Research article

Study of uric acid and microalbuminuria in preeclampsia and normal pregnant women

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ABSTRACT

Introduction and Aim: Pregnancy is complicated by the hypertension disease known as pre-eclampsia. The development of hypertension to a level of 140/90 mmHg or greater in the presence of proteinuria after the 20th week of gestation characterises this condition, a multisystem disorder with an unclear cause. Uric acid and microalbuminuria were assessed in preeclamptic women (PW) and normal pregnant women (NPW).

Materials and Methods: For the present study 120 women (60 NPW and 60 PW) were selected from the hospital at Mullana, Ambala, Haryana. The level of uric acid and microalbuminuria were estimated in all subjects.

Results: Preeclamptic women had microalbuminuria levels that were substantially (p<0.001) greater than those of normal pregnant women, and their uric acid levels were significantly (p<0.001) higher.

Conclusion: Preeclampsia patients had significantly higher uric acid and microalbuminuria levels than normal pregnant women. We deduced from the study that uric acid and microalbuminuria can be helpful in diagnosing preeclampsia risk.

Keywords: Uric acid; microalbuminuria; preeclampsia; hypertension.

INTRODUCTION

One of the frequent pregnancy problems is preeclampsia. Preeclampsia affects 4-5% of pregnant women, and its pathogenesis is unknown (1,2). At the 20th week of pregnancy, preeclampsia manifests as hypertension, proteinuria, dyslipidaemia, an intensified systemic inflammatory response, and oedema. It is also associated with thrombocytopenia, disseminated intravascular coagulation, and liver damage in its most severe form (3,4).

The primary by-product of purine metabolism is uric acid. Fay stated in 1990 that an increase in the disintegration of placental cells may result from an overproduction of uric acid (5). Jeyabalan *et al.,* (6) reported that elevated levels of serum uric acid in preeclamptic as a result of reduced renal clearance. Pre-eclampsia and gestational hypertension patients share a number of risk factors. The extent of placental cell apoptosis and the severity of the illness are both reflected in an elevated uric acid level. such as older mothers, obesity, low serum Ca and Mg levels, and higher uric acid concentrations(7). It has been suggested that either a reduction in uric acid excretion or an increase in uric acid synthesis is what causes the hyperuricemia in preeclampsia (5,6).

In the absence of clinically evident nephropathy, urine albumin excretion above normal levels are regarded as evidence of microalbuminuria (8-10).

Urinary albumin levels between 30 and 300 mg/24 hours are considered to indicate the presence of microalbuminuria (11). One of the defining characteristics of preeclampsia is microalbuminuria. It is confirmed that abnormalities in renal function are present in some otherwise symptom-free patients in whom pre-eclampsia would subsequently develop by the presence of microalbuminuria. Microalbuminuria levels in the early stages of pregnancy have a significant negative predictive value as indicators of preeclampsia (12). In pregnancy, persistent microalbuminuria has substantial diagnostic significance as a potential indicator of developing PE because it suggests a high likelihood of kidney glomerular filtration capacity impairment (13).

MATERIALS AND METHODS

The current study was conducted in Maharishi Markandeshwar Institute of Medical Sciences and Researches, Mullana Ambala, Haryana, India, which had 120 participants (60 healthy pregnant women and 60 preeclamptic women), in a hospital setting. The institution's ethical review board had approved the study. Women who were 20 weeks or more gestation and had a systolic blood pressure of less than 140 mm Hg and a diastolic blood pressure of less than 90 mm Hg were deemed to have hypertension-preeclampsia. The research also excluded participants who refused to take part or who had already given

birth. All patient data, including age and sex, was collected, and the intended proforma was followed while filling out specific information on the patient's previous and present medical history, including any illnesses and medications.

The glucose oxidase peroxidase (GOD) test was used to measure RBS, the urease-GLDH kinetic technique was used to estimate urea, the uricase (14,15) method was used to assess uric acid, and the pyrogallol red method was used to assess microalbuminuria (16). The unpaired t-test was used to analyse the gathered data. For statistical analysis, the statistical package for social sciences software (SPSS) version 27.0 is employed.

RESULTS

In the current study, microalbuminuria and uric acid levels were examined in 120 women, 60 of whom were preeclampsia patients (group 1) and 60 of whom were healthy pregnant women (group 2).

Table 1 displays the distribution of patients by age group for control and preeclampsia cases. In the control group, there were 2 (3.3%) females under the age of 20, 47 (78.3%) females between the ages of 21 and 30, 10 (16.7%) females between the ages of 31 and 40, and 1 (1.7%) female between the ages of 41 and 50. Most typically pregnant ladies fall within the age range of 21 to 30 years.

Among preeclamptic cases, 1 (1.7%) of the females were under the age of 20, 34 (56.7%) were between the ages of 21 and 30, 23 (38.3%) were between the ages of 31 and 40, and 2 (3.3%) were between the ages of 41 and 50. The majority of patients fall into the 21 to 30 age range. Groups 1 and 2 were statistically significant (p<0.05) based on age distribution.

Table 1: Comparison of age distribution between preeclampsia cases and normal pregnancies.

Age in Years	Normal Pregnancy		Preeclampsia		P Value
	Number	Percentage (%)	Number	Percentage (%)	
≤20	2	3.3	1	1.7	0.049**
21-30	47	78.3	34	56.7	
31-40	10	16.7	23	38.3	
41-50	1	1.7	2	3.3	
Total	60	100	60	100	

The distribution of several parameters among pregnant women with normal physiologies is shown in Table 2. In control group 2, 59 (98.3%) of the female participants had RBS less than or equal to 140 mg/dL, while one (1.7%) had RBS more than 140 mg/dL.

In control group (2), 36 (60.0%) females were with Serum Creatinine less than 0.6 mg/dL and 24 (40.0%) females were within range 0.6 to 1.1 mg/dL and no female was above 1.1 mg/dL.

In control group (2), 24 (40.0%) females were with Blood Urea less than 15 mg/dL and 36 (60.0%) females were within range 15 to 45 mg/dL.

In control group (2), 8 (13.3%) females were with Uric Acid less than 2.6 mg/dL and 48 (80.0%) females were within range 2.6 to 6.0 mg/dL and 4 (6.7%) females were above 6.0 mg/dL.

Table 2: Distribution of different parameters among normal pregnant women

Parameters	Range	Numbers (n=60)	Percentage (%)
RBS	≤140	59	98.3
	>140	1	1.7
Serum Creatinine	<0.6	36	60.0
	0.6-1.1	24	40.0
	>1.1	0	0.0
Blood Urea	<15	24	40.0
	15-45	36	60.0
Uric Acid	<2.6	8	13.3
	2.6-6.0	48	80.0
	>6.0	4	6.7

Biological indicators including RBS, urea, uric acid, and microalbuminuria levels in both of the studied groups changed significantly (p<0.001)., as shown in Table 3. There was a statistically significant difference between the two groups (p<0.001). in the

RBS mean and standard deviation, which were 104.67±24.11 in group 1 and 83.16±18.31 in group 2. Blood urea had a statistically extremely significant difference between groups 1 and 2, with a mean and standard deviation of 22.53±8.15 and 17.37±5.43

respectively (p<0.001). Uric acid had mean and SD of 5.09±1.10 in Group 1 and 3.79±1.21 in Group 2, respectively. Preeclampsia patients had much higher uric acid levels than normal pregnant women did; this difference was statistically very significant (p<0.0001). Moreover, the mean and SD of microalbuminuria in groups 1 and 2 were 1.37±0.66 and 0.52±0.33 respectively. Preeclampsia patients have much greater levels of microalbuminuria than typical pregnant women; this difference was statistically highly significant (p<0.0001).

Table 3: Comparison of different parameters between normal pregnancy and preeclampsia cases by using t-test

Parameters	Normal Pregnancy		Preeclampsia		P Value
	Mean	S.D.	Mean	S. D.	
RBS	83.16	18.31	104.67	24.11	<0.001*
Blood urea	17.37	5.43	22.53	8.15	<0.001*
Uric acid	3.79	1.21	5.09	1.10	<0.001*
Microalbuminuria (mg/day)	0.52	0.33	1.37	0.66	<0.001*

Table 4 shows serum uric acid level among preeclampsia. In mild condition, no female was with serum uric acid less than 2.6 mg/dL, 18(90%) females were in the range 2.6 to 6.0 mg/dL and 2(10%) females were above 6.0 mg/dL.

In moderate condition, no female was with serum uric acid less than 2.6 mg/dL, 15(75%) females were in the range 2.6 to 6.0 mg/dL and 5(25%) females were above 6.0 mg/dL.

In severe condition, no female was with serum uric acid less than 2.6 mg/dL, 17(85%) females were in the range 2.6 to 6.0 mg/dL and 3(15%) females were above 6.0 mg/dL.

Here, the serum uric acid was statistically non-significant (P >0.05) in preeclampsia cases (on the basis of classification).

Table 4: Serum uric acid level among preeclampsia on the basis of classification by using t-test.

Serum Uric acid (mg/dL)	Preeclampsia n (%)			P Value
	Mild	Moderate	Severe	
<2.6	0	0	0	
2.6-6.0	18 (90)	15 (75)	17 (85)	0.432
>6.0	2 (10)	5 (25)	3 (15)	
Total	20 (100)	20 (100)	20 (100)	

DISCUSSION

Preeclampsia is a complicated condition with multiple contributing factors. Insufficient penetration of the uterine wall by trophoblast cells during early pregnancy may be the main factor contributing to the development of a disease. The pathophysiology of disease cannot be explained by any single body of scientific data. However one theory for its pathophysiology is because shallow invasion and lower placental perfusion cause enhanced lipid peroxidation and the production of oxygen radicals without antioxidant protection. Maternal endothelial dysfunction is further exacerbated by this stimulation of neutrophils and macrophages, which further encourages the release of cytokines (17).

The current study demonstrates that preeclampsia patients' uric acid levels are much greater than those of typical pregnant women. Similar to how preeclampsia went from mild to severe, the serum uric acid level rose much more in severe instances than in mild cases. The correlation between elevated uric acid levels and preeclampsia has been documented by Redman *et al.,* (18), Boneu *et al.,* (19), Acien *et al.,* (20), and Yoshimura *et al.,* (21). Moreover, Lim *et al.,* discovered that serum uric acid levels rise as the severity of the condition worsens (22).

Pre-eclampsia has been linked in recent years to significant vascular dysfunction in both the mother and the placenta. (23) Several biochemical markers were discovered to be elevated in cases of micro-vascular injury, and among these, microalbumin is frequently utilized due to its low cost and simplicity in estimating. Microalbuminuria may be a reliable indicator of this illness with a high sensitivity but a poor positive predictive value, according to Salako *et al.,* (23). Microalbuminuria early in the third trimester of pregnancy is a good indicator of hypertensive problems in pregnancy, according to Bar et al. study (24,25).

We found in this study that patients with microalbuminuria will experience preeclampsia. It is obvious that additional clinical research is required to confirm the value of micro-albumin in the early detection of preeclampsia.

Limitations and future perspectives

The small sample size of various comparison groups constitutes a key constraint because the present was restricted to the question of whether uric acid was

equally as effective as proteinuria at identifying risk in a group of high-risk women. Evaluations of serum uric acid and microalbuminuria will also help to show the relationship between preeclampsia and both conditions. Prior to implementing any practised modifications, however, additional follow-up studies with bigger sample size are first required to corroborate these findings and to investigate maternal risk in order to demonstrate the diagnostic capabilities of uric acid and microalbuminuria.

CONCLUSION

Our study was done in a small group of preeclampsia and normal pregnant women to study the levels of uric acid and microalbuminuria along with measurement of another established marker. We therefore conclude that uric acid and microalbuminuria levels may be helpful to predict severity of disease. Assessing the predictive usefulness of microalbuminuria in pregnant women will be necessary to determine the long-term risk of developing preeclampsia. The incidence of maternal fatalities and systemic problems brought on by preeclampsia may be decreased with early identification.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

REFERENCES

1. Selahattin, K., Ahmet, G., Selim, K., Zeynep, O. Correlation of maternal serum high-sensitive C-reactive protein levels with biochemical and clinical parameters in preeclampsia. Eur J Obstet Gynecol Reprod Biol. 2006;124:164-167.
2. Sibai, B.M. Diagnosis and management of Gestational Hypertension and Preeclampsia, Obstetrics and Gynecology 2003;102(1):181-192.
3. Mehdi, F., Hossein, A., Maliheh, H., Hamid, R. A Comparative Study of Serum Level of Vascular Cell Adhesion Molecule-1 (sVCAM-1), Intercellular Adhesion Molecule-1(ICAM-1) and High Sensitive C - Reactive Protein (Hs-CRP) in Normal and Pre-Eclamptic Pregnancies. Ira J Bas Med Sci. 2013;16(5):689-693.
4. Report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in pregnancy. Am J Obstet Gynecol. 2000;183(1):S1-S22.
5. Fay, R. A. Uric acid in pregnancy and preeclampsia: an alternative hypothesis. Aust N Z I Obstet Gynecol.1990; 30(2):141-142.
6. Jeyabalan, A., Conrad, K. P. Renal function during normal pregnancy and preeclampsia. Front Biosci. 2007;1(12):2425-2437.
7. Roberts, J.M., August, P.A., Bakris, G., Barton, J.R., Bernstein, I.M., Druzin, M., *et al.,* Hypertension in pregnancy. Report of the American College of Obstetrician

8. and Gynecologists task force on hypertension in pregnancy. Obstet Gynecol. 2013;122(5):1122-1131.
8. Mogensen, C.E. Early Change in Kidney Function, Blood Pressure and Stages in Diabetic Nephropathy. Prevention and Treatment of Diabetic Nephropathy, H. Keen and M. Legrain, ed. Boston, MTP Press. 1983; 57-83,99-105.
9. Mogensen, C.E., Christensen, C. K., Vittinghus, E. The stage in diabetic renal disease with emphasis on the stage of incipient diabetic nephropathy. Diabetes. 1983;32(2):64-78.
10. Viberti, G.C., Mackintosh, D., Bilous, R.W., Pickup, J.C., Keen, H. Proteinuria in diabetes mellitus: Role of spontaneous and experimental variation of glycemia. Kidney Int. 1982;21(5):714-720.
11. Rodriguez, M.H., Masaki, D.I., Mestman, J., Kumar, D., Rude R. Calcium/creatinine ratio and microalbuminuria in the prediction of pre-eclampsia. Am J Obstet Gynecol. 1988;159(6):1452-1455.
12. Beaulieu, M.D. Prevention of preeclampsia. In: Canadian Task Force on the Periodic Health Examination. Canadian Guide to Clinical Preventive Health Care. Ottawa: Health Canada. 1994 ;136- 143.
13. Robson, S.C., Edmond, D.K. Hypertensive and renal disease in pregnancy. Dewhurst's Textbook of Obstetrics and Gynaecology for Postgraduates 6th ed. United Kingdom: Blackwell Science Ltd. 1999;166-168.
14. Recommendations of the German society for Clinical Chemistry. Standard method for the determination of creatine kinase activity. Revised draft of 1976. J Clin. Chem. Clin. Bioch. 1977; 15:255-260.
15. Di, W., Trendelenburg, C. Quantitative determination of creatine kinase in serum. J Clin Chemie Clin. Bioch. 1982; 20:235.
16. Phillipou, G., James, S.K., Seaborn, C.J., Phillips, P.J. Screening of microalbuminuria by use of rapid, low-cost colorimetric assay. Clinical Chemistry. 1989; 35: 456-458.
17. Christopher, W.G. R., Gavin, P.S., Ian, L. S. Preeclampsia: An excessive maternal inflammatory response to pregnancy. Am J Obstet Gynecol. 1999; 180: 499-506.
18. Redman, C.W., Beilin, L.J., Bonnar, J., Wilkinson, R. H. Plasma-Urate measurements in predicting fetal death in hypertensive pregnancy. Lancet. 1976;1(7974):1370-1373.
19. Boneu, B., Fourine, A., Sie, P., Grandjean, H., Bierme, R., Pontonnier, G. Platelet production time, uricemia and some hemostasis tests in preeclampsia. Eur J Obstet Gynecol Reprod Biol. 1980;11(2): 85-94.
20. Acien, P., Lloret, G., Lioret, M. Perinatal morbidity and mortality in Pregnancy hypertensive disorders: prognostic value of the clinical and laboratory findings. Int J Obstet Gynecol, 1990;32(3): 229-235.
21. Yoshimura, A., Ideura, T., Iwasaki, S., Koshikawa, S. Significance of uric acid clearance in preeclampsia. Am J Obstet Gynecol. 1990;162(6):1639-1640.
22. Lim, K. H., Friedman, S.A., Ecker, J. L., Kao, L., Kilpatrick, S. J. The clinical utility of serum uric acid measurements in hypertensive diseases of pregnancy. Am J Obstet Gynecol. 1998;178(5): 1067-1071.
23. Salako, B.L., Olayemi, O., Odukogbe, A.T., Adedapo, K.S., Aimakhu, C.O., Alu, F. E., *et al.,* Microalbuminuria in pregnancy as a predictor of preeclampsia and eclampsia. West Afr J Med. 2003;22(4):295-300.
24. Bar, J., Hod, M., Erman ,A., Friedman, S., Gelerenter, I., Kaplan, B., *et al.,* Microalbuminuria as an early predictor of hypertensive complications in pregnant women at high risk. Am J Kidney Dis. 1996; 28(2):220-225.
25. Poon, L.C., Kametas, N., Bonino, S., Vercellotti, E., Nicolaides, K.H. Urine albumin concentration and albumin-to-creatinine ratio at 11(+0) to 13(+6) weeks in the prediction of pre-eclampsia. British Journal of Obstetrics and Gynaecology. 2008;115(7):866-873.