Estimation of serum uric acid as a predictor of the severity of Pre-eclampsia & eclampsia

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Abstract

Introduction-uric acid production is a normal phenomenon in normotensive pregnancy, however in preeclampsia and eclampsia uric acid production exaggerated may result in greater potential for endothelial oxidative damage. It has been reported that higher UA is indicative in women with preeclampsia and eclampsia.

Material and method-Prospective study was done for duration of 16 months i.e. may 2019 to Sep.2020 in the department of Biochemistry of central research laboratory of Magadh Medical College, Gaya, India. A total no.100 women in which 50 cases (30 Preeclampsia & 20 Eclampsia) and 50 control (30 were normal pregnant & 20 normal non- pregnant women with reproductive age group)

Result-The mean serum UA , 24hours urinary protein were higher in preeclampsia and eclampsia compared to control.

Conclusion-A significantly increased serum UA in preeclampsia and eclampsia than control group indicate the significant role in pathogenesis of PIH. Total serum Protein levels are reduced in preeclampsia and eclampsia compared to control.

Key word- PIH (Pregnancy induced hypertension) UA (Uric acid), Serum Total protein, Preeclampsia and Eclampsia

Introduction

Pre-eclampsia, a syndrome peculiar to pregnancy characterized clinically by hypertension and Proteinuria.[1] It is a rapidly progressive condition, which originates in placenta and affects both mother and fetus.[2] Preeclampsia is a common pregnancy disorder with a reported incidence rate of 2-5% worldwide.[3] In India the incidence of pre-eclampsia is reported to be 8-10 % of pregnancies.[4] It is among the main causes for pregnant women being admitted into intensive care unit in developed countries[5] and is leading cause of maternal -fetal mortality and "sever morbidity including cardiac ,respiratory, renal and hepatic failure" in both in developed and

developing countries.[6] Preeclampsia is hypertension more than or equal to 140/90mmHg accompanied by proteinuria more than 300mg /24hrs first time after 20th week of gestation and both resolving after with 12th week postpartum.[7] Suprimposed preeclampsia is following three cases

(i)New onset proteinuria (more than or equal to 300mg per 24hrs)in hypertensive women. (ii) Hypertension and proteinuria which is detected before 20th week of gestation which is progressing after 20th week of gestation. (iii)Renal disease with proteinuria detected before 20th week of gestation, which are accompanied by new onset hypertension after 20th week of gestation.

Eclampsia is defined as onset of convulsions in women with pregnancy induced hypertension.[8] Uric acid is end product of Purine catabolism by xanthine oxidase and other enzyme and is responsible for uric acid production coupled with production of free radicals superoxide (O^{2-}),which contribute to oxidative stress on endothelial lining of arteries .These may contribute to development of gestational hypertension.[9] Hyperuricemia caused by utero placental disruption and decreased renal perfusion.[10] Several studies suggested that UA is " the most sensitive indicator of preeclampsia available to clinicians".[11] In this study we concluded that UA is predictor of preeclampsia and in women with hypertension, UA 6.69mg/dl can predict the occarance of preeclampsia latter in pregnancy .In Sharmila Krishnal et al study serum UA level 7.2 mg/dl were signigicantly increased in preeclampsia. [12]

Aim and objectives - Aim of our studies is to estimate serum uric acid levels in cases of gestational hypertension has been established previously, so that oxidative stress induced endothelial damage leading to plaque formation resulting in pregnancy induced hypertension could be prevented. In several studies an increase in serum uric acid levels has been observed in cases of gestational hypertension. This condition is very difficult for patient as well as doctors, because morbidity and mortality both are increased in cases of gestational hypertension, particularly with increased serum uric acid. We started estimation of uric acid levels in first trimester (less than 12 week of gestation),so that prevention of gestational hypertension and effect of uric acid on its generation could be possible.

By early institution of treatment of pregnancy induced hypertension we can prevent morbidity and mortality of patient.

Material and methods- The prospective study was carried out in Biochemistry department of Central Research Laboratory in collaboration with department of Obstetrics & Gynaecology at Anugrah Narayan Magadh Medical College, Gaya over a period of 16 months from May 2019 to Sep.2020 .Approval was obtained by ethical committee of Anugrah Narayan Magadh Medical College, Gaya,Bihar,India. Total 100 cases were selected of which 20 cases were clinically normal non-pregnant women of reproductive age group (15-45years) and 30 cases were normal pregnant women of different age group. 50 cases were grouped as control. 50 cases of toxemia of pregnancy were taken for study, further cases categorized as 30 cases of preeclampsia and 20 cases of eclampsia. They were non smokers, not taking tobacco and free from other metabolic disorders. We had collected necessary information about cases and control.

Inclusion Criteria

1. Cases of pre-eclampsia and eclampsia patient in primi with age group of 15-45 years and with gestation age more than 20 weeks.
2. Controls of normotensive primi with gestation age more than 20 weeks and normal non pregnant women with reproductive age group15-45 years.

Exclusion Criteria

1. Gestational diabetes
2. Chronic hypertension
3. Cardiovascular disease
4. Liver disease
5. Endocrine disorder
6. Renal disease

Sample Collection

Blood sample were collected by venous puncture of cubital space, on spot urine in sterile urine pot and next day collect the 24hours urine by on duty nurses in presence our volunteers in Obsteretics & Gynecology Department.

Serum was separated after 30 minutes standing and 5minutes centrifugation at 3000 rpm, then clear serum transferred to sterile tube analysis was done on the same day in Biochemistry department of central research laboratory.

The presence of Proteinuria was screened by one urine deep stick test, then proceed to 24hrs. urine protein.

Quantitative estimation of uric acid was carried by uricase method, which has many advantages. It is very easy method and uric acid can be determined within minutes and very small amount of serum required. It is very sensitive and specific method.

Principle-Uric acid is enzymatically oxidized by oxygen to produce hydrogen peroxide, allantoin, and carbon dioxide. Quantity of hydrogen peroxide react with 4 aminoantipyrine and 2,4,6 tribromo 3-hydroxy benzoic acid in presence of peroxydase to produce intensity of chromogen (Quininoneimimine) formed is proportional to the uric acid concentration and this color is measured at 505 (500-540 nm).

Reagent- 4-Aminoantipyrine,2,4,6 –Tribromo,3-hydroxy benzoic acid, Uricase, Peroxidase & Tris Buffer.

Procedure- One ml of working reagent take in each Blank, Standard,Test marked sterile khan tube and mixed $20\mu l$ distilled water, standard and serum in respective tube and incubate for 5 minutes in incubator at37°c. Read the absorbance of standard and test at 505nm with Spectrophotometer against the reagent blank.

Calculation-Ratio of absorbance of Test and Standard multiply by concentration of standard (6mg/dl).

Serum total protein, serum albumin, globulin, A/G ratio determined and blood pressure was measured.

The data of various biochemical parameters was compared between case and control groups and students "t" test was used as statistical method.

Observation The present study of observation of serum uric acid was carried out on total of 100 cases of which 20 cases were clinically normal non-pregnant women of reproductive age group

(15-45years) and 30 cases were normal pregnant women in different trimester of pregnancy. 50 cases were grouped as control. 50 cases of toxemia of pregnancy were taken for study, further categorized as 30 cases of preeclampsia and 20 cases of eclampsia.

Table-1: Mean and standard deviation of various biochemical parameters in controls and total cases (preeclampsia and eclampsia)

S.N	Biochemical Parameters	Mean & SD of controls	Mean &SD of cases	T value	p value	Remarks
1.	S.Uric Acid	3.82±1.143	6.69±0.395	10.61	<0.001	Significant
2.	Total Protein	5.78±0.76	4.66±0.75	4.84	<0.01	Significant
3.	24hrs urine Protein	5.8±0.70	866±519.7	7.42	<0.001	Significant

Table -2: Mean and standard deviation of various biochemical parameters in preeclampsia and eclampsia

S.N	Biochemical Parameters	Mean & SD of Pre-eclampsia	Mean &SD of Eclampsia	T value	p value	Remarks
1.	S.Uric Acid	6.9±1.53	7.92±1.89	1.3	>0.05	Non-Significant
2.	Total Serum Protein	5.0±0.89	4.25±0.75	3.1	>0.05	Non-Significant
3.	24hrs urine Protein	756±390.50	1040.552..7	1.83	>0.05	Non-Significant

Table 2 shows there is no significant change in mean serum uric acid level in pre -eclampsia and eclampsia but table 1 shows there is significant increase in mean serum uric acid in pre -eclampsia and eclampsia as compared to control group (non pregnant and normal pregnancy).There is significant increase in mean serum uric acid in eclampsia compared to pre-eclampsia.

Results-A total number of 30cases of pre-eclampsia and 20 cases of eclampsia in 3rd trimester have been studied. All pre-eclampsia patients show classical triad of hypertension, Proteinuria & edema. The mean serum uric acid level in the study group was 6.69±0.395 and in control group 3.82±1.143. The difference between mean of two groups was statically significant (p<0.001) .The mean of pre-eclampsia case 6.9±1.53 and mean in eclampsia cases is 7.92±1.89. The mean 24 hour urinary protein in the study group was 866.9±519.7 and in control group 5.8±0.70. The difference between mean of two groups was statically significant (p<0.001) .The mean of pre-eclampsia case756.2±390.50 and mean in eclampsia cases is 1040.52±552.7.

Discussion- Uric acid is end product created during break down of Purine, most of it is excreted in urine to regulate normal level. A total number of 30cases of pre-eclampsia and 20 cases of eclampsia in 3rd trimester have been studied. All pre-eclampsia patients show classical triad of hypertension, Proteinuria & edema. The mean serum uric acid level in the study group was 6.69 ± 0.395 and in control group 3.82 ± 1.143. The difference between mean of two groups was statically significant ($p<0.001$) .The mean of pre-eclampsia case 6.9 ± 1.53 and mean in eclampsia cases is 7.92 ± 1.89 The mean 24 hour urinary protein in the study group was 866 ± 519.7 and in control group 5.8 ± 0.70. The difference between mean of two groups was statically significant ($p<0.001$) .The mean of pre-eclampsia case756.2 ± 390.50 and mean in eclampsia cases is 1040.52 ± 552.7.

Uric acid is most common routine investigation done in all laboratories for assessing the severity of preeclampsia. It also differentiates the either hypertensive or preeclampsia. In hypertensive pregnancy, uric acid level is usually not raised. It is also useful prognostically i.e., the higher level of urate the greater is the perinatal mortality.[13]

A raised urate in the maternal blood results from tissue ischemia and reduced renal clearance, urate is actively secreted by distal convoluted tubules damage to the distal convoluted tubules in preeclampsia result in decreased urate secretion which result in increase in circulation.

Mainly uric acid levels were estimated to indicate the degree of severity of toxemia pregnancy. A high uric acid is predictor of severity of disease and perinatal mortality has been suggested by several authors.[13]An increase in uric acid is for runner of Proteinuria.

 Toxaemia of pregnancy remain enigma despite many advances made. These constitute one of the common complication of gestation and contribute to be responsible for maternal and perinatal morbidity and mortality. The incidence of this disease has been considerably declined as nutritional education and socioeconomic status of population raisen. Table-2 showed serum uric acid in different group of cases. There was significant increase in serum uric acid in preeclampsia and eclampsia.

 Mustaphi R et al study, Toxemia of pregnancy is associated with maternal and fetal morbidity and mortality[14].

Shikha Saxena et al study a similar significant difference ($p<0.001$)was noted for serum uric acid level in PIH cases(6.65 ± 1.36) and the control subjects(4.72 ± 0.85).[15] Eclampsia (severe form of preeclampsia) is major obsteretics emergency which require mobilization of efforts and adequate management to avoid catastrophic events. Unfortunately continued scientific probe into understanding the pathophysiology of this disease and causative factor is still unclear. But in spite of all these factors, the incidence of this disease can be lowered by reducing serum uric acid.

Conclusion – It was from the present study that the trend was increase in serum uric acid in preeclampsia and eclampsia as compared to control group was significant statistically.

          Hyperuricemia is one of the important observation noted in toxaemia of pregnancy and is important predictor of perinatal morbidity and mortality.

          The measurement of serum uric acid is of great diagnostic and prognostic value in toxaemia pregnancy and useful to assess maternal and perinatal morbidity and mortality and worsening of the condition can be prevented.

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