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Original Research Article

Assessment of Biochemical Markers of Hepatorenal Dysfunction in Hypertensive Disorders of Pregnancy

Girija Priyadarshini

Post Graduate, Dept. of Physiology, S.C.B Medical College, Cuttack, Odisha, India.

Corresponding Author: Girija Priyadarshini

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ABSTRACT

Background: Hypertensive disorders like preeclampsia remain a frequent and dangerous complication of pregnancy leading to hepatorenal dysfunction. Uric acid is a potent mediator of inflammation and hyperuricemia is considered as a risk factor of hypertension, cardiovascular and renal disease.
Objective: Aim of the study is to assess the biochemical markers of hepatorenal dysfunction in patients with preeclampsia and to determine accuracy with which serum uric acid predicts severity o preeclampsia.
Material and methods: The study comprised of 100 pregnant women with preeclampsia in age group 18-45years. 100 healthy age matched pregnant women served as controls. Biochemical parameters studied were urinary protein, serum urea, serum creatinine, serum uric acid, serum bilirubin, alkaline phosphatase (ALP). Serum Glutamate Oxaloacetate Transaminase(SGOT) Serum Glutamate Pyruvate Transaminase (SGPT).
Result: In severe preeclampsia 3.4% cases have trace, 21% cases moderate and maximum 76% cases severe proteinuria. A significant incline in the value of serum bilirubin (p value<0.01) liver enzymes (ALP, SGOT, SGPT) (p value <0.001) and serum uric acid (p value <0.001) seen in preeclampsia as compared to normal pregnancy. 94% of severe preeclamptic patients had high serum uric acid level (>6 mg%)
Conclusion: It is concluded from present study that, elevation of serum uric acid and liver enzymes levels are early persistent signs of disease process with multi-system involvement and serum uric acid is a consistent predictor of severity of preeclampsia and may have a role in pathogenesis of the disorder.
Key word: preeclampsia, hepatorenal dysfunction, serum uric acid, serum creatinine

INTRODUCTION

Hypertensive disorders complicate 2-10% of all pregnancies of which preeclampsia is the most common often resulting in multi organ failure. [1,2] It is one of the greatest unsolved mysteries in obstetrics, leading to high maternal and perinatal mortality and morbidity. There is a considerable decline in the incidence of preeclampsia over the years in the developed countries but due to lack of antenatal supervision in developing countries it has not yet achieved any significant decline. This is mainly due to low socioeconomic status, apathetic attitude and poor health education. [3] Hence proper antenatal care, early diagnosis and timely interference of the cases will reduce the incidence of

preeclampsia. In liver peripheral and periportal haemorrhagic necrosis occurs as a result of which levels of serum liver enzymes and serum bilirubin increase in preeclampsia which may be associated with haemolysis, decrease in platelet count, designated as HELLP syndrome. [4]

Normally in pregnancy the clearance of urate is high whereas in preeclampsia the renal tubular function is affected earlier than the glomerular function and decreased clearance of uric acid precedes changes in glomerular filtration rate leading to hyperuricemia. [5,6]

Hyperuricemia is also considered as a risk factor of hypertension, cardiovascular and renal disease. Uric acid is a potent mediator of inflammation. It increases the concentration of the chemokine monocyte chemoattractant protein-1 (MCP-1) and also stimulates human monocytes to produce the pro-inflammatory cytokines Interleukin-1β Interleukin-6 and Tumor Necrosis Factor-α, which are elevated in the circulation of preeclamptic women. [7-9]

Elevated uric acid decreases endothelial cell proliferation, migration, placental development, inhibits placental amino acid uptake, trophoblast invasion and the incorporation of trophoblast into endothelial monolayers. [10]

All these lead to a hypothesis that uric acid is not just a marker of disease severity but contributes directly to the pathogenesis of the disorder. A number of studies are available to assess hepatorenal dysfunctions in preeclampsia but with conflicting and confusing results. Several studies have reported a positive correlation between elevated maternal serum uric acid levels and adverse maternal and fetal outcome yet other studies report uric acid to be a poor predictor of any complication of pre-eclampsia.

Such confusing results have encouraged us to carry out a detailed study of hepatorenal functions in preeclampsia by assessing serum levels of liver enzymes, bilirubin and serum levels of urea, creatinine and uric acid.

MATERIALS AND METHODS

The present cross sectional, hospital based study was carried out in the Department of Physiology, along with collaboration of Department of Obstetrics and Gynaecology and Department of Biochemistry of S.C.B. Medical College, Cuttack from the period of March 2013 to June 2014.

The study group comprised of 100 preeclamptic women from the outdoor, indoor and labour room of Department of Obstetrics and Gynaecology within age group of 18-35 years. 100 healthy pregnant women selected from antenatal outdoor of Obstetrics and Gynaecology department of S.C.B. Medical College and Hospital, Cuttack served as the control group. All were age matched and were in their third trimester and singleton pregnancy.

Exclusion Criteria:

Women with previous history of hypertension, diabetes mellitus, history of recurrent miscarriages, previous hepatic or renal disease, multiple foetuses, idiopathic thrombocytopenic purpura (ITP) or any other bleeding diathesis, immunosupression or history of illicit drug use were excluded from the study

The preeclamptic women were selected based on the following criteria:

Pregnant women with blood pressure over the baseline ≥ 140 /90 mm of Hg with proteinuria ≥ 0.3 gm / l or >1 + measured by dipstick.

The preeclamptic women were categorized into Mild (140-159 /90-109 mm Hg) and severe (≥160 /110) on the basis of blood pressure based upon classification of American College of Obstetrician & Gynecologist (ACOG, 2002) [2]

After taking informed written consent from each patient and approval of institution ethical committee, detailed history of the preeclamptic patients admitted to Department of Obstetrics and Gynaecology, was recorded regarding gravida, parity, history of diabetes mellitus, hypertension and other obstetrics and gynaecological complications. Ultrasonography was done in all cases to confirm the gestational age and to exclude any obstetrical and gynaecological complications.

Complete clinical examination was done at the start of the test. The anthropometric parameters like height and weight of subject were measured. Blood pressure was measured with patients in supine position and resting comfortably on her right hand at 30 degrees to the horizontal with the sphygmomanometer cuff at the level of the heart.

Blood was collected from all the admitted patients who were not given any therapy for preeclampsia and the tests were done in Department of Biochemistry and Physiology during the duty hours of 10a.m to 4 p.m.

Biochemical Parameters studied were:

- Urinary protein : Urine analysis kit
- Serum urea: GLDH / KINETIC Method, autokit from Diagnova
- Serum Creatinine :Modified Jaffe's method, kit from DIALAB
- Serum Uric acid :Uricase POD–Enzymatic Colorimetric method
- Serum bilirubin :Estimation of serum bilirubin was done by Jendrassik Grof procedure using reagents from DIALAB.
- Estimatation of SGOT / AST (Modified IFCC)
- Estimation of SGPT /ALT(Modified IFCC)
- Estimation of Alkaline Phosphatase (OPT, DGKC) :

Statistical analysis

SPSS version 19 was used for statistical analysis. All data were expressed as Mean±SD. Student's unpaired t test was used to detect the level of significance within the two groups. A level of p value <0.05 was used to indicate statistical significance in all analyses.

RESULTS

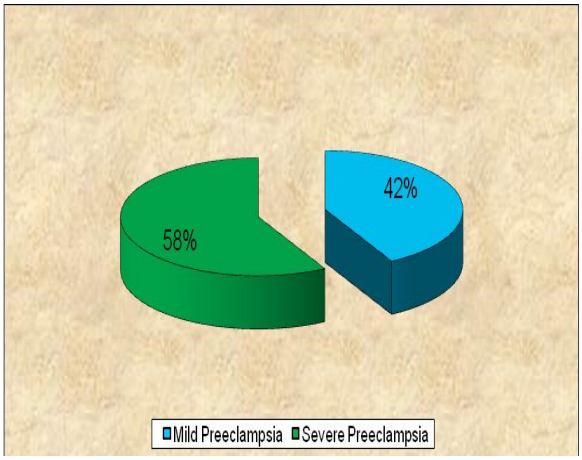

Figure 1 shows the distribution of preeclamptic women in the study group.

Out of 100 cases of preeclampsia, 42 cases have mild preeclampsia and 58cases with severe preeclampsia.

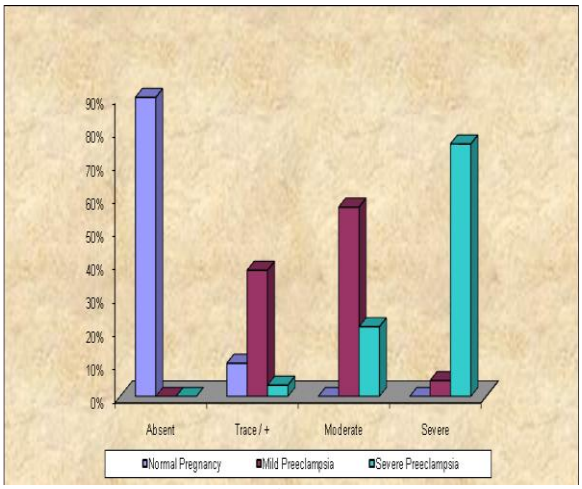

Figure 2 depicts the degree of proteinuria in study and control group.

In normal pregnancy 10% cases have trace (+) proteinuria and 90% cases have no proteinuria. In mild preeclampsia 38% cases have trace, 57% moderate and 4.8% cases have severe proteinuria. In severe preeclampsia 3.4% cases have trace, 21% cases moderate and maximum 76% cases severe proteinuria.

Table 1 shows the liver function tests in preeclampsia and normal pregnancy

Parameters	Preeclampsia (n=100)	Normal Pregnancy (n=100)	P value
	Mean ± SD	Mean ± SD	
S.Bilirubin (mg/dl)	0.98 ± 0.38	0.83 ± 0.20	<0.01**
SGOT (IU/L)	52.89±27.4	26.87±0.8	<0.001***
SGPT (IU/L)	43.45±21.6	27.8 ± 7.3	<0.001***
ALP (IU/L)	311 ± 138.06	199.14±30.4	<0.001***

Statistical analysis was done using student's unpaired t test (p>0.05- Not significant(NS),p<0.05=*, p<0.01=** ,p<0.001=***)

Significant rise in the value of serum bilirubin (p value<0.01) and liver enzymes (p value<0.001) seen in preeclampsia in comparison to the normal pregnancy.

Table-2 shows the renal function tests in preeclampsia and normal pregnancy

Parameters mg/dl	Preeclampsia (N=10) Mean±SD	Normal Pregnancy (N=100) Mean ± SD	P. value
S. urea(mg/dl)	34.3 ± 15.02	30.76 ± 6.8	0.13(NS)
S. Creatinine (mg/dl)	1.09 ± 0.52	1.05 ± 0.44	0.67(NS)
S. Uric Acid (mg/dl)	6.35 ± 0.96	4.12 ± 0.56	<0.001***

Statistical analysis was done using student's unpaired t test(p>0.05- Not significant(NS),p<0.05=*, p<0.01=** ,p<0.001=***)

Mean serum urea in preeclampsia to be 34.3 ± 15.02 mg/dl and creatinine 1.09 ± 0.52 mg/dl and in normal pregnancy with mean serum urea 30.76 ± 6.8 mg/dl and creatinine 1.05 ± 0.44 mg/dl. There is a significant increase in serum uric acid in preeclampsia as compared to normal pregnancy (p value<0.001)

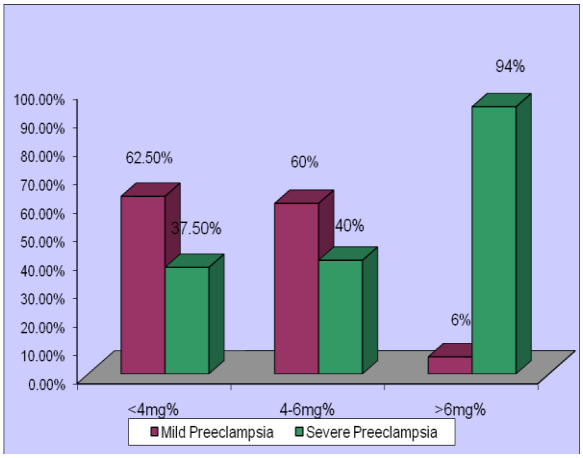

Figure 3 depicts the uric acid level according to severity of preeclampsia.

Majority (94%) of severe preeclamptic patients are having high serum uric acid level (>6 mg%) and majority (62.5%) of mild preeclampsia patients have serum uric acid < 4 mg.

DISCUSSION

Several qualitative results can be drawn on the basis of available results of the present study.

The present study documents significant proteinuria in severe preeclampsia cases which may be due to vasospasm of afferent glomerular arterioles, glomerular endotheliosis and increased capillary permeability. [11]

A significant rise in serum bilirubin and liver enzyme levels was observed in preeclampsia patients as compared to normal pregnant controls. Similar increase in liver function tests were seen in many other studies where they obtained

54%abnormality in liver function in preeclamptic cases. [4,12]

In the present study a significant rise in serum uric acid was documented in preeclampsia patients however the rise in serum uric acid and creatinine was not statistically significant as compared to control group. In majority of mild preeclampsia cases the serum uric acid level is below 6 mg/dl where as maximum cases of severe preeclampsia has uric acid levels more than 6 mg/dl. Several studies showed hyperuricemia as the biochemical characteristics of preeclampsia which may be correlated with the severity of maternal disease. [13, 14]

Cunningham FG et al and Kang DH et al observed similar increase in serum uric acid in preeclampsia and hypothesized that elevated uric acid levels is due to decrease in urate clearance by the proximal convoluted tubules of the kidneys. Levels of serum uric acid did show a high positive correlation with the severity of PIH in relation to hypertension and proteinuria. Hyperuricemia more than 5.5 mg% is associated with increased perinatal mortality. [5,6]

Shannon A in his study observed that the elevation of uric acid in preeclamptic women often precedes hypertension and proteinuria. Increased uric acid production from maternal, fetal or placental tissues through heightened tissues breakdown could also explain the increased concentration. [15]

According to a study by Laughon et al, higher uric acid concentrations in the first trimester (>3.56 mg/dL) were associated with an increased risk of developing preeclampsia but not gestational hypertension. [16]

Several studies documented uric acid to be an independent risk factor for developing hypertensive disease, and it is elevated prior to the development of hypertension. [17-19]

However, various studies reported although uric acid is a marker of value in detecting pre-eclampsia, it has been identified as a poor predictor of any complications of pre-eclampsia. [20-23]

Similar to the present study few studies observe insignificant rise in serum urea and creatinine. These parameters have no predictive value in preeclampsia. [24,25]

CONCLUSION

Thus from the present study we conclude that, elevation of serum uric acid and liver enzymes levels are early persistent signs of disease process with multi-system involvement. Clinical prediction of preeclampsia may facilitate initiation of timely management to avert maternal and fetal mortality Reducing uric acid concentration might be a potential therapeutic strategy for preeclamptic women as well.

Limitations & future scope of the study

Sample size is less. Lack of urinary measurements of uric acid, creatinine and urea and measurement of oxidative stress including substances.

Broad spectrum, multicentric studies are strongly recommended.

Competing Interests

Author doesn't have any competing interest.

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