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URIC ACID : AN INFLAMATORY MARKER IN PREECLAMPSIA ?

Biochemistry

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ABSTRACT

The pregnancy is the state of carrying a developing embryo or fetus within female body[1]. Preeclampsia affects 3-5% of pregnancies. Placental ischemia and inflammation occur due to impaired trophoblastic invasion in uterine spiral artery. Preeclampsia is an idiopathic multisystem disorder that typically starts after the 20th week of pregnancy; high blood pressure is a main contributing factor. Ten million women develop preeclampsia each year around the world. In hypertensive pregnancy however, there is incomplete trophoblastic invasion upto decidual vessels, but not upto myometrial vessels. Because of this, myometrial spiral arteriolar lumen remains narrow which impairs blood flow to produce placental hypoxia.

Aim and Objectives: Aim of the study is to study wheather Uric Acid is an inflammatory marker of Preclampsia.

Results : 30 women in preeclamptic compared with 30 normal pregnant with similar age and period of gestation . The mean SBP of the cases and controls are 157.7 mm of Hg and 113.6 mm of Hg with significant p value < 0.0001. The mean DBPin cases and controls is 101.4 mm of Hg and 77.47 mm og Hg with significant $p< 0.0001$. The mean serum uric acid in cases and controls are 6.41 mg/dl and 4.33 mg/dl respectively With $p < 0.0001$.

KEYWORDS

INTRODUCTION :

Pregnancy is a physiological state associated with many alterations in metabolic, biochemical, physiological, hematological and immunological processes. If there are no complications, all these changes are reversible following a few days to a few months after delivery.[1]Preeclampsia is an idiopathic multisystem disorder that typically starts after the 20th week of pregnancy; high blood pressure is a main contributing factor.[2] Ten million women develop preeclampsia each year around the world. Worldwide about 76,000 pregnant women die each year from preeclampsia and related hypertensive disorders. Approximately 500,000 babies die from these disorders every year. [3]

Preeclampsia is defined as presence of elevation of BP ≥140/90 mm of Hg after 20 weeks of gestation and proteinuria ≥ 300mg/24 hours or ≥1+ by dipstick method in a random urine sample. It occurs in approximately 6-8% of all pregnancies, 10% of first pregnancies, and 20-25% of women with a history of chronic hypertension.[4] It accounts for approximately a quarter of all antenatal admissions.[5]

Uric acid is a marker of oxidative stress, tissue injury and renal dysfunction, and therefore might be helpful in the prediction of complications of preeclampsia . [6] Hypoxia and Ischemia of the placenta and cytokines such as interferon induce the expression of xanthine oxidase and therefore increase the production of uric acid and also reactive oxygen species. [7]

In 1917, the association between elevated serum uric acid and preeclampsia was reported for the first time. [8] From that time on, uric acid measurement was considered a component in work up of pregnant women with preeclampsia to monitor the severity of the disease and its management.

Some of the hypothesis proposed in favour of raised serum uric acid levels such as abnormal renal clearance, increased tissue breakdown, acidosis and raised in the activity of the xanthine oxidase / dehydrogenase enzyme.[9] Reduction in clearance of uric acid due to the reduction in the glomerular filtration rate, increased absorption and decrease in the secretion may be the cause for the raise in the level of serum uric acid in preeclampsia .[10]

In hypertensive pregnancy however, there is incomplete trophoblastic invasion upto decidual vessels, but not upto myometrial vessels. Because of this, myometrial spiral arteriolar lumen remains narrow which impairs blood flow to produce placental hypoxia. It leads to release of placental debris that incites a systemic inflammatory response. Uric acid is also a mediator of inflammation stimulating the production of monocyte chemoattractant protein -1, IL-1, IL-6, and TNF – α.[11]

Uric acid contribute to failed placental bed vascular remodeling by impending trophoblast invasion with resultant with reduced placental perfusion, setting the stage for ischemia reperfusion injury to the placenta and oxidative stress. Maternal tissue may experience ischemic injury due to vasospasm secondary to endothelial dysfunction . Ischemic injury and oxidative stress promotes a feed-forward cycle of uric acid production. With tissue injury , purines are liberated and with hypoxia, ATP is degraded to both adenine and xanthine (substrate). Hypoxia is the potent inducer of the xanthine oxidase/dehydrogenase enzyme. With the parallel increase in both substrate and enzyme concentrations, uric acid production will increase[9].

METHODOLOGY

It is a case control study which comprise of preeclamptic primigravida patients of gestational age above 20 weeks in Department of Obstetrics and Gynecology, Vani Vilas Hospital and Bowring & Lady Curzon Hospital attached to Bangalore Medical College and Research Institute. Study is from November 2011 to May 2013.

A. Selection of study subjects

Based on inclusion and exclusion criteria a total number of 60 subjects (30 cases and 30 controls) were selected for the present study.

Inclusion Criteria used to select the study subjects:

a. Preeclamptic primigravida of gestational age above 20 weeks.
b. The diagnosis of preeclampsia was made according to the criteria by

American College of Obstetrics and Gynecology [116]

i. Blood pressure higher than 140/90 mmHg.
ii. Edema.
iii. Proteinuria >300mg/24 hours or 1+ dipstick method after 20th weeks of gestation.

Controls –

It includes 30 normal pregnant women of same gestational age group without any complications.

Exclusion criteria

a. Patients with history of Gestational Diabetes Mellitus.
b. Patients with history of Essential Hypertension, Diabetes Mellitus and other Cardio-Vascular Diseases.

Based on the inclusion and exclusion criteria, age matched cases and controls were included in the present study after obtaining informed consent. A proforma was used to record relevant information and patient's data.

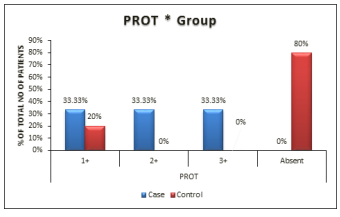
B) Collection of blood samples:
Following selection of subjects and after obtaining informed consent about the proposed study, clinical history was taken from subjects and examination findings were noted down. About 5ml of fasting venous blood sample was collected from median cubital vein by venepuncture.

RESULTS :

Of the 30 cases and 30 controls included in the study, the Systolic and Diastolic Blood Pressure was significantly higher in pre-eclamptic pregnancies as compared with healthy pregnant women. (P<0.001)

	Case	Control	P value
AGE			0.749
Sample size	30	30	
Mean ± Stdev	24.37 ± 3.21	23.73 ± 2.78	
Median	23.5	24	
Min-Max	20-32	18-29	
Inter quartile Range	22 – 26	22 – 26	
POG			0.329
Sample size	30	30	
Mean ± Stdev	36.07 ± 0.83	36.3 ± 0.47	
Median	36	36	
Min-Max	34-37	36-37	
Inter quartile Range	36 – 37	36 – 37	
SBP			<.0001
Sample size	30	30	
Mean ± Stdev	157.73 ± 15.41	113.6 ± 5.67	
Median	150	111	
Min-Max	140-184	106-126	
Inter quartile Range	146 – 170	110 – 120	
DBP			<.0001
Sample size	30	30	
Mean ± Stdev	101.4 ± 9.2	77.47 ± 4.52	
Median	100	78	
Min-Max	90-120	68-84	
Inter quartile Range	94 – 106	74 – 82	

The preeclamptic women had an equal distribution (33.3%) of urine protein as 1+, 2+ and 3+ on dipstix whereas control group had 80% nil and 20% in 1+ category.`



UA			<.0001
Sample size	30	30	
Mean ± Stdev	6.41 ± 1.58	4.33 ± 1.23	
Median	5.4	4.14	
Min-Max	4.6-9.2	2.52-6.91	
Inter quartile Range	5.190 - 8.040	3.580 - 5.060	

Thirty women in preeclamptic group compared with 30 normal pregnant women with similar age and period of gestation . The mean systolic blood pressure of the cases and controls are 157.7 mm of Hg and 113.6 mm of Hg with significant p value < 0.0001. The mean diastolic blood pressure in cases and controls is 101.4 mm of Hg and 77.47 mm og Hg with significant p value of < 0.0001.

The preeclamptic women had an equal distribution (33.3%) of urine protein as 1+, 2+ and 3+ on dipstix whereas control group had 80% nil and 20% in 1+ category.
The mean serum uric acid in cases and controls are 6.41 mg/dl and 4.33 mg/dl respectively with p valvue of < 0.0001.

DISCUSSION :

In our study , the mean serum uric acid in cases is significantly higher (6.42 mg/dl) than when compared to controls (4.33 mg /dl) with p value of < 0.0001.

A similar study by Amir Taefl et al showed that the mean uric acid level in preeclampsia and normal healthy pregnancy is 5.8 mg/dl and 4.9 mg /dl , which is in accordance with our study.[12]

In a study by Triveni et al, the showed that uric acid was very significantly higher in severe preeclampsia (<0.01) and in eclampsia (p<0.01) than in normal healthy pregnant controls .[13]

In a study by Shirish T et al , which is is in accordance with our study, where the serum uric acid in cases was 7.52 mg/dl which is much higher than in controls was 4.55 mg/dl with p value of p < 0.0001.[14]

Studies by Krishna et al, concluded that high serum uric acid level could be a useful indicator of the maternal and fetal complications.[15]

In hypertensive pregnancy however, there is incomplete trophoblastic invasion upto decidual vessels, but not upto myometrial vessels. Because of this, myometrial spiral arteriolar lumen remains narrow which impairs blood flow to produce placental hypoxia. It leads to release of placental debris that incites a systemic inflammatory response. Uric acid is also a mediator of inflammation stimulating the production of monocyte chemoattractant protein -1, IL-1, IL-6, and TNF – α.[11]

Uric acid contribute to failed placental bed vascular remodeling by impending trophoblast invasion with resultant with reduced placental perfusion, setting the stage for ischemia reperfusion injury to the placenta and oxidative stress. Maternal tissue may experience ischemic injury due to vasospasm secondary to endothelial dysfunction . Ischemic injury and oxidative stress promotes a feed-forward cycle of uric acid production. With tissue injury , purines are liberated and with hypoxia, ATP is degraded to both adenine and xanthine (substrate). Hypoxia is the potent inducer of the xanthine oxidase/dehydrogenase enzyme. With the parallel increase in both substrate and enzyme concentrations, uric acid production will increase[9].

CONCLUSION :

Hyperuricemia is one of the earliest and most consistent observation noticed in preeclampsia. We speculate that uric acid may play direct role in pathological processes of preeclampsia at both the level of placental and maternal vasculature. The importance of continous antenatal surveillance and thereof uricacid by laboratory cases of hypertension in pregnancy is thus evident. The disease can be identified early and its deterioration prevented by proper management.

REFERENCES

1. Maternal physiology. In Cunningham F, Lenevo K, Bloom S, Hauth J, Rouse D, Spong C (Edts). Williams Obsterrics, 23rd ed. USA: The McGraw-Hill companies. 2010; 107-131.
2. Ob-Gyns Issue Task Force Report on Hypertension in Pregnancy: Preeclampsia Diagnosis No Longer Requires Presence of Proteinuria
3. Kuklina EV, et al. Hypertensive Disorders and Severe Obstetric Morbidity in the United States. Obstet Gynecol 2009; 113:1299-306.
4. Kamath S. Hypertension in pregnancy. [Editorial]. JAPI. 2006; 54: 269-270.
5. Bansal S. Hypertension in pregnancy. In: Desai P, Malhotra N, Shah D (Edts). Principles & practice of Obstetrics & Gynecology for post-graduates. 3rd ed. New Delhi: Jaypee Borthers. 2008; 100-107.
6. Powers RW, Bodnar LM, Ness RB. Uric acid concentration in early pregnancy among preeclamptic women with gestational hyperuricemia at delivery. Am J Obstet Gynecol 2006;194:160.
7. Many A, Hubel CA, Roberts JM. Hyperuricemia and xanthine oxidase in preeclampsia , revisited. Am J Obstet Gynecol. 1996; 174: 288-91.
8. Slemmons J, Bogert L. The uric acid content of maternal and fetal blood. J bio Chem 1917;32: 63-9.
9. Bainbridge SA, Roberts JM. Uric acid as a pathogenic factor in preeclampsia . Placenta 2008: 29: 67-72.
10. Thangaratinam S, Ismail KM, Sharp S, Coomarasamy A, Khan KS. Tests in prediction of preeclampsia severity review group. Accuracy of serum uric acid in predicting complications of preeclampsia; a systemic review. BJOG 2006: 113 : 369-78.
11. Johnson RJ, Kang DH, Feig D, Kiilvighn S, Kannellis J, Wantanabe S et al. Is there a pathogenic role of uric acid in hypertension and cardiovascular and renal disease ? Hypertension . 2003 ; 41: 1183-90. [Pubmed: 12707287].
12. Amir Taefl, Ashraf Sadat Jamal, Human Delavari MD. The role of serum uric acid in preeclampsia . Journal Of Family and Reproductive Health 2008: 2(3): 159-162.
13. Triveni K. Prathap T. Uric Acid As An Important Biomarker In Hypertensive Disorders In Pregnancy . International Journal Of Reproduction , Contraception , Obstetrics and Gynaecology. 2016:5(12): 4382.
14. Krishna TS, Krishnamma M, Rajeswari DR, Rao V, Naidu JN et al,. Alterrations of serum uric acid concentrations in preeclampsia. Int J Applied Bio Pharmaceutical Tech . 2015;6(2):165-7.