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Role of spot urine albumin-creatinine ratio in predicting pre-eclampsia between 20-28 weeks of gestation

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ABSTRACT

Background: Preeclampsia is best characterized as a condition unique to pregnancy that can affect almost any organ system. Appropriate treatment can be given and its effects can be closely monitored. The only widely recognized procedure remains the 24hour urine collection. However, the protracted time involved in sample collection to final reporting in this method, renders it impractical. The current research was therefore aimed at determining the accuracy of the spot urine ratio of albumin-creatinine in asymptomatic pregnant women. Appropriate treatment if started at early stage of the disease helps in closely monitoring of the disease process.

Materials and Methods: A hospital based prospective, observational study was conducted with 150 patients to establish whether a spot urine albumin-creatinine ratio measured between 20-28 weeks gestation could predict pre-eclampsia in asymptomatic pregnant woman in Department of Obstetrics and Gynecology, Kalinga Institute of Medical Sciences and PBM Hospital, Bhubaneswar between September 2018 and April 2020.

Results: Of the study group, 28 patients had high ACR value, with 25(89.3%) developed pre-eclampsia and 3(2.4%) remained normotensive whereas among 122 (81.3%) patients that were ACR negative 3 (10.7%) patients developed pre-eclampsia. ACR had a sensitivity of 89.29%, specificity 97.54%, positive predictive value of 89.29% and the negative predictive value is 97.54%.

Conclusion: Our analysis showed that in pre-eclampsia patients, urine albumin-creatinine ratio (UACR) values were higher and UACR >35.5 mg/mmol predicted pre-eclampsia well before clinical manifestations started. It is an easy, rapid and reasonably reliable method for predicting and assessing the severity of pre-eclampsia.

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1. Introduction

Pre-eclampsia (PE) is defined as a pregnancy-specific syndrome of reduced organ perfusion secondary to vasospasm and endothelial dysfunction. It is the second highest cause of maternal mortality, accounting for 12-18% of deaths linked to pregnancy. The prevalence of the disease is estimated to be 4–18% in developing nations. Pre-eclampsia is diagnosed when the blood pressure is at or above 140/90 mmHg occurring on two occasions

at least 6 h apart, associated with proteinuria greater than 300 mg / 24h after 20 weeks of gestation. The pathogenesis of Hypertensive Disorders of Pregnancy is ambiguous; although it is believed to occur in two stages. The first stage comprises of the defective invasion of the deciduas by the fetal trophoblasts along with local placental hypoxia. The second stage is the release of placental blood-related components into the maternal circulation and aberrant expression of angiogenic, anti-angiogenic and proinflammatory factors. ²

It appears to involve the systemic activation and injury of maternal endothelial cells, manifested by elevated blood

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pressure (BP), proteinuria, systemic inflammatory response, and the accumulation of antiangiogenic factors that appear to cause the disease by depriving essential growth factors of the glomerular endothelial cells.³ Permeability of the glomerular basement membrane to proteins, including albumin, is key to the diagnosis. While 24-hour urine collection is the gold standard for urinary albumin excretion quantification, it is tedious and the diagnosis results in delay of at least 24 hours. In an attempt to predict preeclampsia in early pregnancy, several previous studies have assessed microalbuminuria, postulating that the gross proteinuria stage is followed by the microalbuminuria stage. Not only is there a delay in diagnosis due to waiting time, but this approach often proves ineffective when immediate delivery is required due to worsening of maternal and fetal conditions. Considering these problems, alternate approaches for the diagnosis of proteinuria in pregnancy, including dipstick and spot urinary protein: creatinine ratio, urine albumin-creatinine ratio.

Therefore the present research was carried out at our tertiary care centre to evaluate the spot urinary albumin-creatinine ratio (ACR) assessed in asymptomatic pregnant women between 20-28 weeks of gestation to predict pre-eclampsia.

2. Materials and Methods

A hospital based prospective observational study was conducted with 150 patients to establish whether a spot urinary ACR measured between 20-28 weeks gestation can predict pre-eclampsia in asymptomatic pregnant women in Department of Obstetrics and Gynecology, Kalinga Institute of Medical Sciences and PBM Hospital, Bhubaneswar between September 2018 and April 2020.

A detailed clinical history and physical examination was done according to the profoma. After approval from the Institutional Ethics Committee a valid informed consent was obtained and data was collected from all research participants. For the study the inclusion criteria were all antenatal cases of singleton pregnancy above 18 years of age visiting the OPD and emergency department from 20-28 weeks gestation and no proteinuria upon dipstick measurement.

At each visit, their blood pressure was assessed and all signs and symptoms of pre-eclampsia were evaluated. Urine ACR estimation was done by collecting spot mid stream urine sample and subjecting it to immunoturbidimetric microalbumin method for albumin and modified Jaffe's method for creatinine estimation. Variables used in the study are patient age, BMI(Body Mass Index), parity, gestational age at delivery, BP(blood pressure), UACR, mode of delivery, birth weight of neonates.

3. Results

In this prospective observational study of 150 patients, 28(18.7%) patients developed preeclampsia. Majority of the patients who developed preeclampsia were in the age group of 21-25 years (46.5%) followed by 26-30 years (25%), 18-20 years (17.8%) and >30 years (10.7%). The mean age of the patients was 24.71 ± 4.50 years.

As per the distribution of the patients according to BMI, mean BMI of unaffected and preeclampsia patients were $24.62 \pm 3.06 \text{kg/m}^2$ and $24.78 \pm 2.45 \text{kg/m}^2$ respectively. As per the parity, incidence of preeclampsia was slightly higher in primigravida 16(57.2%) than multigravida 12(42.8%).

In 13 (46.4%) and 15 (53.6%) preeclampsia patients, delivery occurred at gestational age <37 weeks and \ge 37 weeks respectively. The mean gestational age at delivery of unaffected patients was significantly higher compared to preeclampsia patients.

The mean systolic blood pressure (SBP) in normotensive and pre-eclamptic women was 109.17±8.73 and 149.2±6.7 mmHg respectively, and the mean diastolic blood pressure (DBP) recorded in normotensive and pre-eclamptic women were 74.59±11.22mmHg and 95.4±4.7mmHg. (Table 1)

Out of 28 women who developed preeclampsia, 9 (32.1%) and 19 (67.9%) preeclampsia patients had vaginal delivery and LSCS delivery respectively. The mean birth weight of neonates (2.85±0.49kg vs. 1.98±0.51kg) was significantly higher in unaffected patients compared to preeclampsia patients.

The mean urine albumin-creatinine ratio (UACR) value of unaffected patients was significantly lower compared to preeclampsia patients. The UACR cut off value was taken as 35.5mg/mmol as in the earlier study.⁴ The number of patients according to test positivity and negativity is 18.7% and 81.3% respectively.

Association of UACR with preeclampsia is shown in Table 2 in which out of 28 (18.7%) patients that were UACR positive, 25 (89.3%) patients developed preeclampsia and 3 (2.4%) patients remained unaffected, whereas among 122 (81.3%) patients that were UACR negative 3 (10.7%) patients developed preeclampsia. The sensitivity and specificity of UACR were calculated at 89.29% and 97.54% respectively. The positive predictive value is 89.29% and the negative predictive value is 97.54%.

4. Discussion

Currently, preeclampsia is the leading cause of maternal as well as fetal mortality and morbidity. The complex pathophysiology of preeclampsia begins with endothelial dysfunction, impaired placental growth, and immunologic aberrations, possibly related to genetic susceptibility. Although the diagnosis of severe preeclampsia is no longer dependent on existence of proteinuria, women with hypertensive disorders of pregnancy with elevated ACR

Table 1: Distribution of patients according to blood pressure parameters

Parameters	Unaffected		Pre-eclampsia		n Volus
	Mean	SD	Mean	SD	p Value
SBP	109.17	8.73	149.2	6.7	>0.05
DBP	74.59	11.22	95.4	4.7	

Table 2: Association of UACR with preeclampsia

UACR	Unaffected	Pre- eclampsia	Total	p value
Test positive	2.40%	89.30%	18.70%	
Test negative	97.60%	10.70%	81.30%	< 0.05
Total	100%	100%	100%	

might be considered serious, and we should not delay the management of preeclampsia in these patients.⁵

For the diagnosis of preeclampsia, proteinuria ~ 300 mg / 24hour urine collection or dipstick reading 1+ is needed. However, the guidelines are now revised and new recommendations suggest that it is not a necessary component for the diagnosis of preeclampsia. 6

Typically, preeclampsia manifests in third trimester of pregnancy, but the underlying mechanisms start functioning as early as 8-18 weeks of pregnancy. ⁷ Although preeclampsia is not preventable, it is possible to prevent deaths occurring due to this condition. Women who do not receive prenatal care are more likely to succumb to the complications related to preeclampsia-eclampsia than those women who received. ⁸

In our study, the incidence of preeclampsia is 18.7% and it was shown that ACR is significantly higher in patients with preeclampsia than those who are unaffected which is comparable to Mishra et al.¹ and Baweja et al.⁴ Also, urine albumin-creatinine ratio (UACR) ≥35.5 mg/mmol was considered as test positive. The number of patients according to test positivity and negativity is 18.7% and 81.3% respectively. This finding was consistent with the studies of Devi LT et al. 9 The sensitivity and specificity of UACR were calculated at 89.29% and 97.54% respectively. The positive predictive value is 89.29% and the negative predictive value is 97.54%. Similar observations were noted in the studies of Mishra VV et al., Devi LT et al. ^{1,9}

Adequate knowledge about a disorder contributes greatly to its prevention, control and management. Women experiencing PE premonitory signs and symptoms will report early to the hospital, receive timely medical intervention and have fewer adverse outcomes. This emphasizes the need for women to have adequate knowledge of the disease.²

5. Conclusion

In developing countries the identification of risk groups for preeclampsia through accessible and effective technology will lead to better maternal and fetal health outcomes as prenatal care will be initiated prior to the disease process being identified. In near future, UACR could be very useful test not only for the prediction of development of preeclampsia, but also predict its magnitude and fetomaternal outcomes.

Our study showed that UACR values were higher in preeclamptic womens and UACR > 35.5mg/mmol predicted preeclampsia well before the clinical manifestations occurred. It is a simple, fast and reliable tool for prediction of preeclampsia.

6. Source of Funding

None.

7. Conflict of Interest

The authors declare that there is no conflict of interest.

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