Research Article

Comparison of lipid profile and malondialdehyde with severity of blood pressure in pregnancy-induced hypertension

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Abstract

Background: Abnormal lipid profile and increased lipid peroxidation have a basic role in pathogenesis of pregnancy-induced hypertension (PIH). The association of dyslipidemia and lipid peroxidation product malondialdehyde (MDA) with severity of PIH has emerged as important diagnostic tool in predicting its progression.

Objective: To establish the correlation of serum lipid profile and lipid peroxidation product MDA with severity of PIH considering systolic and diastolic blood pressure (BP).

Materials and Methods: Study subjects included 70 women with diagnosed PIH and divided into two groups taking cutoff point of systolic BP 160 mm Hg and diastolic BP 110 mm Hg, respectively. Level of lipoproteins and MDA in patients with PIH was compared in both groups of systolic and diastolic BP. Statistical analysis was done by applying independent Student's *t*-test, coefficient of correlation *r* was determined, and *p*-value <0.05 was considered to be statistically significant.

Result: A significant higher level of total cholesterol (TC), very-low-density lipoprotein cholesterol (VLDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides (TGs), and MDA was estimated in PIH subjects with systolic BP ≥160 mm Hg. PIH patients had significantly elevated serum TC, VLDL-C, LDL-C, TGs, TC/high-density lipoprotein cholesterol (HDL-C), and LDL-C/HDL-C ratio and MDA with diastolic BP ≥110 mm of Hg. A positive and statistically significant correlation was found between BP (systolic and diastolic) and TC, VLDL-C, LDL-C, TGs, TC/HDL-C, LDL-C/HDL-C, and MDA.

Conclusion: Dyslipidemia and increased lipid peroxidation contributes to the pathogenesis and severity of PIH hence their early detection would aid in better management of PIH. Diastolic BP has come out as better criteria than systolic BP for assessing severity of PIH.

KEY WORDS: Pregnancy-induced hypertension, dyslipidemia, malondialdehyde, diastolic blood pressure, systolic blood pressure

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Introduction

Pregnancy-induced hypertension (PIH) is the most important cause of maternal and neonatal morbidity and mortality complicating approximately 6% of pregnancies globally.[1] Incidence of preeclampsia varies between 2% and 10% of pregnancies worldwide.[2] The World Health Organization estimates seven times higher incidence of preeclampsia in developing countries than in developed countries.[3] Oxidative stress increases

during preeclampsia resulting in increased production of lipid peroxides, reactive oxygen species to cause endothelial injury and dysfunction, and platelet and neutrophil activation causing vasospasm.[4] In spite of numerous researches carried out, no single marker has proved to be an accurate predictive tool for preeclampsia till date. A combination of history, clinical examination along with various urine or blood parameters has been the basis to diagnose and assess the severity of PIH by the clinicians. A great need for development of predictive tools for the severity of PIH is warranted in the present scientific era. The association of serum lipid profile and malondialdehyde (MDA) with severity of PIH has emerged as important predictive and diagnostic tool.

This work was conducted to establish the correlation of serum lipid profile and lipid peroxidation product MDA with severity of PIH considering systolic and diastolic blood pressure (BP).

Materials and Methods

The prospective 1-year (January–December 2012) study was conducted in the department of Biochemistry in collaboration with the Department of Obstetrics & Gynaecology, Rohilkhand Medical College & Hospital, Bareilly, Uttar Pradesh, India, after getting approval from institutional ethical committee. After explaining objectives, informed and understood consent was obtained from all individual participants included in the study. Study subjects included 70 women with diagnosed PIH at gestational age of >20 weeks. The term pregnancy-induced hypertension is defined as the hypertension that develops as the direct result of gravid state. It includes (1) gestational hypertension, (2) preeclampsia, and (3) eclampsia.[5] The severity of PIH in pregnant women is expressed in terms of systolic and diastolic BP. Systolic BP ≥160 mm Hg and diastolic BP ≥110 mm Hg was considered as severe PIH. Study subjects were divided into two groups taking cutoff point of systolic BP 160 mm Hg and diastolic BP 110 mm Hg, respectively. Level of lipoproteins and MDA in PIH patients were compared for systolic BP at cutoff point of 160 mm Hg (n = 40 and 30) and diastolic BP at cutoff point of 110 mm Hg (n = 35 each). The subjects with history of familial hyperlipidemia, use of antihyperlipidemic agents, use of vitamin C/vitamin E or antioxidant supplementation, obesity, gestational diabetes, diabetes mellitus, chronic hypertension, coronary heart disease, impaired renal function, liver disorder, hypothyroidism, smoking, tobacco addiction, and alcoholism were excluded from the study. Four milliliters of venous blood was obtained from each subject aseptically after 10–12 hours of fasting in a serum separator vacutainer. Samples were allowed to clot at 37°C for 30 min followed by centrifugation at 2000 rotations per minute (rpm) for 15 min to get a clear and cell-free serum. Biochemical analyses were performed on ERBA Chem-5 semiautoanalyzer and spectrophotometer.

Biochemical analysis included:

- Total cholesterol (TC) by cholesterol oxidase-peroxidase-aminoantipyrine enzymatic method
- High-density lipoprotein cholesterol (HDL-C) by phosphotungstic acid method
- Very-low-density lipoprotein cholesterol (VLDL-C) and low-density lipoprotein cholesterol (LDL-C) by Friedewald's formula
- Triglycerides (TGs) by glycerophosphate oxidase-peroxidase (GPO-Trinder) method
- MDA by thiobarbituric acid method

The data were processed and appropriate statistical analysis was done by using Microsoft Excel 2010 and Statistical Package for Social Science software version 17 (SPSS Inc., Chicago, IL). All values of analyzed parameters were expressed as mean (standard deviation). Independent Student's t-test was applied to see the statistical significance of the variables between the groups of PIH. Coefficient of correlation r was determined between different biochemical indices and systolic and diastolic BP by using Pearson product moment correlation. A p-value <0.05 was considered to be statistically significant.

Results

A statistically significant higher levels of TC, VLDL-C, LDL-C, and TG were estimated in PIH subjects with systolic BP ≥160 mm Hg when compared with their levels in PIH subjects with systolic BP <160 mm Hg. However, changes observed in HDL-C, TC/HDL-C, and LDL-C/HDL-C ratio, but significant difference could not be established between the groups ($p > 0.05$). We noted a significant increase in serum MDA level in women with PIH having systolic BP ≥160 mm Hg as compared to those with systolic BP <160 mm Hg [Table 1].

Patients with PIH had significantly elevated serum TC, VLDL-C, LDL-C, TG, TC/HDL-C, and LDL-C/HDL-C ratio with diastolic BP ≥110 when compared with levels in PIH women with diastolic BP <110 mm Hg. Difference in mean value of HDL-C was nonsignificant at the cutoff points of diastolic BP. We noted a significant increase in serum MDA level in women with PIH having diastolic BP ≥110 mm Hg as compared to those with diastolic BP <110 mm Hg [Table 2].

Different variables were correlated with systolic and diastolic BP using Pearson product moment correlation. A moderate positive and statistically significant correlation was found between systolic BP and TC, VLDL-C, LDL-C, TG, TC/HDL-C, and LDL-C/HDL-C, whereas a strong positive and statistically significant correlation was observed between systolic BP and MDA. There was no statistical correlation between systolic BP and HDL-C. A moderate positive and statistically significant correlation was found between diastolic BP and TC, VLDL-C, LDL-C, TG, TC/HDL-C, LDL-C/HDL-C, and MDA, whereas a negative statistically significant correlation was observed between diastolic BP and HDL-C [Table 3].

Discussions

PIH may be due to various factors such as vasospasm, vascular endothelial cell activation and dysfunction, increased

Table 1: Comparison of serum lipid profile and MDA with systolic blood pressure in PIH subjects

Lipoproteins and other variables	Systolic BP <160 mm Hg (mean ± SD) *N* = 40	Systolic BP ≥160 mm Hg (mean ± SD) *N* = 30	*p*
TC (mg/dL)	212.24 ± 33.34	244.69 ± 49.73	<0.01*
HDL-C (mg/dL)	40.82 ± 9.02	42.64 ± 9.08	0.41
VLDL-C (mg/dL)	52.83 ± 13.45	61.82 ± 15.10	0.01*
LDL-C (mg/dL)	118.59 ± 35.11	140.26 ± 42.24	0.02*
TAG (mg/dL)	264.09 ± 67.26	309.11 ± 75.51	0.01*
TC/HDL-C ratio	5.36 ± 1.07	6.12 ± 2.39	0.08
LDL-C/HDL-C ratio	3.02 ± 1.00	3.59 ± 1.87	0.11
MDA (mmols/L)	0.96 ± 0.25	1.22 ± 0.18	<0.001*

SD, standard deviation; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; VLDL-C, very-low-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TAG, triacylglycerol; MDA, malondialdehyde; PIH, pregnancy-induced hypertension.

*Statistical significance.

Table 2: Comparison of serum lipid profile and MDA with diastolic blood pressure in PIH subjects

Lipoproteins and other variables	Diastolic BP <110 mm Hg (mean ± SD) *N* = 35	Diastolic BP ≥110 mm Hg (mean ± SD) *N* = 35	*p*
TC (mg/dL)	212.85 ± 30.23	239.44 ± 51.36	0.01*
HDL-C (mg/dL)	43.17 ± 8.66	40.03 ± 9.24	0.15
VLDL-C (mg/dL)	53.14 ± 13.74	60.22 ± 15.11	0.04*
LDL-C (mg/dL)	116.55 ± 34.36	139.20 ± 41.56	0.02*
TAG (mg/dL)	265.67 ± 68.65	301.09 ± 75.60	0.04*
TC/HDL-C ratio	5.06 ± 0.97	6.31 ± 2.18	<0.01*
LDL-C/HDL-C ratio	2.78 ± 0.92	3.74 ± 1.73	<0.01*
MDA (mmol/L)	0.97 ± 0.22	1.17 ± 0.25	<0.01*

SD, standard deviation; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; VLDL-C, very-low-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TAG, triacylglycerol; MDA, malondialdehyde; PIH, pregnancy-induced hypertension.

*Statistical significance.

pressor responses, and decreased prostacyclin: thromboxane A_2 ratio.[6] As the severity of the PIH increases, there is increase in the severity of the pathophysiological phenomenon leading to the accentuation of BP. Several investigators have hypothesized that the relation between a deranged lipid profile, endothelium cell dysfunction, and oxidative stress is of major importance in the development of pathophysiology of PIH.[7,8] Statistically significant higher level of TC, VLDL-C, LDL-C, and TG in PIH subjects with systolic BP ≥160 mm Hg; and significantly elevated values of serum TC, VLDL-C, LDL-C, TC, TC/HDL-C, and LDL-C/HDL-C ratio in PIH women with diastolic BP ≥110 mm Hg in our study was well supported by Mohanty et al.[9] who also observed similar statistically significant rise in various fractions of lipid except HDL-C when compared with the systolic BP at cutoff point of 150 mm Hg and diastolic BP at cutoff point of 100 mm Hg. Irinyenikan et al.[10] also compared serum lipids of the patients with the severity of systolic BP using cutoff point at 150 mm Hg. In their study, all fractions of lipid were elevated similar to our study except the HDL-C, which was noted at lower side in contrast to our findings. But when they compared lipid fractions with the severity of diastolic BP at cutoff point of 110 mm Hg, TC and LDL-C were lower and TG and VLDL-C were higher, whereas HDL-C was almost at similar level. These differences however are not clear but the differences in racial, dietary, and environmental factors may be attributed to it. Iftikhar et al.[11] also compared lipid variables according to the severity of preeclampsia, and in contrast to our observations they found no statistically significant difference between mild and severe group except for TC that was significantly found elevated in severe preeclampsia as compared to the mild group. Islam et al.[12] in their study showed that mean cholesterol

Table 3: The correlation between serum lipids and MDA and systolic and diastolic blood pressure using Pearson's correlation coefficient

Blood pressure	Variables	Coefficient of correlation *r*	*p*-Value of *r*
Systolic BP	TC	0.435	<0.001*
	HDL-C	–0.076	0.53
	VLDL-C	0.319	<0.01*
	LDL-C	0.382	<0.01*
	Triglycerides	0.319	<0.01*
	TC/HDL-C	0.394	<0.01*
	LDL-C/HDL-C	0.371	<0.01*
	MDA	0.567	<0.001*
Diastolic BP	TC	0.440	<0.001*
	HDL-C	–0.239	0.04*
	VLDL-C	0.411	<0.001*
	LDL-C	0.389	<0.01*
	Triglycerides	0.411	<0.001*
	TC/HDL-C	0.475	<0.001*
	LDL-C/HDL-C	0.425	<0.001*
	MDA	0.443	<0.001*

TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; VLDL-C, very-low-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TAG, triacylglycerol; MDA, malondialdehyde.

*Statistical significance.

level was not significantly different between preeclamptic, eclamptic, and normal subjects. But there was significant rise in TG and fall in HDL-C concentration in preeclamptic subjects while eclamptic women showed significant fall in HDL-C and rise in LDL-C as compared to normal pregnant women. They concluded that altered lipid metabolism played a key role in the pathophysiology of preeclampsia and eclampsia. Similar results were reported by Bayhan et al.[13] from Turkey. These findings suggest that there is a significant relationship between lipid levels and systolic as well as diastolic BP in PIH increasing susceptibility to vascular disease associated with TC, VLDL-C, LDL-C, and TG in these patients. Similarly, there is an association between TC/HDL-C and LDL-C/HDL-C with diastolic BP, but our study could not establish association between these ratios and systolic BP. This finding supports the diastolic BP as better criteria for diagnosing PIH. The study suggested that low HDL-C levels and high TG, LDL-C levels with increased lipid peroxidation are the main dangers for atherosclerosis among women with PIH. The altered TC/HDL-C and LDL-C/HDL-C ratios point toward more threats in PIH. The TC/HDL-C ratio is one of the determinants of the predisposition to the risk of atherosclerosis, with an accepted value of <4.5 and <5.0 in males and females, respectively, beyond which they become at risk of atherosclerosis. The TC/HDL ratio has also been shown to be high in PIH and preeclampsia compared to normal pregnancy.[14] In our study we noted the higher ratio of TC/HDL-C in severe PIH subjects when compared with mild PIH subjects but the ratio of TC/HDL-C in both the groups is beyond the accepted value of <5 denoting the risk for atherosclerosis.

A significant positive correlation between MDA and systolic ($r = 0.567$, $p < 0.001$) and diastolic ($r = 0.443$, $p < 0.001$) BP was observed in our study. A significant positive association was also noted by Bayhan et al.[13] between serum level of MDA and systolic BP in women with severe preeclampsia ($r = 0.375$, $p = 0.049$) supporting our findings. In contrast to our findings, Sahu et al.[15] noted a negative correlation of diastolic BP with MDA ($p < 0.05$) in PIH women. This observation might be because of the lower mean diastolic BP of the cases (89.8 ± 10.57 mm Hg) and smaller number of PIH subjects ($n = 30$). Increased levels of oxidative stress markers and decreased levels of antioxidants in preeclamptic women suggested that oxidative stress markers play a significant role in the pathophysiology of PIH.[16] There is a strong significant relationship between MDA and systolic–diastolic BP in PIH, which suggests an increased susceptibility to vascular disease and development and progression of PIH associated with MDA in these patients. The increased MDA level in PIH is known to be due to increased generation of reactive oxygen species and reduction in antioxidants activity. Reactive oxygen species thus produced can cause enhanced lipid peroxidation in PIH.[17] Highly significant reduction in antioxidant activity was observed in the preeclamptic patients in the study by Adiga et al.[18] Excessive lipid peroxidation occurring in PIH can be attributed to hypercholesterolemia, which promotes the formation of free radicals. Increased oxygen

demand to meet the bodily functions in pregnancy is also a contributory factor for the oxidative stress that results in the formation of free radicals. Further, lipid alterations observed may also promote oxidative stress, leading to endothelial dysfunction in preeclampsia.

Our study has been focused on comparison of lipid profile and MDA with severity of BP in PIH and to some extent we have succeeded in correlating BP with the severity of PIH showing altered lipid profile and lipid peroxidation product MDA. However, our study involved small sample size due to limited time period and therefore the result inferred may not be considered as the reflection of larger population. In view of the small sample size in this study, we suggest larger sample size in future study. Various clinical parameters and biomarkers related to PIH need to be taken into consideration so as to have major clinical implications; and to clinch a definite correlation between different parameters.

Conclusion

In this study, most of the lipid fractions were elevated in severe PIH, which suggested its association with deranged lipid level along with lipid peroxidation product MDA. The study inferred that altered serum lipid levels and the significant rise in MDA indicating lipid peroxidation contributes to the pathogenesis of PIH. Diastolic BP has come out as better criteria than systolic BP for assessing severity of PIH, which is evident by its better correlation with deranged serum lipid fractions and MDA. Early detection of dyslipidemia and lipid peroxidation with increasing BP would aid in better management thereby preventing progression of PIH and improving maternal and fetal outcome.

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