Abstract:
Aims and objectives To predict pre-eclampsia using serum uric acid levels in antenatal normotensive patient and to assess the severity of pre-eclampsia using the serum uric acid levels. Study design It is a prospective observational study of 120 patients visiting our institution at 20 weeks of gestation. The cut-off value of serum uric acid was taken as 6 mg. They were followed for the development of signs of pre-eclampsia.
Result It was observed that 64 patients had uric acid 6mg percent of which 55 developed pre-eclampsia (86 percent) and about 9 remained normotensive (14 percent). Twenty four (37 Percent) patients with pre-eclampsia developed complications like (15 percent)7 eclampsia, (6 percent)3 placental abruption , (4 percent)1 HELLP syndrome, one pulmonary edema and 12 with signs of imminent eclampsia.
Conclusion In our study patients with uric acid 6mg became pre-eclamptic and also the serum uric acid levels correlated with the maternal complications of pre-eclampsia.

Keyword: uric acid, pre-eclampsia, hyperuricemia, maternal complications

Introduction:
Many clinical and biochemical parameters have been used to detect pre-eclampsia and assess its severity. But most of the available parameters are neither specific nor sensitive. Hyperuricemia, a common finding in pre-eclamptic pregnancies is evident from early gestational weeks. Uric acid is a terminal metabolite of the degradation of nucleotides, which increases their blood levels in patients with preeclampsia-eclampsia, increasing its synthesis by damage and death of trophoblastic cells in proliferation and decreased urinary excretion due a lower glomerular filtration rate and increased absorption in the proximal tubule. Uric acid can promote endothelial dysfunction, damage and inflammation, which leads to oxidation which is evident in Pre-eclampsia [1]. Hence a study was done to predict pre-eclampsia using serum uric acid levels.

Aims: To predict pre-eclampsia using serum uric acid levels.
acid levels in normotensive antenatal patients at 20 weeks gestation. To predict the complications of pre-eclampsia using serum uric acid levels. **Study design** It was a prospective observational study of 120 patients who were normotensives visiting our institution.

**Inclusion criteria:**
The patients with no albuminuria and normotensives with singleton pregnancy with pedal edema at 20 weeks Gestation were admitted & included in the study.

**Exclusion criteria**
Women with renal disease, liver disease, cardiac causes, gout and hematological disorder, H/o diuretic intake. H/o hypertension prior to pregnancy, and women received diet containing of meat and other sources of nucleoprotein and drugs known to influence serum uric acid level were excluded.

**Methods:**
The patients were explained about the study and consent obtained. Five ml of blood was collected between 8.30 -11.30 am to avoid diurnal variation in serum uric acid level at 20 weeks of gestation. Samples were analysed within 24 hrs of collection in the clinical biochemistry laboratory colorimetrically in Semi autoanalyser. Cases were followed for the development of maternal complications like pre-eclampsia, eclampsia, abruption and HELLP syndrome. The cut-off value of serum uric acid was taken as 6 mg%. Repeat samples were taken at (i) Third trimester, (ii) Before delivery in patients with uric acid > 6 mg%. Proteinuria was defined as >300 mg/24hrs urine collection or >2+ on a voided urine or >1+ on a catheterized random urine sample. Data analysed with SPSS 16 software using appropriate statistical test.

**Results:**

**Serum uric acid and pre-eclampsia:**
The sensitivity and specificity of the test were 90% and 84% . The positive predictive value for serum uric acid to predict pre-eclampsia is 85%. Serum uric acid levels significantly correlated with the development of pre-eclampsia (p < 0.001), ROC curve AUC 0.855, 95% CI, 0.778-0.931.

**Serum Uric acid and maternal complication:**
It was observed that 24 patients of pre-eclampsia (37%) with repeat uric acid level (taken at third trimester) higher than the previous value developed complications - 7 eclampsia (15%), 3abruption (6%) , 1 HELLP syndrome (4%), one case of pulmonary edema and 12 cases with signs of imminent eclampsia . The mean uric acid level for the patients who went in for complications was 9.7 mg%. The remaining thirty one patients with no complications but with serum uric acid >6 mg%, the mean was 7.2 mg%. Only two of the 6 pre-eclamptic patients with serum uric acid level <6 mg% had maternal complication (eclampsia).The remaining patients had no complications.

**Table 2: Patients with complications in relation to uric acid level**
The maternal complications have significant correlation with serum uric acid levels (p < 0.001), ROC curve AUC 0.742, 95% CI, 0.641-0.843, with the negative predictive value of 96%. The maternal complications were less in patients with uric acid level <6 mg%.
DISCUSSION:
Uric acid is produced as a result of the enzyme oxidase and its production is associated with formation of free radicals. Its raised levels are usually secondary to altered renal functions [2]. According to Vazquez – Rodriguez JG et al, hyperuricemia (> 4.5 mg/dL) is the first biomarker of the clinical chemistry considered as an early evidence of disease (< or = 20 weeks gestation). Uric acid concentrations are not only a criterion for establishing the correct diagnosis and the differential with other hypertensive states, but an indication of termination of pregnancy. Hyperuricemia has also demonstrated its usefulness as a predictor of maternal and fetal complications and maternal sequelae of late postpartum. Several studies have demonstrated its influence on the genesis of preeclampsia-eclampsia, either alone or jointly with other known processes (metabolic syndrome, oxidative stress, inflammation cascade, and angiogenesis) that have a proven role in perpetuating the endothelial damage and maternal vascular smooth muscle cells [3]. According to Bainbridge et al, elevated uric acid decreases endothelial cell proliferation and migration, which could lead to poor placental development, and ultimately preeclampsia [4]. In healthy pregnancies, uric acid decreases from an average of 4.2 mg/dl pre-pregnancy to 3.1 ± 1.1 mg/dl in the first trimester, and slowly increases during gestation to an average of 5.1 ± 1.2 mg/dl from 35 weeks gestation to term. A normal Indian adult female have uric acid level of < 5.7 mgs% (<340 µmol/L). Hence the cut-off value was taken as 6 mg%.

Serum uric acid and pre-eclampsia:
In our prospective study of 120 patients, those with uric acid levels > 6 mg% were associated with an increased risk of developing pre-eclampsia with a positive predictive value of 84%. Banu Dane et al showed that maternal serum uric acid level in second trimester may be used in prediction of PIH with a sensitivity of 40.4% and specificity of 79.8%. In our study specificity has concordance with Banu Dane et al study [5].

Serum uric acid and maternal complications:
In our study twenty four patients with repeat uric acid levels greater than the previous value developed maternal complications. The mean uric acid level in patients who developed complications was 9.5 mg%. However the negative predictive value of maternal complications was 96.4%, which showed that the patients with normal uric acid levels were less prone to complications. Thangaratinam S et al showed in a systematic review that in women with preeclampsia a positive test results of uric acid > 350 µmol/l threshold predicted Eclampsia with a likelihood ratio of 2.1. It was therefore concluded in his review that use of therapeutic measures such as magnesium sulfate or planning early delivery should not be based on uric acid levels [6]. Annabel et al, concluded his study that plasma levels of uric acid approximately correlated with the severity of pre-eclampsia [7]. And H E Fadel et al has also showed in his study that uric acid level has been shown to roughly parallel the severity of maternal syndrome [8]. These studies support our observation that raised uric acid levels have predicted the development of preeclampsia and maternal complications.
**Conclusion:**

Pre-eclampsia is a pregnancy specific syndrome and a leading cause of maternal and fetal morbidity and mortality. Our study observed raised serum uric acid level at 20 weeks gestation predicted pre-eclampsia and maternal complications. An increased serum uric acid level often pre-dates the onset of clinical manifestation of pre-eclampsia. It is also a marker of metabolic syndrome known to increase the risk of pre-eclampsia. Thus serum uric acid level can be used as a predictor of pre-eclampsia and manage expectantly those patients for a good maternal outcome.

**References:**


7. Annabel C. Martin & Mark A. Brown, Could uric acid have a pathogenic role in pre-eclampsia?, *Nature Reviews Nephrology (December 2010) 6, 744-748*.