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A Clinical Study of Prediction of Preeclampsia in Early Pregnancy by Estimating the Spot Urinary Albumin/ Creatinine Ratio

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Abstract:-

BACKGROUND:

Hypertensive disorders complicate 5% to 10% of all pregnancies and are associated with significant maternal morbidity and mortality[1,2]. The latest analysis by the World Health Organization suggests that, in developed countries, 16% of maternal deaths in pregnancy were a result of hypertensive disorders[2]. In women presenting with hypertension in the latter half of pregnancy, detailed laboratory evaluations are essential to determine whether a patient has a diagnosis of preeclampsia.Measurement of protein excretion in a 24-hour urine collection has been the longstanding gold standard for the quantitative evaluation of proteinuria in pregnancy. 24- hour urine collection is time consuming, inconvenient, and not always reliable because of the difficulty in collecting the sample correctly. An alternative method for quantitative evaluation of proteinuria is the measurement of the spot Urinary albumin: creatinine ratio (UACR)[3,4,5], which avoids the influence of variations in urinary solute concentration[6] and provides a more convenient and rapid method as predictor for risk of developing preeclampsia. The prevention of morbidity and feto-maternal mortality by early detection of preeclampsia in early second trimester by a simple SACR helps in proper interpretation and more frequent clinical, hematological and biochemical surveillance by accurate interpretation by clinicians.

AIMS & OBJECTIVES:-

- *To predict preeclampsia by estimating the spot urinary albumin/ creatinine ratio in early pregnancy between 12 to 20 weeks.*
- *To correlate spot urine albumin creatinine ratio and severity of preeclampsia*
- *To correlate spot urine albumin creatinine ratio and gestational hypertension, IUGR*

METHODS:-

This study was conducted on 200 antenatal women with gestational age of 12-20 weeks attending OPD from November 2017 to June 2019 at Gandhi Hospital, Secunderabad. The participants were followed until delivery and observed for the correlation between the spot urine albumin creatinine ratio and subsequent development of preeclampsia and other outcomes.

RESULTS:-

The mean age group of subjects was 23.44 ± 3.63 . Most of the cases (74%) were multigravida and 26% were primigravidae. The mean SACR value of unaffected women is 2.95 ± 1.93 mg of Albumin/gm of Creatinine ranging between 0.5 – 8.5 mg/gm of creatinine, women who developed GHTN is 5.85 ± 3.5mg/g ranging between 0.9 – 10.2 and women who developed preeclampsia is 31.83 ± 17.14mg/g ranging between 10.9 – 68.52mg/g. 1% belonged to BMI < 18.5Kg/m2,83.5% to BMI 18.6- 24.9 Kg/m2. 15.5% to BMI 25–29.9Kg/m2 i.e overweight. The chances of developing preeclampsia is more in the patients with higher BMI. 80 % of women with SACR more than 9.75 mg/g had a term delivery, 20 % had a preterm delivery. 5% had NICU admissions and 2 % had babies with IUGR. 53.33% of women with SACR more than 9.75 mg/g had a vaginal

delivery and 46.66% of women underwent a cesarean section.13.33 % of women with SACR more than 9.75 mg/g had babies with birthweight<2 kg. 40 % had babies with birthweight between 2.6 – 3 Kg. 40 % had babies with birthweight more than 3.1 Kg. 40 % of women with SACR more than 9.75 mg/g were induced due to preeclampsia, 20% due to oligohydramnios who also had preeclampsia and 13.3% due to PROM.

CONCLUSION:-

The level of urinary protein excretion has considerable clinical implications in the course of pregnancy and on the perinatal and maternal outcome. The value of the spot urine albumin-creatinine ratio in a single urine sample is potentially more accurate as it avoids collection errors and gives more physiologically relevant information. A spot urinary albumin-to-creatinine ratio of more than 9.75 mg of Albumin/1 gm of creatinine between 12 and 20 weeks of gestation can predict the development of preeclampsia in later pregnancy with the sensitivity and specificity of 77 and 95%, respectively. It was also shown that SACR is significantly higher in patients with severe preeclampsia and IUGR.

Keywords:-*Preeclampsia, Spot urinary albumin-to-creatinine ratio, Proteinuria*

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I. Introduction:-

Hypertensive disorders complicate 5% to 10% of all pregnancies and are associated with significant maternal morbidity and mortality[1,2].In women presenting with elevation in BP in the latter half of pregnancy (defined as a sustained elevation in blood pressure of ≥140 mm Hg systolic and/or ≥90 mm Hg diastolic), detailed laboratory evaluations are essential to determine whether a patient has a diagnosis of preeclampsia.The pathophysiological events resulting in pre-eclampsia begin early in gestation, and precede the onset of the clinical features[6]. One of the early pathophysiological hallmarks is endothelial cell damage[6,7]. Microalbuminuria is a marker of endothelial dysfunction and, in the general population, is associated with hypertension, obesity, diabetes, and renal disease, and also with an increased risk for myocardial infarction, stroke, and premature death. 24- hour urine collection is time consuming, inconvenient, and not always reliable because of the difficulty in collecting the sample correctly. An alternative method for quantitative evaluation of proteinuria is the measurement of the spot Urinary albumin: creatinine ratio (UACR)[8,9,10], which avoids the influence of variations in urinary solute concentration and provides a more convenient and rapid method as predictor for risk of developing preeclampsia.

II. Aims & Objectives:-

•To predict preeclampsia by estimating the spot urinary albumin/creatinine ratio(Albumin in mg/1gm Creatinine) in early pregnancy between 12 to 20 weeks.

•To correlate spot urine albumin creatinine ratio and severity of preeclampsia

•To correlate spot urine albumin creatinine ratio and gestational hypertension, IUGR

III. Materials And Methods:-

This is a prospective study of 200 women between 12 to 20 weeks of gestation with singleton pregnancy attending the antenatal OPD between November 2017 to June 2019 at Gandhi Hospital, Secunderabad. Women attending antenatal OPD were included in the study after taking the informed consent. Urine spot albumin creatinine ratio was measured between 12 – 20 weeks of gestation. Urine albumin was measured by immunoturbidimetric method through Beckman AU 480 fully automated biochemistry analyzer. Urine creatinine was measured by the Jaffe's reaction. These participants were followed until delivery and were observed for the correlation between the spot albumin creatinine ratio and subsequent development of preeclampsia and other outcomes. The Sample was further divided into Group A with Urine Spot Albumin Creatinine Ratio(SACR)<9.75:1 (9.75 mg of albumin/gm of creatinine) and Group B with SACR>9.75(mg of albumin):1(gm of creatinine) and the outcomes were observed and compared.

INCLUSION CRITERIA:-

1. Singleton pregnancy.
2. Gestational age between 12 and 20 weeks.
3. Urine sample provided at gestational age between 12-20 weeks.
4. Normal renal function and no evident proteinuria on measurement with dipstick.
5. Women willing to come for regular antenatal checkups and deliver at Gandhi Hospital.
6. Normal blood pressure between 12 to 20 weeks

EXCLUSION CRITERIA:-

1. Multi fetal pregnancy
2. Women with hematuria, dipstick positive proteinuria, ongoing urinary tract infection,acute renal failure or chronic kidney disease
3. Gestational age below 12 weeks or above 20 weeks
4. Known major fetal anomaly or fetal demise

IV. Results And Analysis:-

1. AGE WISE DISTRIBUTION OF SUBJECTS:

In the present study, women with SACR>9.75,7% belonged to <20 years of age,35% aged between 21-25 years,35% aged between 26-30 years, 21% aged between 31-35 years. The mean age of the subjects was 23.44 ± 3.63

Age(yrs)	Group A(SACR<9.75) (185)	Group B(SACR>9.75) (15)
<20	45(24%)	1(7%)
21-25	92(49%)	5(35%)
26-30	43(23%)	5(35%)
31-35	5(2.7%)	3(21%)
>35	0	0

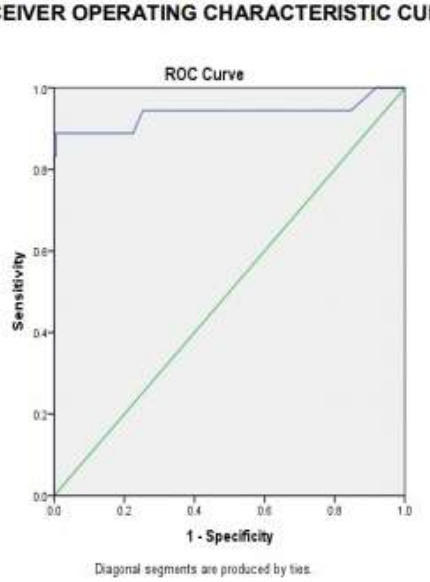
2. SPOT URINE ALBUMIN CREATININE RATIO (SACR) VALUES:

The mean SACR value of unaffected women is 2.95 ± 1.93 ranging between 0.5 – 8.5 , women who developed GHTN is 5.85 ± 3.5 ranging between 0.9 – 10.2 and women who developed preeclampsia is 31.83 ± 17.14 mg/g ranging between 10.9 – 68.52.

MATERNAL OUTCOME	SACR(mg/g)	MEAN±SD	MEDIAN
HEALTHY(185)	0.5-8.5	2.95±1.93	4.2
GHTN(4)	0.9-10.2	5.85±3.5	10.2
PREECLAMPSIA(11)	10.9-68.52	31.83±17.14	25.75

3. RECEIVER OPERATING CHARECTERISTIC CURVE:

Spot Urine Albumin creatinine Ratio - The area under the ROC curve - 0.93 (95% CI:0.842, 1) p =0.001 . The optimal cutoff point was 9.75; this cutoff yielded a sensitivity 77% and Specificity = 95%.



Area Under the Curve

Test Result Variable(s): SACR

Area	Std. Error	P VALUE	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.937	0.049	0.001	0.842	1.000

4. BMI WISE DISTRIBUTION OF SUBJECTS:

In the present study, women with SACR>9.75, 0% belonged to BMI < 18.5Kg/m2, 35% belonged to BMI 18.6-24.9 Kg/m2. 64% belonged to BMI ranging between 25–29.9Kg/m2i.e overweight. The chances of developing preeclampsia is more in the patients with higher BMI.

BMI	Group A(SACR<9.75) (185)	Group B (>9.75) (15)
<18.5	2(1%)	0
18.6-24.9	160(86%)	5(35%)
25-29.9	22(11%)	9(64%)
>30	0	o

5. GRAVIDA WISE DISTRIBUTION OF SUBJECTS:

In the present study,women with SACR>9.75, 28% women are primigravida and 72% women are multigravidae.

GRAVIDA	GROUP A(SACR<9.75) (185)	GROUP B(SACR>9.75) (15)
PRIMI	42(22%)	4(28%)
G2	79(42%)	6(42%)
G3	30(16%)	2(14%)
G4 AND ABOVE	34(18%)	2(14%)

6. HISTORY OF PREECLAMPSIA IN PREVIOUS PREGNANCY:

In the present study, women with SACR>9.75, 64 % had the history of preeclampsia in previous pregnancy. 11% women had history of preeclampsia in women with SACR<9.75mg/g.

H/O PREECLAMPSIA	GROUP A(SACR<9.75) (185)	GROUP B(SACR>9.75) (15)
PRESENT	22(11%)	9(64%)
ABSENT	163(88%)	5(35%)

7. FAMILY HISTORY OF HYPERTENSION:

85 % of the women who had SACR>9.75had a family history of hypertension. 34 % of women with SACR< 9.75 mg/g had a family history of HTN.

FAMILY H/O HYPERTENSION	GROUP A(SACR<9.75) (185)	GROUP B(SACR>9.75) (15)
PRESENT	63(34%)	12(85%)
ABSENT	122(65%)	2(14%)

8. OUTCOME OF PREGNANCY:

80 % of women with SACR more than 9.75 had a term delivery, 20 % had a preterm delivery. 33 % had NICU admissions and 6% had babies with IUGR.

OUTCOME	GROUP A (SACR<9.75) (185)	GROUP B (SACR>9.75) (15)
TERM	173(93%)	12(80%)
PRETERM	22(11%)	3(20%)
NICU ADMISSION	15(8%)	4(26%)
IUGR	1(0.5%)	1(6%)
IUD	1(0.5%)	1(6%)

9. MODE OF DELIVERY:

53 % of women with SACR more than 9.75had a vaginal delivery and 46% of women underwent a cesarean section.

MODE OF DELIVERY	GROUP A(SACR<9.75) (185)	GROUP B(SACR>9.75) (15)
SPONTANEOUS VAGINAL	101(54%)	0
INDUCED VAGINAL	34(17%)	5(33%)
OUTLET	2(1%)	0
VBAC	1(0.5%)	3(20%)
EM.LSCS	33(16.5%)	2(13%)
EL.LSS	29(14%)	5(33%)

10. INDICATION FOR INDUCTION OF LABOUR:

40 % of womenwith SACR more than 9.75 were induced due to preeclampsia,20 % women with SACR more than 9.75 were induced due to oligohydramnios,13.33 % had to be induced due to PROM.

INDICATION FOR INDUCTION	GROUP A(SACR<9.75) (185)	GROUP B(SACR>9.75) (15)
PREECLAMPSIA	1(0.5%)	6(40%)
OLIGOHYDRAMNIOS	8(4%)	3(20%)
PROM	11(5%)	2(13%)
PPROM	5(2%)	0
EDD	1(0.5%)	0

11. NICU ADMISSIONS:

6% of NICU admissions in Women with SACR >9.75 were each due to Low Birth Weight, Meconium Aspiration syndrome, Poor apgar, forObservation and the babies were discharged healthy.

REASON	GROUP A(SACR<9.75) (185)	GROUP B(SACR>9.75) (15)
LOW BIRTH WEIGHT	3(1.6%)	1(6%)
PRETERM	2(1%)	0
RESPIRATORY DISTRESS SYNDROME	2(1%)	0
MECONIUM ASPIRATION SYNDROME	2(1%)	1(6%)
POOR APGAR	2(1%)	2(14%)
OBSERVATION	2(1%)	0

12. BIRTHWEIGHT OF BABIES:

13 % of women with SACR more than 9.75 had babies with birthweight less than 2 kg.6 % had babies with birthweight ranging between 2.1 – 2.5 Kg. 40 % had babies with birthweight ranging between 2.6 – 3 Kg. 40 % had babies with birthweight more than3.1 Kg.

BIRTHWEIGHT	GROUP A (SACR<9.75) (185)	GROUP B (SACR>9.75) (15)
<2KG	5(2%)	2(13%)
2.1-2.5KG	15(8%)	1(6%)
2.6-3KG	115(62%)	6(40%)
>3.1KG	50(27%)	6(40%)

V. Discussion:-

Pre-eclampsia is distinguished from gestational hypertension by the presence of significant proteinuria. An accurate and rapid detection of proteinuria is essential in the management of hypertensive disorders in pregnancy. This can help us to know the severity of condition much earlier which can alter the course of management.The gold standard for the diagnosis of significant proteinuria remains the 24hours urine protein. The need for a 24hr collection is because of high degree of variation in the urine protein concentration during the course of the day. However, the method is cumbersome, time consuming and can be inaccurate because of incomplete collection. For these reasons simpler methods which can measure urinary protein in spot samples like urinary dipstick and urine protein-creatinine ratio, urine albumin creatinine ratio, are proposed. Spot Urine albumin creatinine ratio showed sensitivity-77%, specificity-95%.A significant positive correlation was seen between Spot Urine-creatinine ratio and development of preeclampsia, $p = 0.001$. Higher the SACR, more was the severity of preeclampsia and IUGR was seen in patients with high SACR values. The mean SACR of the women who developed preeclampsia is 31.83 ± 17.14mg/g and the median is 25.75mg/g. 80 % of women with SACR more than 9.75 mg/g had a term delivery, 20 % had a preterm delivery. 33 % had NICU admissions and

6 % had babies with IUGR. 42.8 % of the women who developed had a vaginal delivery and 57.2 % underwent caesarean section. 53.33 % of women with SACR more than 9.75 mg/g had a vaginal delivery and 46.66 % of women underwent a caesarean section. The perinatal outcome in women with higher levels of proteinuria was poor with increased incidences of fetal growth restriction, prematurity, low birth weight (LBW) and Neonatal Intensive Care Unit (NICU) admission.

VI. Conclusion:-

The level of urinary protein excretion has considerable clinical implications in the course of pregnancy and on the perinatal and maternal outcome. Hence the early detection of even minor degrees of proteinuria is important.A spot urinary albumin-to-creatinine ratio of more than 9.75 mg of Albumin/1gm of creatinine between 12 and 20 weeks of gestation can predict the development of preeclampsia in later pregnancy with the sensitivity and specificity of 77 and 95%, respectively. For years, 24 hour urine collection has been the gold standard for quantification of proteinuria in the management of women with pre eclampsia. However, this method necessarily imposes poor patient compliance, a delay of more than 24hrs on the diagnostic process and sometimes yields inaccurate results because of collection errors.Our conclusion was that, the value of the spot urine albumin-creatinine ratio in a single urine sample is potentially more accurate as it avoids collection errors and gives more physiologically relevant information. Also use of the ratio negates the uncertainty associated with the dilute or concentrated urine.Our study demonstrates spot urine albumin-creatinine ratio as a good predictor of preeclampsia when measured between 12 to 20 weeks of gestation .It was also shown that SACR is significantly higher in patients with severe preeclampsia, IUGR.

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