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Research Protocol

Evaluation of the Correlation between Spot Urinary Protein/Creatinine Ratio and Serum Uric Acid and its Association with Feto-maternal Outcome in Hypertensive Pregnancy

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ABSTRACT

Background: Hypertension complicating pregnancy affects almost 7- 15% of all gestations and accounts for approximately one-fourth of all antenatal admissions. Serum uric acid is a predictor of oxidative stress, tissue injury and renal impairment, and thus may be useful in detecting preeclampsia complications. The Spot Urinary Protein / Creatinine Ratio (P/C) predicts with high accuracy the amount of urinary protein excretion 24 hours a day. Objective: To study the Spot Urinary P/C Ratio and Serum Uric Acid levels as prognostic indicators and their effect on feto-maternal outcome in females with singleton pregnancy suffering from pre-eclampsia.

Methodology: A basic head to toe examination followed by a systemic examination of CVS and RS system would be done.

BP values would be recorded for all cases and controls at 4 hourly intervals. A complete obstetric examination will be conducted to clinically assess various maternal and fetal parameters. Investigations will include complete blood count (CBC), liver function test, kidney function tests, Urine test, and level of uric acid and lactate dehydrogenase (LDH). Clinical follow up till of all cases till delivery to look for progression of preeclampsia/eclampsia. Involvement of other organ systems will be noted if any.

Results: There exists a positive correlation between Spot Urinary P/C Ratio and Serum Uric Acid and adverse feto-maternal outcome.

Conclusion: Urine collection is easy and hassles free in addition to being non-invasive and cost-effective. It requires simple instruction for collection. Hence, Spot Urinary P/C Ratio and Serum Uric Acid is a useful approach for monitoring women with pre-eclampsia at community and hospital setting.

Key Words: Urinary protein, Urinary creatinine, Serum uric acid

INTRODUCTION

Hypertension complicating pregnancy affects almost 7- 15% of all gestations and accounts for approximately one-fourth of all antenatal admissions. Preeclampsia is a hypertensive disorder of pregnancy is a multi-organ system disease and can lead to severe hepato-renal, neurological and cardio-pulmonary complications.[1,2] Proteinuria can be measured in preeclamptic women by the 24-hour ratio of urinary protein excretion and spot Urinary protein/creatinine (P/C). The Spot Urinary Protein / Creatinine Ratio (P/C) predicts with high accuracy the amount of urinary protein excretion 24 hours a day. In the present time, there is a need for validation of non-invasive tests for earlier prediction & necessary intervention. Henceforth, we purpose to study the Spot Urinary P/C Ratio and Serum Uric Acid levels as prognostic indicators and their effect on feto-maternal outcome in females with singleton pregnancy suffering from pre-eclampsia.[4,5]

Out of the triad of infection, haemorrhage and hypertension, which are the top causes of maternal morbidity and mortality, the first two have been controlled to a great extent. Moreover, they are amendable to available modalities of treatment. Only hypertensive disease of pregnancy, as a group, remains difficult to prognosticate and manage. Among the many vari-

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ables which indicate the severity of hypertensive pregnancy, Urine Protein/Creatinine Ratio (P/C) and Serum Uric Acid levels are important indices.[6,7] In this research, therefore, we propose to create the association between the levels of urine protein/creatinine (P / C) and serum uric acid with the intensity of hypertensive pregnancy and the feto-maternal outcomes.

OBJECTIVES

- To study the Urine Protein/Creatinine Ratio in Pregnant females at or more than 34 weeks GA with Blood pressure levels equal to or more than 140/90mm Hg.
- To study the Serum Uric Acid levels in Pregnant females at or more than 34 weeks GA with Blood pressure levels equal to or more than 140/90mm Hg.
- To study the Urine P/C Ratio and Serum Uric Acid levels in Pregnant females at or more than 34 weeks GA with Blood pressure levels equal to or more than 140/90mmhg and its correlation with feto-maternal outcome.

MATERIALS AND METHODS

Place of study: Department of obstetrics and gynaecology JNMC, AVBRH, DMIMS (Deemed to be University), Wardha

Study design: Cross-Sectional Observational Study

Study group (n=100): Pregnant Women at or > 34 weeks GA with a Blood Pressure reading of equal or more than 140/90 mmHg visiting the ANC clinic or admitted in the ward at ABVRH.

Study group (n=100): Pregnant Females with a Normal Blood Pressure Reading visiting the ANC clinic or admitted in the ward at ABVRH.

Sample size: 100

This will be calculated by using the following formulae

$$\frac{Z\ x/2(sq)\ x\ P(1-P)}{D(sq)}$$

Statistical Analysis

Chi square test and Student's unpaired t-test will be employed using softSPSS 24.0 VERSION, Graph Pad 7.0 VERISON

Level of Significance: 5%

Power of Test: 80%

Side of Test: One-Sided

EXPECTED OUTCOMES/RESULTS

Descriptive data: Proteinuria And Blood Pressure

Outcome data: Case study will be done on 100 subjects and correlation between Spot Urinary P/C Ratio & Serum Uric Acid with adverse feto-maternal outcome shows a positive correlation.

Main results: To establish the relation between Spot Urinary P/C Ratio and Serum Uric Acid and its association with adverse fetomaternal outcome.

The proposed study will be sufficient to demonstrate a good correlation between the two variables, i.e. Urine Protein/Creatinine Ratio (P/C) and Serum Uric Acid levels & progression of PIH, and hence a good clinical tool for mapping of the management policies.

DISCUSSION

Preeclampsia is a hypertensive disorder unique to pregnancy. It leads to multisystem implications including endothelial dysfunction, affecting almost 3-5% of all pregnancies. It is a great contributor to feto-maternal morbidity and mortality. Proteinuria caused a result of renal insult along with hyperuricemia have been implicated as predictors of adverse outcomes in hypertensive pregnancy. 24-h urine protein estimation has been considered the gold standard for testing proteinuria but has the disadvantage of consuming time, delaying diagnosis, and thus delaying initiation of appropriate management. Alternative testing methods like P/C ratio have proved to be at par with the gold standard.[1,2,3] There is a strong association between the spot urine P/C ratio and 24-h urine protein excretion, the former cannot measure proteinuria quantitatively.[2]

Preeclampsia induces changes in glomerular permeability and changes in tubular reabsorption of diluted proteins, thereby displaying proteinuria that is a hallmark of the disease. Proteinuria severity has been seen as an indicator of adverse maternal and fetal outcomes. A 24-hour urinary protein greater than 300 mg was considered essential for proteinuria.[1,4,5] The incidence of very low birth weight (< 1500 g) increased significantly as the 24-h urine protein exceeded 300 mg.[1,6,7] NICU admission rate and fetal complications such as IUGR and neonatal sepsis also increased as protein levels of 300 mg or more in 24-hour urine increased. One stillborn death was also reported when the 24-h urine protein was more than 300 mg. Maternal complications such as abruptio placentae, intrapartum eclampsia, HELLP syndrome, were also seen at high levels of proteinuria.[1] Another study indicated that high random spot urine P / C ratio values (0.3) led to a higher likelihood of having unfavourable maternal and fetal clinical results. There was no significant association between worsening of the outcomes and any ad-

ditional increment of the values thereby indicating the diagnostic nature of the test as opposed to one used for clinical monitoring.[3,8,9] The optimal capacity of spot P/C ratio to detect significant proteinuria had high sensitivity and specificity values (above 75%).[4] No significant correlation existed between women with preeclampsia and massive proteinuria and maternal morbidity compared to women with severe or mild proteinuria.[5,10]

Hyperuricemia is another key factor in the pathogenesis of preeclampsia. Higher levels of uric acid correlate with significant maternal and fetal morbidity and mortality. The utility of serum uric acid as a marker of severity of preeclampsia has been substantiated by several studies.[11,12] Yassaee found a clear link between weak neonatal outcomes (apgar< 7) and increased levels of uric acid in the serum (almost 6 mg / dL).[6,13] Association of proteinuria with serum uric acid concentrations using spot P/C and 24-hour urine protein is also reported. Coefficients of correlation showed a moderate correlation with the ratio of urine spot P / C and uric acid.[1]

The findings were excellent in a paper by Bellomo et al, where serum uric acid was examined to aid in pre-eclampsia diagnosis and prognosis. Uric acid conferred 8–9 times the risk of preeclampsia and 1.5 times the risk for children with SGA (neonatal outcome).[7] Few articles related to different aspects of this study were reviewed.[8-10] Bhriegu et al. assessed maternal and perinatal outcome in postdated pregnancy.[11] Bhayani et al studied the profile of urinary tract infection in a rural tertiary care hospital[12]. Kshirsagar et al. conducted an evaluation of serum ferritin level in anaemic and nonanemic pregnant women and its correlation with maternal and perinatal outcome. Few pieces of evidence from the Global Burden of Disease study are available.[13-15]

CONCLUSION

Urine collection is easy and hassle-free in addition to being non-invasive and cost-effective. It requires simple instruction for collection. Hence, Spot Urinary P/C Ratio and Serum Uric Acid is a useful approach for monitoring women with pre-eclampsia at community and hospital setting.

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