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A Comparative Study of Serum Fasting Lipid Profile, Serum Magnesium and Serum Inorganic Phosphate Concentration in Hypertensive and Normotensive Women in Third Trimester of Pregnancy

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ABSTRACT

INTRODUCTION
Hypertensive disorder during the period of pregnancy is a major cause of maternal death in India and also the rest of the world. The incidence and prevalence of hypertensive disorders in pregnancy is about 7-10%. Hypertensive disorders during pregnancy are one of the main causes of maternal death worldwide. Derangement of serum lipid profile and serum magnesium concentration in pregnant women may lead to develop preeclampsia. Therefore there may be a relationship between hypomagnesaemia and preeclampsia.
AIM
So this study was undertaken to assess serum Fasting Lipid profile level, serum Magnesium and Serum Inorganic Phosphate concentration and also to correlate any difference found in hypertensive and normotensive women in their third trimester of pregnancy.
METHODS
The present study comprised of 100 cases of clinically established Hypertensive Pregnant women and 100 cases of normotensive pregnant women in their third trimester. Serum fasting lipid profile, Serum Magnesium and Phosphate were estimated in Semi-auto analyzer from the study sample. Statistical analysis of the data was performed by using Microsoft Excel software.
RESULTS
The serum fasting lipid profile and Mean Magnesium concentration in hypertensive were found to be significantly altered ($p<0.01$) in hypertensive study participants than in the normotensives participant.
CONCLUSION
Fasting lipid profile and serum Magnesium can very well be used as biochemical markers of the new onset hypertensive pregnant women and also can be used in better management of established cases of eclampsia or preeclampsia patients.

KEYWORDS Pre-eclamsia, Eclamsia, Cholesterol, Triglyceride, HDL, Magnesium, Phosphorus

INTRODUCTION

Hypertensive disorders during pregnancy are one of the main causes of maternal death worldwide. Hypertensive disorders complicating pregnancy are common and form one of the deadly triad, along with haemorrhage and infection that contribute greatly to maternal morbidity and mortality. Hypertensive disorder during the period of pregnancy is a major cause of maternal death in India and also the rest of the world. In India, the estimated maternal mortality is around 254/1, 00,000 of pregnancies during the period of 2004-2006 as published in the special bulletin of MMR in India 2004-2006. Eclampsia is an acute disorder of pregnancy, labour and puerpuerium, characterized by Preeclampsia with convulsion followed by loss of consciousness with or without oedema. The incidence and prevalence of hypertensive disorders in pregnancy is about 7-10%1.

Kaaja et al., (1995) postulated that lipid abnormalities play a role in the pathogenesis of gestational hypertension, causing altered endothelial function and vascular damage2.

Sattar N et al., (1996) postulated Serum Triglyceride, Low Density Lipoprotein Cholesterol (LDL-C) was found to be significantly higher in PIH case than normal controls3.

Magnesium has been shown to be an effective treatment option for the prevention of eclampsia. Its mechanism of action is likely to be both vascular and neurological. Due to antagonist effect to calcium, its effect on vascular smooth muscle to promote relaxation and vasodilation which may lead to lowering of total peripheral vascular resistance. Moreover, Magnesium may have an effect on the cerebral endothelium to limit vasogenic edema by decreasing stress fibre contraction and Para cellular permeability via calcium-dependent second messenger systems. In addition, Magnesium may also act centrally to inhibit NMDA receptors, providing anticonvulsant activity by increasing the seizure threshold4.

There are reduced extracellular calcium and magnesium concentrations in patients with pre-eclampsia and eclampsia. Reduced concentration of magnesium may have a cause and effect relationship with these disorders. These data may therefore be found useful when considering interventional management of preeclampsia and eclampsia using magnesium and calcium supplementation Therefore there may be a relationship between hypomagnesaemia and preeclampsia5.

Taking all the facts into consideration "A comparative study of serum Magnesium concentration and Lipid profile in Hypertensive and Normotensive women in third trimester of pregnancy" was undertaken in the Department of Biochemistry, Assam Medical College & Hospital, Dibrugarh to find out any disorders of lipid and magnesium metabolism that may occur during pregnancy which would be reflected in the blood levels of magnesium and Lipid profile. So this study was undertaken to assess serum Fasting Lipid profile level, serum Magnesium and Serum Inorganic Phosphate concentration and also to correlate any differences found in hypertensive and normotensive women in their third trimester of pregnancy.

MATERIALS AND METHODS

The present study comprised of 100 cases of clinically established Hypertensive Pregnant women in their 3rd trimester of pregnancy and 100 cases of normotensive pregnant women. The clinically established hypertensive 100 cases of pregnant women who were admitted in the antenatal ward in the Department of Obstetrics & Gynaecology, at Assam Medical College & Hospital, Dibrugarh were taken as study case group. The 100 cases of age matched normotensive pregnant women in their 3rd trimester were taken as control group.

Inclusion criteria

Pregnant women in 3rd trimester (> 24 weeks of gestation) suffering from hypertension were taken as 'Hypertensive Study Group'.

The cases for study were composed of already diagnosed cases of hypertension on the basis of following criterion: Blood pressure > 140/90 mm of Hg on at least two occasions 6 or more hours apart after 24 weeks of gestation.

Only those cases were included from whom informed consent could be taken.

Exclusion criteria

Patients with history of hypertension, renal disease, collagen vascular disease, diabetes mellitus, severe anaemia, hydatiform mole, multiple pregnancies were excluded from the study.

The venepuncture was done in the cubital fossa. About 2 ml of blood was transferred to sterile empty vials and samples were centrifuged at 5,000 rpm for 10 minutes as soon as after formation of the clot. The supernatant clear serum was then pipetted out using dry piston pipettes with disposable tips. The samples were analysed on the same day. Serum Fasting Lipid profile level, serum Magnesium and Serum Inorganic Phosphate concentration were estimated in Semi-auto analyzer from the study sample.

Serum Triglyceride estimation (GPO/PAP method)6

Principle: Triglycerdes are hydrolysed by lipase to glycerol and free fatty acids. Glycerol is phosphorylated by ATP in the presence of glycerol kinase to glycerol 3-phosphate, which is oxidized by the enzyme glycerol 3-phosphate oxidase (GPO) producing hydrogen peroxide. Hydrogen peroxide so formed reacts with phenolic compound and 4-aminoantipyrine to give a red coloured quinoneimine complex which is proportional to the amount of Triglyceride present in the sample.

Serum Cholesterol estimation: (CHOD/PAP method)7

Principle: Cholesterol esterase (CHE) hydrolyses cholesterol ester to free cholesterol. Free cholesterol is oxidized to hydrogen peroxide. Hydrogen peroxide formed reacts with 4amino antipyrine and phenol in the presence of Peroxidase (POD) to produce red coloured quinoneimine dye complex. Intensity of the colour formed is directly proportional to the amount of cholesterol present in the sample.

HDL cholesterol estimation (PEG/ CHOD/PAP method)8

Principle: When the serum is reacted with the Polyethylene Glycol contained in the precipitating reagent, all the VLDL and LDL are precipitated. The HDL remains in the supernatant and is then assayed as a sample for cholesterol using the Cholesterol (CHOD/PAP) reagent.

LDL Cholesterol estimation:

LDL Cholesterol is calculated by using Friedwald's formula.

LDL Cholesterol in mg/dl = Total cholesterol/5 - (HDL-Cholesterol)

Estimation of VLDL:

VLDL is the primary triglyceride carrying form in the fasting state; its concentration can be approximated by dividing the amount of plasma triglyceride by 5.

Estimation of Magnesium (Calmagite method)9

Principle: Magnesium combines with calmagite in an alkaline medium to form a red coloured complex. Interference of protein and calcium is eliminated by the addition of chelating agent and detergent. Intensity of the colour formed is proportional to the amount of magnesium present in the sample.

Estimation of Phosphorus (Molybdate U.V method)10

Principle: Phosphate ions in acidic medium react with ammonium molybdate to form a phosphomolybdate complex. This complex has an absorbance in the ultraviolet range and is measured at 340 nm . Intensity of the complex formed is directly proportional to the amount of inorganic phosphorus present in the sample. Phosphorus+ Ammonium Molybdate Phosphomolybdate complex

RESULT AND OBSERVATIONS

The present study is a randomised case control study. Results were analysed by using unpaired student's t-test.

In the 100 hypertensive cases which were studied, the maximum number of 49 cases (49%) belonged to the 21-25 years age group. The next highest number of cases 24 (24%) were from the age group ≤ 20 years. We get the highest number of 73 cases were less than 25 years age. It was also observed that 67 (67%) cases were primigravidas and 33 (33%) cases were multigravidas in the hypertensive study group.

Table 1
Comparison of mean Serum Lipid profile in hypertensive and normotensive study participants

Parameters	Hypertensive (mg/dl)		Normotensive (mg/dl)		p-value
	Mean	S.D	Mean	S.D	
Total Cholesterol	194.3	44.20	137.9	41.0	<0.01
Triglyceride	204.0	49.98	152.7	40.33	<0.01
HDL Cholesterol	44.7	8.00	38.0	7.35	<0.01
LDL Cholesterol	108.0	33.37	69.1	31.82	<0.01
VLDL Cholesterol	41.1	10.02	30.5	8.11	<0.01

The mean serum levels of Total Cholesterol in hypertensive were 194.3 ± 44.20 mg/dl and in normotensive were 137.9 ± 41.0 mg/dl. Student t-test revealed significant differences (p <0.01) in Total Cholesterol values in between hypertensive and normotensive groups.

The mean serum levels of Triglyceride in hypertensive are 204.0 ± 49.98 mg/dl and in normotensive were 152.7 ± 40.33 mg/dl. Student t-test revealed significant differences (p <0.01) in Triglyceride values in between hypertensive and normotensive groups.

The mean serum levels of HDL Cholesterol in hypertensive were 44.7 ± 8.0 mg/dl and in normotensive were 38.0 ± 7.35 mg/dl. T-test revealed significant differences (p <0.01) in HDL Cholesterol values in between hypertensive and normotensive groups.

The mean serum levels of LDL Cholesterol in hypertensive were 108.0 ± 33.37 mg/dl and in normotensive were 69.1 ± 31.82 mg/dl. T-test revealed significant differences (p <0.01) in LDL Cholesterol values in between hypertensive and normotensive groups.

The mean serum levels of VLDL Cholesterol in hypertensive were 41.1 ± 10.02 mg/dl and in normotensive were 30.5 ± 8.11 mg/dl. T-test revealed significant differences (p <0.01) in VLDL Cholesterol values in between hypertensive and normotensive groups.

Table 2
Comparison of Serum Magnesium concentration in hypertensive and normotensive study participants

Parameter	Hypertensive		Normotensive		p-value
	Mean (mg/dl)	S.D	Mean (mg/dl)	S.D	
Mean Magnesium	2.0	0.25	2.3	0.35	<0.0001

Table 2 shows that mean Magnesium level in hypertensive is 2±0.25 meq/l and in normotensive is 2.3±0.35 meq/l. Student t-test revealed very highly significant differences (p <0.0001) in serum magnesium concentration in between hypertensive and normotensive groups.

Table 3
Comparison of Serum Inorganic Phosphate concentration in hypertensive and normotensive study participants

Parameter	Hypertensive		Normotensive		p-value
	Mean (mg/dl)	S.D	Mean (mg/dl)	S.D	
Serum Phosphate	4.0	0.53	3.8	0.97	0.07

Table 3 shows the levels of mean serum Inorganic phosphate in the study participants. The mean serum levels of Inorganic Phosphate in hypertensive are 4±0.53 mg/dl and in normotensive is 3.8±0.97 mg/dl. Student t-test revealed that the difference was not significant.

DISCUSSION

In the 100 hypertensive cases which were studied, the maximum number of 49 cases (49%) belonged to the 21-25 years age group. The next highest number of cases 24 (24%) were from the age group ≤ 20 years. we get the highest number of 73 cases were less than 25 years age . A study done in Saudi Arabia showed that women at extremes of maternal age, the nulliparous women, and high-parity women are at an increased risk of developing pre-eclampsia11. According to another study maximum incidence of developing pre-eclamsia was in the age group of 15-25 years12.

In the present study there were 67 (67%) cases were primigravidas and 33 (33%) cases were multigravidas in the hypertensive study group. Eclampsia is a very common pregnancy associated disorder in our country mostly affecting primigravida of early age group with poor socioeconomic background13. According to another study they found that Pre-eclamsia is mainly affects in first pregnancy14.

The analysis of total cholesterol in the study participants, show that serum total cholesterol was found to be significantly higher (p<0.01) in hypertensive study participants (194.3±44.20 mg/dl) than in the normotensives (137.9±41.0 mg/dl). M. T. M. Anceschi et al., (2005) also found that serum cholesterol levels were higher in normotensive and gradually increased more in preeclampsia15. Total Cholesterol levels did not increase during normal mid trimester pregnancy, but cholesterol levels were significantly higher in cases with severe hypertension16.

Serum Triacylglycerol in our study was found to be (204.0±49.98 mg/dl) in the hypertensive study participants and (152.7±40.33 mg/dl) in the normotensives, which statistically shows a significant difference (p<0.01) . This finding is consistent with study such as Jayanta D.et al.,(2006), (p<0.001). They found higher Triglyceride levels in hypertensive patients than normotensive controls17.

The VLDL Cholesterol was calculated from Triglyceride level and similarly, the VLDL Cholesterol showed a significant difference (p<0.01) between hypertensive cases (41.1±10.02 mg/dl) and normotensive cases (30.5±8.11 mg/dl).

The analysis of HDL cholesterol in the study participants, show that serum HDL Cholesterol was found to be higher (p<0.01) in hypertensive study participants (44.7±8.0 mg/dl) than in the normotensives (38.0±7.35 mg/dl). Milan S. et al., (2009) {(1.48±.24 mmol/l) vs (1.38±.20 mmol/l)}, found similar results18.

The analysis of LDL cholesterol in the study participants, show that serum LDL Cholesterol was found to be significantly higher (p<0.01) in hypertensive study participants (108.0±33.37 mg/dl) than in the normotensives (69.1±31.82 mg/dl). Shalini M. et al., (2011) {(115.56 ± 12.02 mg/dl) vs (135.71 ± 32.20) mg/dl, (P < 0.01)} found that Lipid abnormalities, mostly elevated levels of Triglyceride, Total Cholesterol, LDL, and VLDL were present in pre-eclamptics. High Triglyceride levels and maternal obesity are associated with preeclampsia among pregnant women19.

The analysis of Magnesium in the study participants, show that serum Magnesium concentration was found to be significantly lower (p<0.0001) in hypertensive study participants (2.0±0.25 meq/l) than to the normotensives (2.3±0.35 meq/l) participants. One study established that Serum Magnesium concentration was found to be significantly lower in pre-eclamsia patients (1.9±0.37 mg/dl vs. 2.29±0.69 mg/dl, p<0.01)20. The levels of zinc, copper, selenium, manganese and magnesium are significantly altered in pregnant women with pre-eclampsia. In order to get these important elements dietary supplementation or direct replacement therapy of these trace elements is suggested for women with pre-eclampsia (0.5 ± 0.2 meq/l vs 1.0 ± 0.2 meq/l,p<.0001)21. Hypomagnesaemia can be said to be one of the etiological factors in pre-eclampsia and eclampsia. Serial estimation of serum magnesium during antenatal period, pre-eclampsia can be predicted and eclampsia can be prevented early22.

The analysis of serum phosphate in the study participants, show that serum phosphate concentration was found to have statistically no significance. The mean phosphate concentration in hypertensive study participants (4.0±0.53 mg/dl) was higher than in the normotensives (3.8±0.97 mg/dl). Hypophosphateuria are important features of severe preeclampsia and probably are indirectly related to the altered renal function seen in toxemia of pregnancy23.

CONCLUSION

So it can be stated that the elevation of blood pressure in hypertension of pregnancy was influenced by the lipid profile and thus the lipid profile of a hypertensive pregnant women can with all probabilities be used as a biochemical marker of the disease. Serial estimation of serum Lipid Profile can very well be used as biochemical markers of the disease and also can be used in better management of established cases of eclampsia or preeclampsia. It can also suggest that a low serum Magnesium level might be linked to explaining the pathogenesis of preeclampsia. Therefore, serial estimation of serum Magnesium can very well be used as biochemical markers of the new onset hypertensive pregnant women and also can be used in better management of established cases of eclampsia or preeclampsia patients. The metabolic disorder that occurs during hypertension of pregnancy may be important and may be a predictor of future systemic diseases in these women. Therefore more investigations are warranted into the implications of hypertension in pregnancy.

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