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ORIGINAL RESEARCH

A Comparative Study of Serum Creatinine, Serum Uric Acid and Blood Urea in Normal Pregnant and Pregnancy Induced Hypertensive Subject

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ABSTRACT

Background: Standard assessment of renal function in pregnancy is by measurement of serum creatinine concentration yet normal gestational ranges have not been established. The aim of this systematic review was to define the difference in serum creatinine in a healthy pregnancy compared with concentrations in non-pregnant women to facilitate identification of abnormal kidney function in pregnancy.

Materials and Methods: The study was performed on 70 pregnant women. Out of which 35 women were pregnancy induced hypertensive and 35 were normal pregnant women.

Results: The result showed significantly high blood pressure (SBP-197.21±21.7 VS 187.28±8.69, DBP 124.36±9.41 VS 99.2±6.28) and Blood urea (42.31 ±7.81 mg% VS 41.30±9.29 mg%), serum creatinine (3.45 ±1.19 mg% VS 3.18±1.38 mg%), serum uric acid level (9.89±3.16 mg% VS 7.34±0.9 mg%) in pregnancy induced hypertensive women compares to normal pregnant women. In the present study, in pre-eclampsia, there is elevation of serum uric acid and serum creatinine elevated values are statistically significant.

Conclusion: There is a renal derangement of parameters in preeclampsia so it may be advised to renal function test to confirm involvement of renal dysfunctions. Measurement of renal function Test could be used as a biochemical indicator in pregnancy induced hypertensive women.

Keywords: Creatinine; kidney function; pregnancy; renal function, Preeclampsia, Uric acid, Early-onset preeclampsia, Late-onset preeclampsia, Pregnancy induced hypertension, Serum Creatinine, Blood Urea, Serum uric acid, renal function tests.

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INTRODUCTION

Outside of pregnancy, glomerular filtration rates (GFRs) are routinely estimated from serum creatinine concentrations using standardized equations, facilitating the diagnosis of chronic kidney disease and grading of disease severity. Such equations use demographic and clinical variables to correct for physiological factors that affect serum creatinine. However, in

pregnancy, estimated GFRs inconsistently underestimate renal function and should not be used.[1] Estimated GFR calculations based on Modified Diet in Renal Disease calculations underestimate GFR in pregnancy by up to 41 ml/min per 1.73 m^2 compared with inulin clearance.[2] Even in women with preeclampsia and contracted maternal plasma volume, estimated GFR remains inaccurate when derived by both Modified Diet in Renal Disease and Chronic Kidney Disease Epidemiology Collaboration methods, compared with inulin and creatinine clearance.[2,3]

Serum creatinine concentration, therefore, remains the only standard, single-point assessment for kidney function in pregnant populations, yet a normal range for serum creatinine in pregnancy has not been established. The upper limit (95th–97.5th centile) of creatinine concentration in healthy pregnancy varies between published cohorts. Reference range limits include values of 72 mmol/l (0.81 mg/dl),[4] 80 mmol/l (0.90 mg/dl),[5] 89 mmol/l (1.00 mg/dl),[6] and 95 mmol/l (1.07 mg/dl).[7] such data have limited generalizability without correction for factors known to cause variance in serum creatinine, including ethnicity, gestation, and the use of different creatinine assay methods. The most widely cited study of trimester-specific creatinine concentration includes only 29 healthy pregnant women.[7] Contemporaneous statements regarding creatinine concentration in pregnancy are largely based on expert opinion, including a "normal" range of 35 to 75 mmol/l (0.40–0.80 mg/dl),[8,9] an "average" creatinine in pregnancy of 53 mmol/l (0.60 mg/dl),[10] and a recommendation that serum creatinine in pregnancy greater than 75 mmol/l (0.85 mg/dl) should raise suspicion of kidney injury.[11]

MATERIALS & METHODS

Study Group:

The present examination was completed on total 70 women from outpatient department. Out of which 35 were normal pregnant women (Group I) and 35 were pre-ecliptic patient (group II) was divided. The investigation was directed in the department of Biochemistry and physiology of Tertiary care teaching Hospital. The Group II further divided into two groups as early-beginning preeclampsia (EOPE) and late- beginning preeclampsia (LOPE) based on their time of diagnose either before or after 34 gestational weeks.

Recording of Systemic Arterial Blood Pressure:

BP was measured in supine position by utilizing mercury sphygmomanometer. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) of all the subjects were recorded.

Selection of Cases: Criteria for selection of the subjects in this examination were as follows-

No previous history of hypertension.

No history of urinary tract infection.

Absence of any other medical complications (cardiovascular disease, renal disease, collagen vascular disease) affiliated with preeclampsia.

Inclusion Criteria:

Age 21-36 years, prim gravida, 28-40 weeks gestations and absence of labor contraction. Informed consent was taken. The preeclampsia was defined as BP always greater than 140/90 mmHg and proteinuria above 0.3 gm/24 hour.

The blood sample was collected in plain vial and analyzed for biochemical investigations which include (1) uric acid, (2) Urea, (3) Creatinine and (4) Total protein.

Biochemical Investigations:

Blood sample was collected in plain vial and incubated at 37°C for 30 minutes, after incubation, clot was removed and remaining sample was taken in centrifuge test tube, test

sample were centrifuged at 3000 rpm for 10 to 20 minutes. Supernatant was collected in clean and dry serum test tube for analysis of uric acid, urea, creatinine and total protein. Biochemical parameter, uric acid was estimated by spectrophotometer in a commercial available kit (Enzymatic-colorimetric tinder methods). Urea was estimated by semi auto analyzer (Enzymatic-UV kinetic method). Creatinine and total protein were estimated by colorimeter (Jaffe kinetic, Biuret reaction method) according to manufacturer's instruction.

Statistical Analysis:

The comparisons between two groups were analyzed by student's t-test. All parameters were given as mean± standard deviation. The criterion for significance was $p<0.05$. Pearson's correlation was used to evaluate the correlations between the variables. Data analysis was performed with the statistical package for the social sciences version 16.00 (SPSS, Chicago, ielinosis USA).

RESULTS

Table 1: Distribution of subjects in the two groups

Groups	Number of subjects
Normal Pregnancy (Group A)	70
Preeclampsia (Group B)	70

Table 2: Age distribution of subjects in the two groups

Age (in years)	Normal Pregnancy	Preeclampsia
	(Group A)	(Group B)
22–25	32	27
26–29	28	30
30–33	08	09
34–37	02	04
Total	70	70

Table 3: Showing the Gravida distribution of control and study groups

Gravida	Normal Pregnancy (Group A)	Pre-eclampsia
		(Group B)
Prim gravida	37	46
Multigravida	33	24
Total	70	70

Table 4: Showing mean and standard deviation of Blood pressure and serum uric acid level in control and study Groups

Subject	SBP(mm Hg)	DBP (mm Hg)	S. Uric Acid (mg/dl)	S. creatinine level	Blood urea
	Mean +/- SD	Mean +/- SD	Mean +/- SD		
Normal pregnant (n=70)	187.28 ± 8.69	99.2 ± 6.28	5.34±0.9	1.08.±0.38 mg/dl	41.30 ± 9.29
PIH (n=70)	197.21 ± 21.7	124.36 ± 9.41	8.89 ± 3.16	2.45±1.19 mg/dl	42.31 ± 7.81
P value	P<0.001	P<0.001	P<0.001	P<0.001	P<0.07

The result showed significantly high blood pressure in Normal pregnant versus PIH (SBP-187.28 ± 8.69 VS 197.21 ± 21.7, DBP 99.2 ± 6.28 VS 124.36 ± 9.41) and Blood urea (41.30 ± 9.29 mg% VS 42.31 ± 7.81 mg%), serum creatinine (1.08±0.38 mg/dl mg% VS 2.45±1.19 mg/dl mg%), serum uric acid level (5.34±0.9 mg% VS 8.89 ± 3.16 mg%) in pregnancy induced hypertensive women compares to normal pregnant women.

DISCUSSION

The controversial reports are available regarding the extent of the elevated values of the serum uric acid levels in pre-eclampsia women. While a majority of available studies generally observe significant elevation in serum uric acid levels in the former group, several studies also find no such clear-cut significance in the respective results.

Similarly, with reference to the extent of blood urea or serum creatinine levels in preeclampsia, often differing results have been observed.

Furthermore, whether or not the elevated levels of serum uric acid (as those of the blood urea or serum Creatinine) can be taken as a predictive indicator for the pre-eclampsia disorder remains to be elucidated. For example, in several studies it was found that the extent of the elevation in serum uric acid level in pre-eclamptics was an indicator for the degree of severity of this disorder.[8-17]

Elevated serum uric acid levels have also been interpreted to act as an important cofactor involved in the pathogenesis and manifestation of pre-eclamptic disorder.[14] Proteinuria rather than hypertension was observed.[8]

One of the most commonly accepted explanations for elevated serum uric acid has been said to be increased reabsorption and decreased excretion of uric acid in proximal tubules, similar to the physiologic response to hypovolemia.[18]

On the basis of observed TOS (Total Oxidant Status) and TAS (Total Antioxidant Status) levels, it has been inferred that increased oxidative stress and ant oxidative defence mechanisms may contribute to the disease process in preeclampsia.[19]

Recently, increased oxidative stress and formation of reactive oxygen species (ROS) have been proposed as another contributing source of hyperuricemia noted in preeclampsia apart from renal dysfunction.[20]

Uric acid (as also Creatinine and to some extent urea), possessing water soluble or hydrophilic antioxidant characteristics, may delay or inhibit cellular damage mainly through the free radical scavenging property; it also presents strong antioxidant activity towards ROS in aqueous phase.[21]

Uric Acid contributes to about 60% of free radical scavenging activity in human serum.[22]

The observed uric acid elevation may be a protective response, capable of opposing harmful effects of free radical activity and oxidative stress. Elevated serum uric acid concentrations predict the development of hypertension.[17]

In addition, an elevated serum uric acid concentration may reflect impaired endothelial integrity, in which endothelial dependent vascular relaxation produced by nitric oxide (NO) is reduced.[23]

Uric acid thus may function as a marker of oxidative stress tissue injury dysfunction. During uncomplicated pregnancies serum uric acid concentrations decrease by about 25 % to 35 % in early pregnancy, but then increase throughout the pregnancy until towards the end of it when they approach non-pregnant levels.[24]

It has been proposed that these pregnancy mediated changes in serum uric acid are often the result of altered renal handling. Increased serum uric acid in preeclampsia is secondary to reduced renal urate clearance because of renal dysfunction.25 and also due to increased Xanthine Oxidase activity.[20]

It is also possible that increased serum uric acid values may indicate the presence of undiagnosed sub-clinical renal disease in some subjects and this may increase the risk for preeclampsia.

However, in several studies it was concluded that the measured elevated serum uric acid level can be taken as an unreliable indicator for development of hypertension.[14,15]

Another review inferred that uric acid is not a consistent predictive factor for the development of preeclampsia, but its level generally increases once the disease manifests and plasma levels of uric acid may often correlate with disease severity.[17]

The differences in each of the mean serum uric acid or serum creatinine concentrations between the preeclampsia and the normotensives respectively were not statistically significant and that these parameters are of little value in the prediction of preeclampsia.[16]

Few studies observe insignificant change in serum creatinine level in the two cited groups.[8,16] On the other hand, an early study showed increased serum creatinine level but said the latter to be of no predictive value in preeclampsia.[18]

Our present study is also in line with two earlier studies wherein small change in blood urea levels both in pre-eclamptics and normotensives are insignificant.[16,18]

In the present study, though the serum uric acid level was higher in pre-eclamptics when compared to the normotensives, the elevated levels of uric acid did not correlate with the raised systolic blood pressure or the raised diastolic blood pressure.

This is in line with an earlier study predicting that the changes in the plasma concentrations of serum uric acid can more prominently be correlated with the degree of this study examined both work and leisure-time activity levels, providing an opportunity to assess their independent and combined effects on the risk of preeclampsia.

CONCLUSION

The study is concluded that the elevated uric acid levels alone does not predict and correlate with the severity of the preeclampsia but in combination with blood urea, serum creatinine levels may predict it. The serum uric levels may provide additional information which is helpful to predict the preeclampsia.

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