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EVALUATION OF SERUM URIC ACID AND LIPID PROFILE IN GESTATIONAL HYPERTENSION.

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ABSTRACT

Gestational hypertension (GH) is one of the causes for increased maternal morbidity and mortality and leads to 15% of preterm births. Dyslipidaemia and hyperuricemia are suggested to have pathophysiological role. 100 women with GH and 100 normotensive pregnant women were included in the study. Serum Glucose, lipid profile and uric acid were estimated by standard enzymatic methods. In our study the total cholesterol, triglycerides, LDL-C, VLDL-C and uric acid were significantly elevated and HDL-C was significantly decreased in GH group compared to control ($p< 0.0001$). Uric acid showed significant positive correlation with systolic blood pressure, TGL, and TGL/HDL ($r = 0.287$, $p < 0.01$; $r = 0.551$, $p < 0.001$; $r = 0.429$, $p < 0.001$ respectively) and negative correlation with HDL/VLDL ($r = -0.415$, $p < 0.001$).TGL showed significant positive correlation with diastolic blood pressure ($r = 313$, $p = 0.001$); uric acid($r = 0.551$, $p < 0.001$), TGL/HDL ($r = 0.762$, $p < 0.001$) and negative correlation with HDL/VLDL ($r = -0.701$, $p < 0.001$). Lipid profile and serum uric acid measurements in the early 2nd trimester can be suggested as cost-effective markers in the prevention of the complications of GH.

KEYWORDS: **Gestational hypertension, Lipid profile, Dyslipidaemia, Uric acid, Preeclampsia.**

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INTRODUCTION

Hypertensive disorders complicate 5-10% of all pregnancies. The deadly triad of hypertensive disorders, haemorrhage and infection contribute greatly to the maternal morbidity and mortality [1]. In India the incidence of preeclampsia is reported to be 8-10% of the pregnancies [2]. The incidence in primigravidae is about 10% and in multigravidae about 5% [3]. It causes IUGR leading to low birth weights. Low birth weight child is prone to suffer from diabetes, hypertension, and coronary vascular disorders in their later life [4]. Working group of the National High Blood Pressure Education Program (2000) describes four types of hypertensive disorders: 1) Gestational hypertension (formerly Pregnancy Induced Hypertension), 2) Preeclampsia and Eclampsia syndrome, 3) Preeclampsia syndrome superimposed on chronic hypertension and 4) Chronic hypertension [1]. According to the norms of American college of obstetrics and Gynaecologists, the diagnostic criteria for gestational hypertension [Pregnancy Induced Hypertension (PIH)] is 1) Systolic Blood pressure ≥140 mm/Hg 2) Diastolic Blood pressure ≥90 mm/Hg Or 3) increase of ≥30 mm/Hg in Systolic pressure Or 4) increase of ≥15 mm/Hg in Diastolic pressure, in a previously normotensive woman [5].Placental implantation with abnormal trophoblastic invasion of uterine vessels and immunological maladaptive tolerance between maternal, paternal (placental) and fetal tissues are some of the etiological factors for the hypertensive disorders. Placental ischemia is the main factor responsible for the disease process. This may be due to various factors like vasospasm, vascular endothelial cell activation and dysfunction, increased pressor responses, and decreased prostacyclin: Thromboxane A2 ratio [1]. It is suggested that the disease is present till the placenta is present; once it is removed the situation improved [5]. This leads to delivery of premature babies. Endothelial activation and altered platelet counts are the markers of the disease progression before the development of signs and symptoms [5]. Hypoestogenemia, predominance of smaller and denser serum LDL and significant concentration of soluble vascular cell adhesion molecule-1 are important contributors for endothelial dysfunction in gestational hypertension [6].In lipid mediated endothelial dysfunction an essential step is oxidation of low-density lipoprotein [7-9]. The atherogenesis itself may be initiated by hypertriglyceridemia. Hypertriglyceridemia leads to elevated levels of small dense LDL particles which is atherogenic. Marked dyslipidaemia occurs with gestational hypertension. In many ways this dyslipidaemia represents an accentuation of the lipid changes noted in normal pregnancy. Mean plasma triglyceride and Free Fatty Acid (FFA) concentrations increase about 2-fold on average in women with gestational hypertension relative to women with uncomplicated Pregnancy [10] Elevated uric acid is another component of the preeclampsia syndrome that was recognized many years ago. It is one of the most consistent and earliest detectable changes in preeclampsia and has been cited as a better predictor of fetal risk than blood pressure [11].This results from decreased uric acid clearance from diminished glomerular filtration, elevated tubular reabsorption and decreased secretion (Lindheimer and colleagues 2008a) [1]. In the present study we evaluated the lipid profile and serum uric acid in gestational hypertensive women compared to normal pregnant women.

MATERIALS AND METHODS

Blood samples were collected from all participants after a 12-hour fast. The samples were immediately centrifuged and processed. The following parameters were estimated using standard Erba kits. Glucose, Cholesterol, Triglycerides and uric acid were estimated by enzymatic methods in ERBA-Chem semi auto-analyzer. HDL-cholesterol was estimated by phosphotungstate method. LDL cholesterol was calculated by Friedewald's formula and VLDL by TGL/5.

STATISTICAL ANALYSIS

The analyses were performed using SPSS software. The mean serum lipid concentrations and uric acid concentration of the cases and controls were compared using paired t test.

Significance was set at P < 0.0001. Correlations between various lipid fractions, uric acid and fasting blood sugar were made using Pearson's correlation coefficient, considering only the group with gestational hypertension. Significance was set at P < 0.05 and P < 0.01.

RESULTS

Both the groups were comparable with respect to age and gestational age. Table-1 shows the demographic characteristics of control and gestational hypertension groups.

Table-1
Demographic characteristics of control and gestational hypertension groups

Variables	Gestational Hypertension (n=100)	Control (n=100)
Age (yrs)	24.57±3.27	23.9±3.50
Gestational age(weeks of pregnancy)	29.33±3.47	28.58±2.86
Systolic BP (mm/Hg)	141.28±3.69	117.6±7.67
Diastolic BP (mm/Hg)	93.8±5.47	76.8±7.90

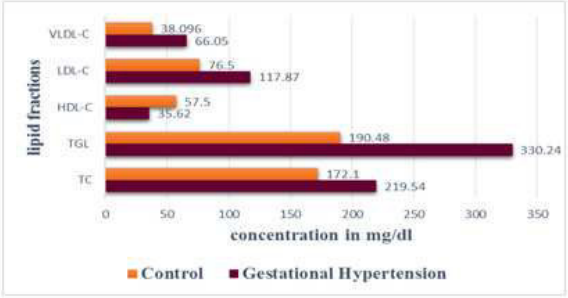
In our study the total cholesterol, triglycerides, LDL-C and VLDL-C were significantly elevated in gestational hypertension group compared to control (p< 0.0001). HDL-C was significantly decreased in gestational hypertension group compared to control (p< 0.0001). All the results were shown in table-2 as mean ± SD and figure-1. Serum uric acid was also significantly elevated in gestational hypertension (p< 0.0001). No significant differences were exhibited between gestational hypertension (GH) group and controls regarding FBS.

Table-2.
Biochemical parameters as mean ± SD

Tests	Gestational Hypertension (n=100)	Control (n=100)	p value
TC (mg/dl)	219.54 ± 32.46	172.10 ±30.16	<0.0001
TGL (mg/dl)	330.24 ± 76.29	190.48 ±37.95	<0.0001
HDL-C (mg/dl)	35.62 ± 7.71	57.50 ±7.90	<0.0001
LDL-C (mg/dl)	117.87 ±34.62	76.50 ±30.22	<0.0001
VLDL-C (mg/dl)	66.05 ±15.46	38.096 ±7.59	<0.0001
UA (mg/dl)	5.008 ±2.03	3.576 ±0.83	<0.0001
FBS (mg/dl)	85.342 ±13.48	88.20 ±13.47	0.1420

[TC-total cholesterol, TGL-triglycerides, HDL-C-high density lipoprotein cholesterol, LDL- C-low density lipoprotein cholesterol, VLDL-C-very low density lipoprotein cholesterol, UA-uric acid, FBS-fasting blood sugar.]

Graph-1
Comparison of lipid parameters between Gestational hypertension (GH) and control groups



Gestational hypertensive patients showed ~70% higher mean serum TG (330.24 versus 190.48 mg/dl, p < 0.0001), and ~ 40% higher mean serum uric acid (5.008 versus 3.576 mg/dl, p < 0.0001). The increase in triglyceride and uric acid levels between gestational hypertensive women and the control group are shown in figures 3 and 4 respectively.

Figure-3
Triglyceride levels in GH and control groups

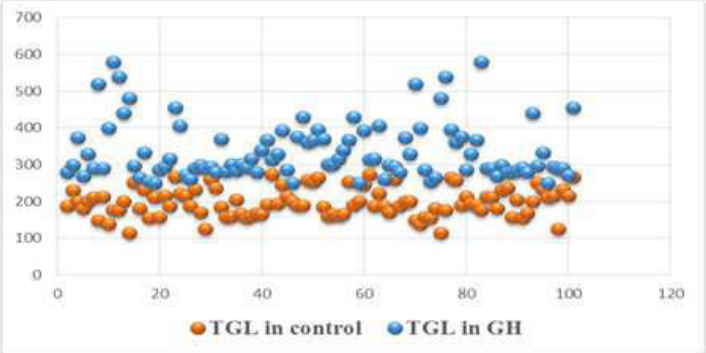


Figure-4
Uric acid levels in GH and control groups

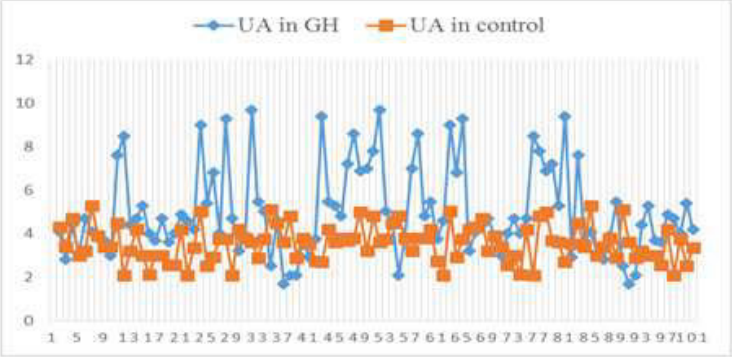


Table-3
Pearson's coefficient of determination (r) of serum uric acid with blood pressure* and *lipid parameters in Gestational hypertensive women.

Lipid parameters	(r)	p value
Total cholesterol	0.145	0.149
Triglycerides	0.551	<0.0001
LDL-C	- 0.090	0.375
VLDL-C	0.551	<0.0001
HDL-C	- 0.090	0.372
Systolic blood pressure	0.287	< 0.01
Diastolic blood pressure	0.235	< 0.05

In gestational hypertension group, all the parameters were correlated using Pearson's correlation (Table-3). That showed significant positive correlation of uric acid with systolic blood pressure, TGL, and TGL/HDL (r = 0.287, p < 0.01; r = 0.551, p < 0.001; r = 0.429, p < 0.001 respectively) and significant negative correlation with HDL/VLDL (r = -0.415, p < 0.001). TGL showed significant positive correlation with diastolic blood pressure (r = 313, p = 0.001); uric acid(r = 0.551, p < 0.001), TGL/HDL (r = 0.762, p < 0.001) and significant negative correlation with HDL/VLDL (r = -0.701, p < 0.001).

DISCUSSION

In our study, all the lipid sub fractions were significantly elevated (p value < 0.0001) and more in the case of triglycerides and VLDL than shown by the normotensive pregnant women. The findings in our study are in consistent with most of the previous studies [12, 13]. The hormonal imbalance is a prime factor for the aetiopathogenesis of gestational hypertension. Gestational hypertension is a state of hypoestrogenemia [6]. Decreased uteroplacental blood flow which is the main pathophysiological event in gestational hypertension leads to impairment in the formation of Dehydroepiandrosterone sulphate (DHEAS) by fetal adrenal glands. DHEAS is the important source of estrogen in pregnancy, (i.e.) 90% of estrogen in maternal circulation is from fetal DHEAS which is converted to estriol in placenta [8]. Hypoestrogenemia also leads to decreased expression of VLDL/apo E receptors resulting in reduced transport of VLDL to fetal compartment and so there is maternal hypertriglyceridemia. Further LDL taken up by the fetus for the synthesis of DHEA is decreased due to reduced fetoplacental perfusion leading to increased LDL. Triglyceride represents an important biomarker of CVD risk because of its association with atherogenic remnant particles and apo CIII [14]. The elevated triglycerides result in increased atherogenic small dense LDL and reduced HDL levels in Gestational hypertension. This may be the result of increased exchange of TGL into LDL and HDL [15].The changes in lipoprotein sub fraction seen in this study were compatible with changes seen in coronary artery disease (Kaaja et al 1995, sattar et al 1997). The dyslipidemia of elevated triglycerides and lowered HDL in our study was similar to that of many other studies [16-18]. In the present study uric acid level was also significantly elevated in gestational hypertensive group which is in consistent with some workers [19]. The currently favored concept is that increased circulating uric acid is secondary to reduced renal urate clearance, as can be seen with hypovolemia. Elevated serum uric acid in hypertensive pregnant patients is associated with poor perinatal outcomes including small for gestational age (SGA) infants and preterm birth (PTB) [20, 21]. Uric acid is the end product of purine catabolism catalyzed by the enzyme xanthine oxidase/dehydrogenase. The oxidase form of the enzyme producing uric acid and superoxide will be increased proportionally with hypoxia. Thus, increased uric acid production occurs in a setting of hypoxia, local acidosis, or increased tissue breakdown or with reduced renal function and can increase oxidative stress—all of which would indicate more severe preeclampsia [11, 22].Uric acid is also found to be associated with carotid atherosclerosis and its increase is an independent risk factor for cardiovascular diseases which mediate altered vascular function and inflammation. Its elevation may be due to imbalance between oxygen free radicals and NO [23]. Because uric acid is also known to have antioxidant activity in the serum, its level may rise as a compensatory mechanism to counteract the increased oxidative stress under the conditions of metabolic syndrome[24] or atherosclerosis [25]. Dyslipidemia is evident during the first and second trimester, far preceding the clinical manifestations of preeclampsia [10]. HDL-C is reduced at earliest measurement (20 weeks gestation) and then throughout gestation in women who later develop the syndrome, again implicating dyslipidemia in the pathophysiology [26]. Hyperuricemia is associated with poor perinatal outcomes and also associated with atherosclerosis. Both dyslipidemia (elevated triglycerides and decreased HDL) and elevated uric acid predict atherosclerosis and also considered to be having pathophysiological role in the clinical manifestations of preeclampsia which was seen in the present study too.

CONCLUSION

Lipid profile and serum uric acid measurements in the early 2nd trimester can be suggested as cost-effective markers that may help in the prevention of the complications of gestational hypertension like, eclampsia, intrauterine growth retardation, HELLP syndrome, future cardio vascular risk of the mother, future

development of Hypertension and stroke. A clinical trial of life style and dietary modification would help in cases of altered lipid metabolism. It has already been suggested in one study that including uric acid in the research diagnosis of preeclampsia identifies a more severe group that is likely to have a more homogeneous pathophysiology than when this marker is not included [11].However our study is limited since the outcomes of the pregnancies are not studied. Similar studies on large study groups with results of the outcome of the pregnancies are needed to establish their usefulness as reliable and cost-effective biomarkers in gestational hypertension.

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