dilemma in clinical interpretation, *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*, 7(10), pp. 4086-4092.
23. Rupali Modak, Amitrajit Pal, Amitava Pal, Mrinal K. Ghosh. 'Prediction of preeclampsia by a combination of maternal spot urinary protein-creatinine ratio and uterine artery Doppler', *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*, 2020;9(2): 635-639.
24. Upadhyay A, Dayal M. Screening for preeclampsia by urine albumin to creatinine ratio. *The New Indian Journal of OBGYN*. 2018; 4(2): 117 – 20.