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BIOCHEMICAL SCREENING OF PREECLAMPSIA

Biochemistry

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ABSTRACT

Background: Preeclampsia (PE), which affects about 2% of pregnancies, is a major cause of maternal and prenatal morbidity and mortality.
Introduction: The aim of the present study was to correlate biochemical parameters like serum uric acid, LDH, AST, ALT with maternal outcomes in Hypertensive diseases in pregnancy.
Material and methods: This prospective study was carried out in Obstetrics and Gynecology and biochemistry department of index medical college, Indore, M.P., India. 100 subjects with 100 controls were enrolled for the study.
Result: We found a statistically significant difference between serum uric acid, LDH, AST, ALT with maternal death in PIH case.
Conclusion: So higher levels of these parameters can be very useful markers to identify the occurrence of the complications of preeclampsia in early pregnancy and help in the management of the women with preeclampsia.

KEYWORDS

preeclampsia, AST, ALT, uric acid.

Introduction: Maternal mortality still remains very high in developing countries including India. Maternal Mortality Ratio (MMR) in India is 200 per 1 lakh live births. Medical conditions like eclampsia, ante-partum hemorrhage, and post-partum hemorrhage all have increased MMR [1]. The mechanisms behind preeclampsia are not fully understood. However, hypertension associated with preeclampsia develops during pregnancy and remits after delivery that leads to the logical implication that the placenta is a central keystone in the process [4]. Removal of the placenta is the only effective treatment to stop disease progression. Hypertension and proteinuria is essential for the diagnosis. Hypertensive disorders during pregnancy are chronic hypertension (known hypertension prior to pregnancy), gestational hypertension (blood pressure > 140/90 mmHg in a normotensive pregnant women who is >20 weeks of gestation and has no proteinuria or any signs of preeclampsia) and superimposed preeclampsia on chronic hypertension (development of preeclampsia in a patient with chronic hypertension or renal disease).[2] Risk factors for pre-eclampsia include a wide array of conditions that reflect the complexity of the disease process and their strengths of association are quantified using risk ratios or odds ratios[3] . These can be categorized based on familial factors, demographic factors, past medical or obstetric history, pregnancy-associated factors, paternal factors and miscellaneous factors.[4] Pre-eclampsia stands out among the hypertensive disorders for its impact on maternal and neonatal health. It is one of the leading causes of maternal and prenatal mortality and morbidity worldwide. However, the pathogenesis of pre-eclampsia is only partially understood and it is related to disturbances in placentation at the beginning of pregnancy, followed by generalized inflammation and progressive endothelial damage. There are other uncertainties too: the diagnosis, screening and management of pre-eclampsia remain controversial, as does the classification of its severity. However, it is generally accepted that the onset of a new episode of hypertension during pregnancy (with persistent diastolic blood pressure >90 mm Hg) with the occurrence of substantial proteinuria (>0.3 g/24 h) can be used as criteria for identifying pre-eclampsia. Although pathophysiological changes (e.g. inadequate placentation) exist from very early stages of the pregnancy, hypertension and proteinuria usually become apparent in the second half of pregnancy and are present in 2%–8% of all pregnancies overall [4]

Materials and Methods:
Study setting, study type: This prospective study was carried out in Obstetrics and Gynecology and biochemistry department of INDEX medical college, Indore, M.P.. , India.

Study participants & study period: All pregnant women admitted between 2011 - 2014 in the hospital were examined. Blood pressure was measured by mercury sphygmomanometer in reclining position in right brachial artery. Three readings were taken at 10 minutes interval. Participants having average systolic blood pressure ≥ 140 mm hg and/or diastolic blood pressure ≥ 90 mm Hg were included in the study. Exclusion criteria: Patients with history of hyperuricemia, diabetes, renal diseases, cardiovascular illness, and symptomatic infectious diseases were excluded.

Sample size and sampling: 100 subjects with 100 controls were enrolled for the study.

Data collection: After enrollment participants were grouped into mild PIH, severe PIH, eclampsia and chronic hypertension. Informed consent was taken from all the participants. The history of all participants was taken. Blood samples of participants were taken from right or left cubital vein and collected in plain and citrate tubes.

Aspartate transaminase (AST) and Alanine transaminase (ALT) was measured by Ultra-violet kinetic method [6]. Uric acid was measured by modified Trinder"s test [5] and lactate dehydrogenase (LDH) was measured by UV kinetic IFCC [7] method. Participants were observed throughout pregnancy and maternal outcome was observed.

Statistical Analysis: We used unpaired„t" test for comparing the mean level of uric acid, LDH, AST, ALT with maternal outcome. p value < 0.05 was considered statistically significant.

Result:

Parameters	MEAN ± SD control	MEAN ± SD Subjects	P-VALUE
ALT	46.47±1.67	55.23± 0.29	0.0001
AST	50.53± 3.54	123.17 ±2.93	0.0001
URIC ACID	3.17 ±1.2	9.33±1.159	0.0001
LDH	210.34± 32.13	470.20 ±246.32	0.0001

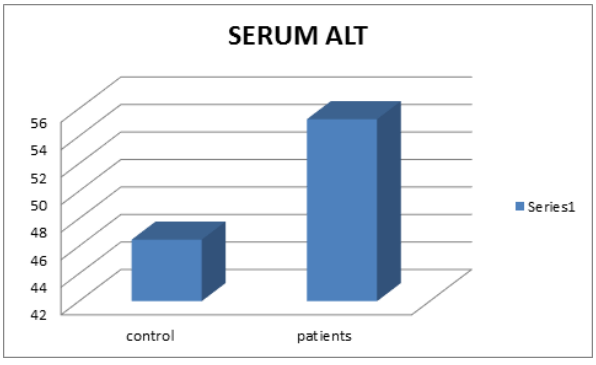

Figure1 : Serum ALT

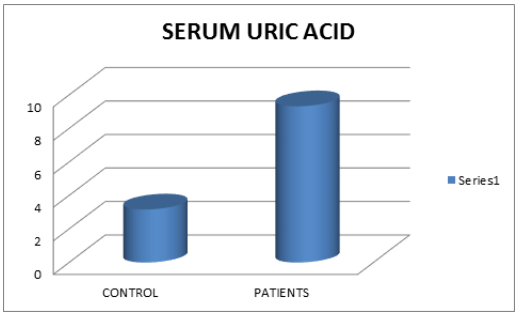

Figure 2 : serum uric acid

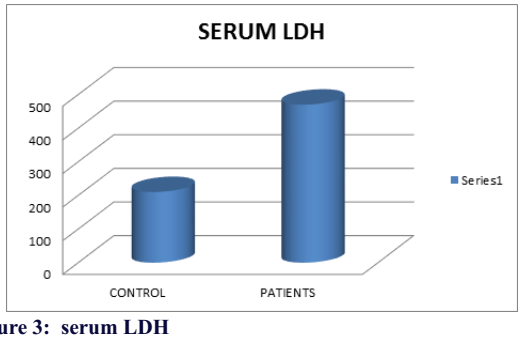

Figure 3: serum LDH

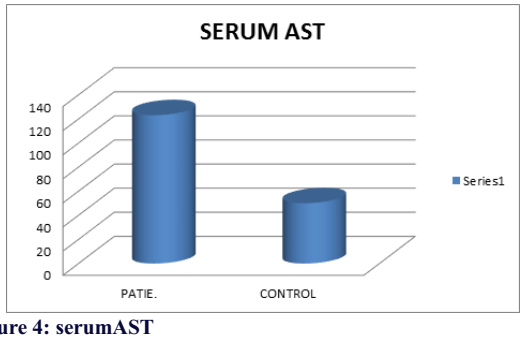

Figure 4: serumAST

Discussion: From the Table it's obvious that there is a statistically significant relation between elevated serum ALT, AST, uric acid, LDH and maternal deaths. There are several potential origins for raised uric acid concentration in preeclampsia, usually it's secondary to altered renal function, increased tissue breakdown, increased oxidative stress and increased activity of xanthine oxidase[8].

In normal pregnancy due to plasma volume expansion Serum uric acid levels are between 2-5mg/dl. Greater then 5.5mg/dl is consistent with preeclampsia and values exceeding 6.0mg/dl suggest more serious disease[9]. Patient with both hyperuricemia and hypertension in the second half of pregnancy is more likely to have preeclampsia even in the absence of proteinuria. Uric acid with > 6mg/dl showed 21.5 fold risk of maternal mortality than in women with < 6mg/dl uric acid levels. Hyperuricemia patients with severe preeclampsia is a strong risk factor for several perinatal complications and increase the risk for intra uterine death by 30.4 times, cesarean section by 6 folds, maternal mortality by 21.5 times, IUGR by 6 folds and eclampsia by 14.3 fold in those with a uric acid level >6mg/dl as compared to a level[8]

Hyperuricemia is a common finding in preeclamptic pregnancies evident from early pregnancy. Despite the fact that elevated uric acid often pre-dates the onset of clinical manifestations of preeclampsia, hyperuricemia is usually considered secondary to altered kidney function. Increased serum uric acid is associated with hypertension, renal disease and adverse cardiovascular events in the non-pregnant population and with adverse fetal outcomes in hypertensive pregnancies. [9]

Elevated level of serum LDH and AST indicates tissue damage related to endothelial vascular damage and is the main cause of the occurrence of preeclampsia HS Qublan showed 92% patients had multi-organ dysfunction in severe preeclampsia women having LDH>800 IU/l. Severely preeclamptic women with LDH >800 IU/l showed significant increase in terms of eclampsia, abruptio placenta, intracranial hemorrhage, HELLP syndrome, acute renal failure, disseminated intravascular coagulation, and pulmonary edema compared with women who had lower levels .[10] Uric acid concentrations are influenced by diet (i.e. high protein, and fructose), alcohol consumption, increased cell turnover, enzymatic defects in purine metabolism or altered kidney function . Estrogen is uricosuric and uric acid concentrations are higher in men and post-menopausal women . In pregnancy uric acid concentrations initially fall 25-35% due to the effects of estrogen, expanded blood volume and increased glomerular filtration rate . However, concentrations slowly rise to those observed in non-pregnant women by term gestation (4-6 mg/dL) [1].

Higher levels of serum LDH and AST are very useful markers to identify the occurrence of the complications of preeclampsia in early pregnancy which may reduce the risk of occurrence of disease [10,11.12,13]. Qublan et al found in their study that the mean LDH levels in normal controls was 299 ± 79 IU/l, in patients with mild preeclampsia was 348 ± 76 IU/l and in patients with severe preeclampsia was 774 ± 69.61 IU/l. Thus they demonstrated a significant association of serum LDH levels with severe preeclampsia ($P < 0.001$). Higher serum LDH levels were associated with increased incidence of maternal complications like abruption placenta, renal failure HELLP syndrome, cerebrovascular accidents etc. in the present study. There was a significant increase in maternal morbidity with increasing serum LDH levels ($P < 0.001$). [7]

Elevated serum level of AST in preeclampsia is explained by the effect of hypoxia on the liver in preeclamptic pregnancy. Disruption of endothelium leads to a reduction of prostacyclin level and increase of thromboxane level. The ratio PgI2/TxA2 is increased in favor of thromboxane, which causes vasoconstriction of blood vessels of the liver. Due to the effects of hypoxia in the liver will cause necrosis and degeneration of hepatocytes and thus would increase AST levels. In preeclampsia there is releasing of different mediators from liver and blood vessel endothelium (fibronectin, thrombomodulin, endothelin-l, thromboxane), which causes vasoconstriction and liver hypoxia. Hypoxia increases the level of ALT, respectively.[13]

Evidence related to the effects of routine postnatal antihypertensive drug therapy compared with no treatment for the prevention of postpartum hypertension in women with antenatal pre-eclampsia and for improving outcomes in women with mild to moderate hypertension was obtained from a Cochrane review of eight RCTs [14.]

Hypertensive disorders of pregnancy are an important cause of severe morbidity, long term disability and death among both mothers and their babies. In Africa and Asia, nearly one tenth of all maternal deaths are associated with hypertensive disorders of pregnancy, whereas one quarter of maternal deaths in Latin America have been associated with those complications. Among the hypertensive disorders that complicate pregnancy, pre-eclampsia and eclampsia stand out as major causes of maternal and perinatal mortality and morbidity.

The majority of deaths due to pre-eclampsia and eclampsia are avoidable through the provision of timely and effective care to the women presenting with these complications. Optimizing health care to prevent and treat women with hypertensive disorders is a necessary step towards achieving the Millennium Development Goals[15.]

Conclusion : Preeclampsia is a multisystem disorder, characterized by vascular endothelial dysfunction. We found a statistically significant difference between serum uric acid, LDH, AST, ALT, and APTT with maternal death in PIH cases. So higher levels of these parameters can be very useful markers to identify the occurrence of the complications of preeclampsia in early pregnancy and help in the management of the women with preeclampsia

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