Original Research Article

Correlation study between serum uric acid and lipid profile in patients with essential hypertension

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Abstract

Background: Essential hypertension (EHT) is a major health problem in developed countries and affects nearly one billion people worldwide. It is postulated that increased serum uric acid (SUA) level plays a pathogenic role in the evolution of EHT. Hyperuricemia can affect adipocytes by reducing production of adiponectin, which in turn decreases lipid catabolism, thereby contributing to dyslipidemia. The aim of the present study is to assess the SUA level, lipid profile and to determine the correlation of SUA with lipid parameters in patients with EHT. **Methods:** In this hospital-based case control study, a total of 50 newly diagnosed and untreated hypertensive patients of age group 35-65 years irrespective of sex were included as cases and a total of 50 age and sex matched, normotensive subjects were included as controls. Patients with history of Diabetes Mellitus, Renal diseases, Chronic liver disease, Familial hyperlipidemia, Gout, smoking, alcohol consumption, obesity and patients on lipid lowering drugs were excluded. SUA and lipid profile were measured in all study and control subjects by standard method. **Results:** Mean serum uric acid levels were significantly higher in the essential hypertension group (7.83±0.16) compared to control group (4.99±0.31) ($p<0.001$). Total cholesterol, Triglyceride, LDL and VLDL levels were significantly higher while HDL level was significantly lower in EHT group as compared to controls ($p<0.001$). SUA had significant positive correlation with total cholesterol, triglyceride, LDL, VLDL, Apo B and Apo B/A1 ratio while SUA had significant negative correlation with HDL and Apo A1 ($p<0.001$). **Conclusion:** In this study, mean SUA levels were significantly higher in the EHT group as compared to control group. SUA was found to be positively and significantly correlated with total cholesterol, triglyceride, LDL, VLDL, Apo B and Apo B/A1 ratio while SUA had significant negative correlation with HDL and Apo A1.

Key words: Hyperuricemia, Hypertensive, Hyperlipidemia

Introduction

Essential hypertension (EHT) is a major health problem in the developed countries and affects nearly one billion people worldwide[1]. It has a strong association with cardiovascular disease and contributes greatly to morbidity, mortality, and economic burden[2]. It accounts for 90% of all the cases of hypertension. In India, according to ICMR survey, the prevalence varies from 17- 21 %. It occurs commonly in the age group between 30-65 years and may be a consequence of interaction between environmental and genetic factors[3]. The association of hyperuricemia with EHT has been reported by several studies[4, 5]. It is postulated that increased serum uric acid (SUA) level is thought to play a pathogenic role in the evolution of EHT[6]. Altered serum lipid and lipoprotein levels are considered as independent modifiable risk factors for EHT which can be corrected by diet, drugs, and exercise. Patients with untreated dyslipidemia are more prone for hypertension[7]. Increased serum total cholesterol, Triglyceride, LDL and VLDL and decreased HDL were observed in patients with essential hypertension[8]. A significant positive correlation between SUA and total cholesterol, triglyceride, LDL levels and negative correlation between SUA and HDL level were observed in a study[9]. Hyperuricemia can affect adipocytes by reducing production of adiponectin, which in turn decreases lipid catabolism, thereby contributing to dyslipidaemia[10-12]. Hypertriglyceridemia can cause insulin resistance which in turn causes hyperuricemia.

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HDL concentration is significantly lower in patients with hyperuricemia[11]. This may account for the low Apo A1 levels in hyperuricemia. ApoB levels are increased with increase in levels of VLDL and LDL. Genest et al[12] observed that VLDL levels are inversely related to urate excretion and cause hyperuricemia. ApoB/Apo A-1 ratio showed linear correlation with serum uric acid. Hyperuricemia and dyslipidaemia in patients with essential hypertension can aggravate its cardiovascular complications. The aim of the present study is to assess the SUA level, lipid profile and to determine the correlation of SUA with lipid parameters in patients with EHT.

Methods

This hospital-based case control study was conducted in the outpatient unit of the Department of Medicine, Government Medical College, Calicut, India between April 2015 to March 2016.

A total of 50 newly diagnosed and untreated patients of age group of 35-65 years irrespective of sex and BP ≥140/90 mm Hg were included as cases. A total of 50 age and sex matched individuals, with Systolic BP 100-140 mm Hg and Diastolic BP 60-90 mm Hg were included as controls in the study. Patients with history of Diabetes Mellitus, Renal diseases, Chronic liver disease, Familial hyperlipidaemia, Gout, and patients on lipid lowering drugs were excluded from the study. Alcoholics, smokers, and obese patients were also excluded from the study.

After obtaining a written voluntary informed consent from all the subjects, data was collected in a detailed proforma along with requisite physical examination. Then blood sample (6 ml) was drawn after an overnight fast (12 h) by venous puncture and serum was separated by a centrifugation at 3000 rpm for 10 minutes.

Following standard methods were used to measure serum uric acid and lipid profile:

- Serum uric acid - Modified Trinder method (13 11)
- Total cholesterol - CHOD – PAP method (14,15 100, 101)
- HDL cholesterol - Phosphotungstic Acid method (16 102)
- Triglycerides - GPO Trinder method (17,18,19 103, 104, 105)
- LDL cholesterol - Friedewald's formulae
- Apolipoprotein A1 - Immunoturbidimetric assay
- Apolipoprotein B - Immunoturbidimetric assay

Serum creatinine and fasting blood glucose was estimated to exclude renal disorder and diabetes mellitus respectively.

The data was analysed by using standard statistical software statistical package for the social sciences (SPSS) version 16. Significance testing of difference for Mean±SD of two groups was done by student t test or Mann-Whitney U test based on the nature of the data. The correlation between continuous variables was assessed by Pearson coefficient of correlation. Association between qualitative variables was tested by Chi-square test and Odds ratio. A p-value of <0.05 was used to establish statistical significance.

Results

The mean Serum uric acid levels were significantly higher in the essential hypertension group (7.83±0.16) compared to the control group (4.99±0.31) (p<0.001). The demographic characteristics were comparable between cases and controls (Table 1). Total cholesterol, Triglyceride, LDL and VLDL levels were significantly higher in EHT group as compared to the controls (p<0.001) while HDL level was significantly lower in EHT group as compared to the controls (p<0.001) (Table 1). Novel lipoprotein markers were also included in the study. Apo B and Apo B/A1 ratio were significantly higher in the cases (p<0.001).

Table 1: Demographic characteristics and SUA and lipid profile of study population

Variables	Case (N=50)	Control (N=50)	P value
Gender (Male/Female)	25/25	29/21	0.42
Age (years) Mean ± SD	51.6 ± 8.9	51.6 ± 9.7	0.97
Serum Uric acid (mg/dl) Mean ± SD	7.83 ± 0.16	4.99 ± 0.31	<0.001
Total Cholesterol (mg/dl) Mean ± SD	227 ± 8.8	173 ± 5.7	<0.001
Triglyceride (mg/dl) Mean ± SD	204 ± 8.6	125 ± 7.8	<0.001
LDL (mg/dl) Mean ± SD	144 ± 8.7	97 ± 5.2	<0.001
VLDL (mg/dl) Mean ± SD	40 ± 1.7	25 ± 1.9	0.001
HDL (mg/dl) Mean ± SD	41 ± 1.9	52 ± 1.5	<0.001
Apo A1 (g/L)	1.05 ± 0.04	1.68 ± 0.05	<0.001
Apo B (g/L)	1.53 ± 0.59	1.00 ± 0.03	<0.001
Apo B/A1 ratio	1.55 ± 0.10	0.60 ± 0.02	<0.001

SUA was found to be positively and significantly correlated with total cholesterol, triglyceride, LDL, VLDL, Apo B and Apo B/A1 ratio while SUA was negatively and significantly correlated with HDL and Apo A1 (Table 2) (Figure 1 and 2).

Table 2: Correlation between SUA and various lipid profile parameters

	Lipid profile parameters	r value	Correlation	P value
Serum Uric acid	Total cholesterol	0.515	Positive	<0.001
	Triglyceride	0.568	Positive	<0.001
	LDL	0.444	Positive	<0.001
	VLDL	0.579	Positive	<0.001
	HDL	-0.291	Negative	0.003
	Apo B	0.658	Positive	<0.001
	Apo A1	-0.607	Negative	<0.001
	Apo B/A1 ratio	0.678	Positive	<0.001

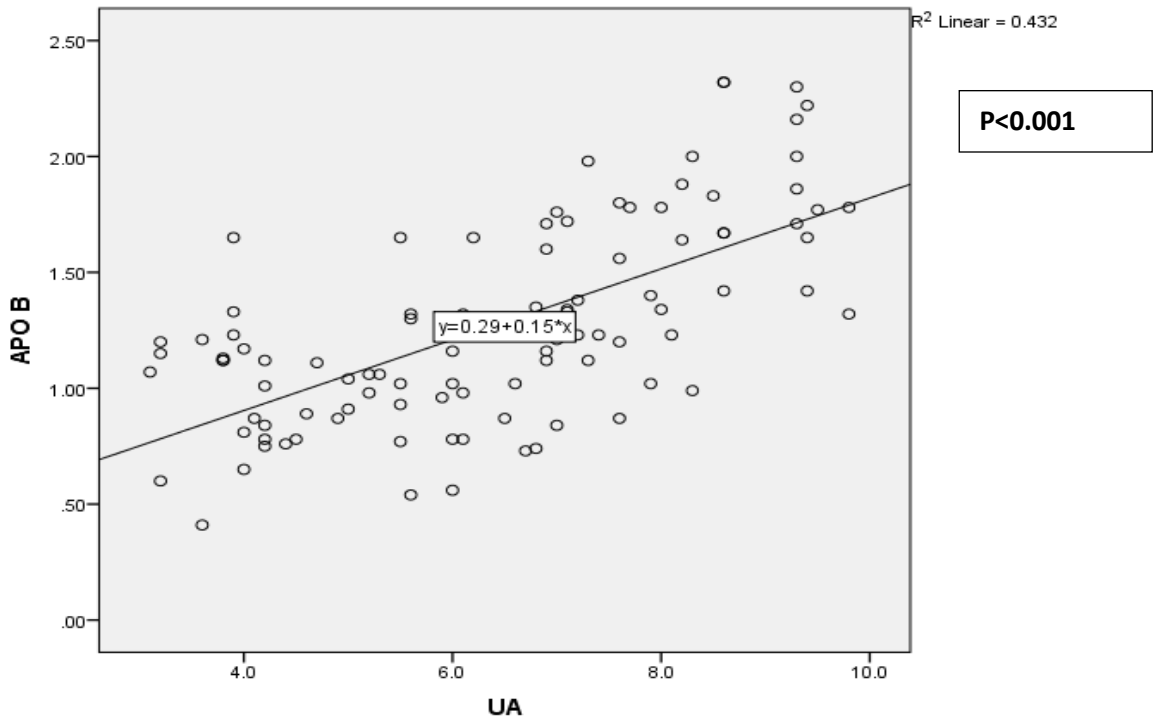

Figure 1: Scatter plot showing correlation between Apo B and SUA

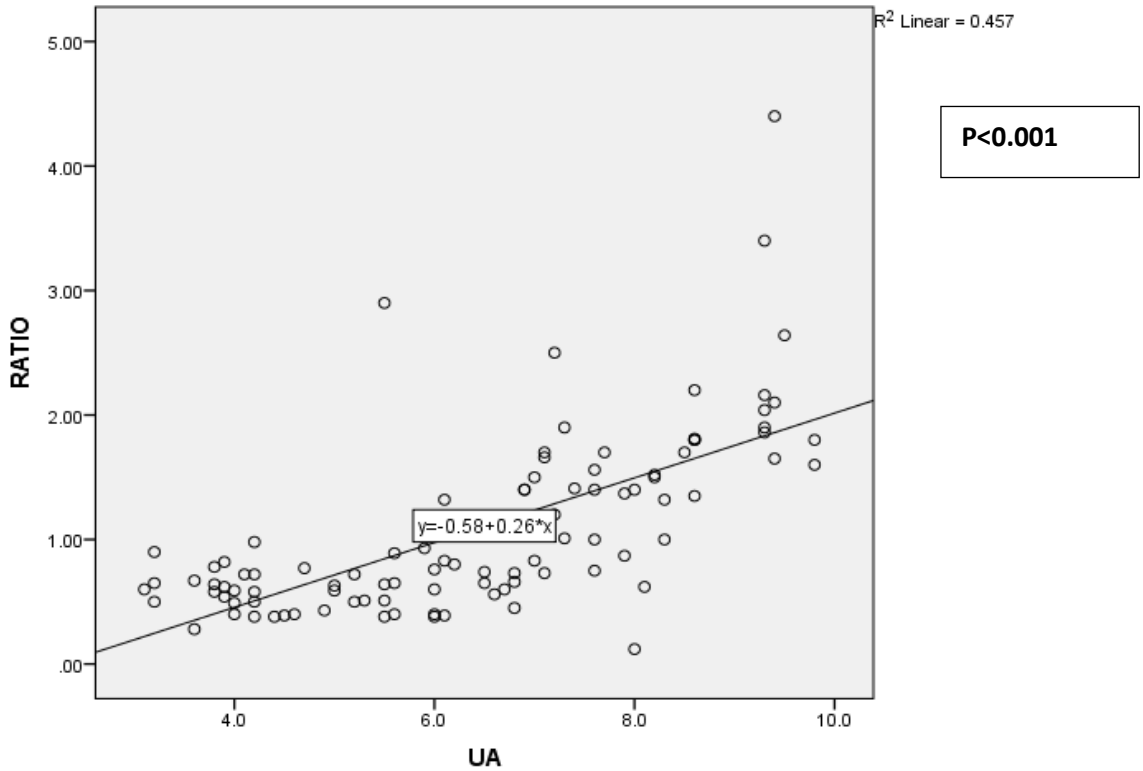

Figure 2: Scatter plot showing correlation between Apo B/A1 ratio and SUA

Discussion

In our study, the mean serum uric acid values were 7.83±0.163 mg/dL in patients with essential hypertension and 4.99±0.179 mg/dL in the control group. The serum uric acid values were significantly elevated in patients with essential hypertension. Similar results were also obtained by Jules Stefan et al[20], Zhang et al[21] and Eshwar et al[22]. Increase in serum uric acid is an important risk factor for the development of essential hypertension[23]. Elevated serum uric acid

in childhood is associated with increased blood pressure in childhood and in adulthood[24, 25]. This suggests that elevated serum uric acid levels may have a role in the early onset of essential hypertension. Elevated serum uric acid levels have been associated with an increased risk for the development of cardiovascular disease[26].

In our study, the mean values of total cholesterol, triglyceride, LDL and VLDL (mg/dL) were significantly higher (p value < 0.001) as compared to the control group. These results were consistent with studies by Venkatesan et al[27], Haperin et al[28] and Davidson et al[29]. The mean HDL values in cases were found to be significantly reduced as compared to the controls. Similar results were obtained by Hersberger et al[30] and Saha et al[31].

In the present study, a significantly decreased value of serum Apo A1 was noted in the hypertensive patients when compared to the controls. The mean Apo B/ Apo A1 ratio in cases were 1.55±0.74 and in the control group were 0.607±0.16. The ratio was found to be significantly higher in cases as compared to the control group. Catalano et al[32], Sherrett et al[33] and McQueen et al[34] reported similar results in their studies. Recent studies suggests that concentration of Apo A1 and Apo B and Apo B/Apo A1 ratio are more sensitive and specific biochemical markers than the conventional lipid and lipoprotein measurements for the risk of development of essential hypertension and cardiovascular disease[35, 36]. Luc et al[37] showed that the severity of atherosclerosis correlated significantly with the serum Apo B level. Meisinger et al reported that Apo B level and Apo B/A1 ratio correlated independently with peripheral atherosclerosis and myocardial infarction[38]. Apo A1 is a major protein component of HDL and associated with fat efflux including cholesterol from tissue to liver for excretion. It activates plasma Lecithin Cholesterol Acyl Transferase which is responsible for the formation of most cholesterol esters. ApoB is the main functional protein for transporting cholesterol to the peripheral cells and responsible for cellular recognition. It is a component of LDL and VLDL. One ApoB molecule is present in each of these lipoprotein particles[39]. Therefore, the ApoB value indicates the total amount of potentially atherogenic lipoproteins[40]. So, ApoB can be regarded as an independent risk marker for essential hypertension and its complications.

SUA was found to be positively and significantly correlated with total cholesterol, triglyceride, LDL, VLDL, Apo B and Apo B/A1 ratio while SUA was negatively and significantly correlated with HDL and Apo A1. These findings were supported by previous studies which showed similar results[40, 41]. Hyperuricemia can affect adipocytes by increasing monocyte chemoattractant protein 1, an adipokine playing an essential role in inducing the proinflammatory state in adipocytes by inhibiting NADPH oxidase and by stimulating peroxisome-proliferator–activated receptor, which in turn reduces the production of adiponectin[42]. This leads to decreases lipid catabolism and contributes to dyslipidemia and inflammation[43]. Recent investigation suggests a positive correlation between hyperuricemia and triglyceride[44]. Dyslipidemia, mainly hypertriglyceridemia, causes insulin resistance, which in turn induces hyperuricemia[45, 46]. This might be since serum uric acid production is linked to glycolysis and glycolysis is controlled by insulin[47]. This association has a close relationship to coronary artery disease. These findings increase the evidence about the relationship among serum uric acid, dyslipidemia, and CAD risk.

Cardiovascular diseases are more likely to occur in patients with essential hypertension when it is associated with dyslipidemia and hyperuricemia[48]. Detection of this correlation at an early stage will prevent complications of essential hypertension. Diuretics use in essential hypertension with hyperuricemia should be limited. It may be a good practice to screen serum uric acid levels and dyslipidemia, especially Apo B/Apo A1 ratio. So, in these patients, lifestyle modification, treatment with hypouricemic drugs and antilipidemic agents along with anti-hypertensive agents will help to reduce cardiovascular complications. In future, serum uric acid level can also be used as a cost-effective screening tool for essential hypertension.

Study design and small sample size are few of the limitations of the study.

Conclusion

In the present study, the mean SUA levels were significantly higher in the EHT group as compared to the control group. Total cholesterol, Triglyceride, LDL and VLDL levels, Apo B and Apo B/A1 ratio were significantly higher in EHT group as compared to the controls while HDL and Apo A1 levels were significantly lower in EHT group as compared to the controls. SUA was found to be positively and significantly correlated with total cholesterol, triglyceride, LDL, VLDL, Apo B and Apo B/A1 ratio while SUA was negatively and significantly correlated with HDL and Apo A1.

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