

# Study of serum uric acid activity in dyslipidemia

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## Abstract

With increasing prevalence of obesity, hypertension, diabetes mellitus, dyslipidemia in the general population due to lifestyle changes, the risk for heart disease, renal disease and cerebrovascular accidents is on the rise. While the topicality of serum uric acid being a risk factor is currently controversial, there is little controversy regarding its association with cardiovascular and renal disease, especially in patients with hypertension, diabetes mellitus and dyslipidemia. The risk for heart failure increases by 21% in patients with hyperuricemia, by 47% in patients with dyslipidemia, and by almost 78% in patients with both hyperuricemia and dyslipidemia. **Aim:** The aim of this study is to evaluate the association between dyslipidemia and hyperuricemia. **Methodology:** The study was conducted as a case control study. The patients attending the OPD of Medicine department of Santosh Medical College and Hospital, Ghaziabad, Uttar Pradesh are included in this study, during a period of July 2014 to June 2015. A written informed consent was taken from the patients inducted into the study. A copy of patient information sheet was also given to the patient, and ethical clearance was taken. **Result:** In the present study, we found 50% of males and 50% of females in cases, and 46% males and 54% females in controls. Hyperuricemia, which is defined as serum uric acid levels of >7 mg/dl in males and >6 mg/dl in females is frequently associated with dyslipidemia. However no consensus has been reached if hyperuricemia in dyslipidemia is a secondary phenomenon or whether hyperuricemia predicts the development of dyslipidemia. **Summary:** The prevalence of obesity, hypertension, diabetes mellitus, dyslipidemia and hyperuricemia has been increasing over the last few decades due to rising living standards with modernisation and urbanisation. Dyslipidemia and hyperuricemia are both individual risk factors for cardiovascular and cerebrovascular diseases. The risk for these increases many fold when both these factors are present in a patient. **Conclusion:** Our study has shown that uric acid elevation is an important component of dyslipidemia. Measuring uric acid is a useful test for a clinician, as it carries important prognostic information. An elevation of uric acid is associated with an increased risk for cardiovascular disease and mortality.

**Keywords:** Hyperuricemia, dyslipidemia.

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## INTRODUCTION

Hyperuricemia or elevated levels of serum uric acid is a biochemical entity that is gaining increasing importance as it has been found by some researchers to be not only a cardiovascular risk factor but also play a role in development of renal and metabolic disease.<sup>1</sup> Hyperuricemia is defined as a S. UA concentration in excess of solubility ie 420 mol/L in men and 360 mol/L in

women.<sup>2</sup> Hyperuricemia is also defined as UA levels > 6 mg/dl or it variates from males (2.5-5.6 mg/dl) and females (3.1-7 mg/dl).<sup>3</sup> Hyperuricemia can be a consequence of increased UA production / decreased UA excretion. The mechanism by which UA causes metabolic disease may involve a reduction in concentration of endothelial nitric oxide.<sup>4</sup> The prevalence of obesity, hypertension, diabetes mellitus, dyslipidemia and hyperuricemia has been increasing over the last few decades due to rising living standards with modernisation and urbanisation.<sup>5</sup> Several previous studies have documented the relationship between serum uric acid levels and CVD.<sup>6</sup> Dyslipidemia is defined as a disorder of lipoprotein metabolism, including lipoprotein overproduction or deficiency. Dyslipidemias may be manifested by elevation of the total cholesterol, low density lipoprotein, very low density lipoprotein, triglyceride concentrations and a decrease in high density lipoprotein. With increase in FFA influx to the liver, increased production of VLDL occurs. Under

physiological conditions, insulin inhibits the secretion of VLDL into the systemic circulation. The other major lipoprotein disturbance is a reduction in HDL cholesterol. This decrease is a consequence of changes in HDL composition and metabolism. In the presence of hypertriglyceridemia, a decrease in HDL cholesterol results from decrease in cholesteryl ester content of the lipoprotein core with a variable increase in triglyceride. Composition of LDL is also modified in a similar way. With fasting S. TGL > 2 mmol/L almost all patients have a predominance of small dense LDL. This change in LDL composition is attributable to the relative depletion of unesterified and esterified cholesterol and phospholipids.<sup>7</sup> In addition to the important finding of elevation in lipoprotein (cholesterol > 250 mg/100ml) being associated with an increase in incidence of coronary heart disease, S. UA seems to be a graded marker of risk factor for the development of CHD when patients with normal UA levels are compared with patients in the lower 1/3<sup>rd</sup> of normal physiological range. Uric acid is an end product of purine metabolism and is related to purine bases of the nucleic acids in humans. S.UA level is determined by the balance between purine intake and UA production, and UA elimination by renal and extra renal routes. Approximately 2/3<sup>rd</sup> of total body urate are produced endogenously, remaining 1/3<sup>rd</sup> by dietary purine.<sup>8</sup>

### MATERIAL AND METHODS

The study has been conducted in the department of General medicine, Santosh medical college, Ghaziabad, Uttar Pradesh during a period of July 2014 to June 2015. A written informed consent was taken from the patients inducted into the study. A copy of patient information sheet was also given to the patient, and ethical clearance was taken. Serum cholesterol was estimated by CHOD-POD enzymatic colorimetric method. HDL was measured by enzymatic clearance assay using Phosphotungstate method, LDL was measured by Friedwald's formula, TG was measured by GPO-PAP method, VLDL was measured by WT formula.

#### Study Design

The study was conducted as a case control study. The patients attending the OPD of Medicine department of Santosh Hospital are included in this study.

#### Study Population

The patients included in the study group were adults of either sex having dyslipidemia. Cases were taken as 100 and controls as 50.

#### Study Period

July 2014 to June 2015

#### Inclusion Criteria

A total of 100 subjects of old and newly diagnosed dyslipidemic patients on the basis of American

Association of Clinical Endocrinologists (AACE) guidelines for the diagnosis of dyslipidemia were selected.

#### Exclusion Criteria

Subjects of the study should not be having any

- 1) Those with history of acute myocardial infarction or cerebral vascular accidents
- 2) History of gout, psoriasis, malignancy and renal stone
- 3) Thyroid disorder
- 4) Renal failure
- 5) Hepatic disorder
- 6) Oncological disease
- 7) Subjects not taking drugs for hypoglycaemia, antioxidants, vitamin supplements or drugs that has known effect on uric metabolism.

### OBSERVATION AND RESULT

Table 1: Clinical parameters studied

S.no	Parameter	Controls (n=50)	Cases (n=100)	P value
1.	Age (yrs)	49.15±9.05	54.42±7.43	0.001*
2.	TC (mg/dl)	173.06±28.01	227.39±74.32	<0.001*
3.	TG (mg/dl)	106.00±34.85	188.09±44.76	<0.001*
4.	HDL(mg/dl)	47.04±12.92	55.20±18.69	0.002*
5.	LDL(mg/dl)	86.52±37.07	141.25±48.54	<0.001*
6.	VLDL (mg/dl)	23.92±6.52	43.72±23.48	<0.001*
7.	Uric acid (mg/dl)	5.67±0.95	6.24±0.95	0.001*

\*Statistically significant (p value <0.05)

Table 2: Age Distribution

Age (yrs)	Control	Percent %	Cases	Percent %
31-40	09	18.0	03	3.0
41-50	23	46.0	27	27.0
51-60	14	28.0	56	56.0
61-70	03	6.0	13	13.0
71-80	01	2.0	01	1.0
<b>Total</b>	<b>50</b>	<b>100.0%</b>	<b>100</b>	<b>100.0%</b>
Mean	49.14±9.05		54.42±7.43	
±SD				

The table shows 56% of cases were in their 5<sup>th</sup> decade of life and 27% of cases were in their 4<sup>th</sup> decade of life and maximum number of controls are present in their 4<sup>th</sup> decade of life (23%).

Table 3: Total Cholesterol (mg/dl)

Total Cholesterol	Control	Percent %	Cases	Percent %
<150	07	14.0	13	13.0
151-200	37	74.0	26	26.0
201-250	06	12.0	31	31.0
251-300	0	0.0	17	17.0
>300	0	0.0	13	13.0
<b>Total</b>	<b>50</b>	<b>100.0</b>	<b>100</b>	<b>100.0</b>
<b>Mean±SD</b>	<b>5.91±0.73</b>		<b>227.39±74.32</b>	

The table shows 31 (31%) patients have TC between 201-250 mg/dl, 17 (17%) have TC between 251-300 mg/dl, 13

(13%) are above 300 mg/dl, 26 (26%) between 151-200 mg/dl and 13 (13%) <150 mg/dl in cases, whereas in controls 37 (14%) patients are below 150 mg/dl, 37 (74%) between 151-200 mg/dl and 06 (12%) lie between 201-250 mg/dl.

**Table 4: Total Triglycerides (mg/dl)**

Total Triglyceride	Control	Percent %	Cases	Percent %
<150	47	94.0	12	12.0
151-200	03	6.0	63	63.0
201-250	0	0.0	12	12.0
251-300	0	0.0	09	9.0
>300	0	0.0	04	4.0
<b>Total</b>	<b>50</b>	<b>100.0</b>	<b>100</b>	<b>100.0</b>
<b>Mean±SD</b>	<b>106.0±34.85</b>		<b>188.09±44.76</b>	

The table shows in cases 63 (63%) patients have TG between 151-200 mg/dl, 12 (12%) have between 201-250 mg/dl, 09 (9%) lie between 251-300 mg/dl, 04 (4%) patients have TG above 300 mg/dl and 12 (12%) have TG below 150 mg/dl, whereas in controls 47 (94%) patients have TG below 150 mg/dl, 03 (6%) lie between 151-200 mg/dl.

**Table 5: High Density Lipoprotein (HDL)(mg/dl)**

HDL	Controls	Percent %	Cases	Percent %
<30	06	12.0	05	5.0
31-40	06	12.0	22	22.0
41-50	23	46.0	23	23.0
51-60	13	26.0	15	15.0
>61	02	4.0	35	35.0
<b>Total</b>	<b>50</b>	<b>100.0</b>	<b>100</b>	<b>100.0</b>
<b>Mean ±SD</b>	<b>47.04±12.92</b>		<b>55.20±18.49</b>	

The table shows 35 (35%) of cases have HDL >61 mg/dl, 15 (15%) between 51-60 mg/dl, 23 (23%) between 41-50 mg/dl, 22 (22%) between 31-40 mg/dl and 05 (5%) <30 mg/dl, whereas in controls 23 (46%) patients lie between 41-50 mg/dl, 06 (12%) <30 mg/dl, 06 (12%) lie between 31-40 mg/dl, 13 (26%) patients lie between 51-60 mg/dl and 02 (4%) lie >61mg/dl.

**Table 5: Very low density lipoprotein (vldl) (mg/dl)**

VLDL	Controls	Percent %	Cases	Percentage %
<20	18	36.0	07	7.0
21-40	31	62.0	52	52.0
41-50	01	2.0	11	11.0
>50	0	0.0	30	30.0
<b>Total</b>	<b>50</b>	<b>100.0</b>	<b>100</b>	<b>100.0</b>
<b>Mean±SD</b>	<b>23.92±6.52</b>		<b>43.72±23.48</b>	

The table shows in cases 52 (52%) of cases have VLDL between 21-40 mg/dl, 11 (11%) have VLDL between 41-

50 mg/dl, 30 (30%) >50 mg/dl, 07 (7%) <20 mg/dl, whereas in controls 31 (62%) patients lie between 21-40 mg/dl, 18 (36%) <20 mg/dl, and 01(02%) between 41-50 mg/dl.

**Table 6: Low density lipoprotein (LDL) (mg/dl)**

LDL	Controls	Percent %	Cases	Percent %
<130	49	98.0	42	42.0
131-200	01	2.0	51	51.0
201-250	0	0.0	05	5.0
>251	0	0.0	02	2.0
<b>Total</b>	<b>50</b>	<b>100.0</b>	<b>100</b>	<b>100.0</b>
<b>Mean±SD</b>	<b>86.52±37.07</b>		<b>141.25±48.54</b>	

The table shows 51 (51%) of cases have LDL between 131-200 mg/dl, 05 (5%) between 201-250 mg/dl, 02 (2%) patients have LDL >251 mg/dl, whereas in controls 49 (98%) subjects have LDL <130 mg/dl and 01 (2%) patients lie between 131-200 mg/dl.

**Table 7: Serum uric acid (mg/dl)**

Uric Acid	Control	Percentage %	Cases	Percentage %
<4.0	04	8.0	01	1.0
4.1-5.0	09	18.0	10	10.0
5.1-6.0	15	30.0	31	31.0
6.1-7.0	20	40.0	40	40.0
>7	02	4.0	18	18.0
<b>Total</b>	<b>50</b>	<b>100.0</b>	<b>100</b>	<b>100.0</b>
<b>Mean±SD</b>	<b>5.67±0.95</b>		<b>6.24±0.95</b>	

The table shows in cases 40 (40%) of cases have uric acid between 6.1-7.0 mg/dl, 31 (31%) patients lie between 5.1-6.0 mg/dl, 18 (18%) patients have uric acid above 7.0 (hyperuricemia), 10 (10%) between 4.1-5.0 mg/dl and 01 (1%) below 4.0 mg/dl, whereas in controls 20 (40%) patients lie between 6.1-7.0 mg/dl, 02 (4%) are above 7.0 mg/dl, 15 (30%) are between 5.1-6.0 mg/dl, 09 (18%) lie between 4.1-5.0 mg/dl and 04 (8%) are below 4.0 mg/dl.

**Table 8: Uric acid with triglycerides**

Variables	Cases (100)	Controls (50)	P value *
TG > 150	88	50	
<b>Mean ± SD of Uric acid</b>	<b>6.31±0.93</b>	<b>5.67±0.95</b>	<b>0.0001</b>

\*Independent sample t test

The table shows there were 88 (88%) patients out of 100 cases whose mean uric acid (6.31±0.93) was compared to mean uric acid of controls (5.67±0.95). The association between controls and cases were statistically significant (p value <0.05)

**Table 9: Uric acid with HDL**

Variables	Cases (100)	Controls (50)	P value *
HDL Males<40	37	50	
Females<50			
<b>Mean ±SD of uric acid</b>	<b>6.23±0.94</b>	<b>5.67±0.95</b>	<b>0.0007</b>

\*Independent sample t test

The table shows there were 37 (37%) patients out of 100 whose mean uric acid ( $6.23 \pm 0.94$ ) was compared to mean uric acid of controls ( $5.67 \pm 0.95$ ). The association between controls and cases was statistically significant ( $p$  value  $< 0.05$ ).

## DISCUSSION

The present study was done to determine the association of serum uric acid in dyslipidemia, and to determine the levels of uric acid with components of dyslipidemia. It's a case control study with 100 cases and 50 controls. Patients were evaluated with detailed history and laboratory investigations. Laboratory investigations included complete lipid profile and serum uric acid. In the present study, we found 50% of males and 50% of females in cases, and 46% males and 54% females in controls.<sup>9</sup> Hyperuricemia, which is defined as serum uric acid levels of  $>7$  mg/dl in males and  $>6$  mg/dl in females is frequently associated with dyslipidemia. However no consensus has been reached if hyperuricemia in dyslipidemia is a secondary phenomenon or whether hyperuricemia predicts the development of dyslipidemia. Also it is not known whether elevated levels of uric acid plays a causal role or a protective role as an antioxidant in conditions of oxidative stress. The finding of our study revealed a significant increase in serum uric acid levels in cases ( $6.24 \pm 0.95$ ) as compared to controls ( $5.67 \pm 0.95$ ), ( $P=0.001$ ). Our finding corroborates with a study conducted by Ishazaka N et al<sup>10</sup> There was positive relation between serum uric acid and triglycerides when mean serum uric acid of triglycerides ( $6.31 \pm 0.93$ ) was compared to mean serum uric acid of controls ( $5.67 \pm 0.95$ ), ( $p=0.0001$ ). the results of our study was in concordance with study conducted by Zhen Zhen Cai, Xiao feng Xu et al<sup>2</sup> which showed significant relation of uric acid with serum triglycerides ( $p < 0.05$ ). Clausen JO et al<sup>11</sup> have put forward an explanation for increased levels of triglycerides seen in hyperuricemia. According to them there is a greater demand for NADPH during synthesis of triglycerides. The synthesis of fatty acids is associated with de novo synthesis of purines, therefore increasing the production of uric acid. In the study we also compared HDL levels with serum uric acid. When means serum uric acid of HDL ( $6.23 \pm 0.94$ ) was compared to means serum uric acid of controls ( $5.67 \pm 0.95$ ). There was a positive relation with HDL levels ( $p=0.007$ ). The results were similar to study conducted by Ahoud F Al Meshaweh et al<sup>12</sup>, which showed a similar result ( $p < 0.05$ ). In the above study conducted, out of 100 patients of dyslipidemia, 18 patients had clear evidence of hyperuricemiaie uric acid level was  $>7$  mg/dl. Hyperuricemia is a risk marker for coronary artery disease<sup>14</sup>, these 18 patients are at risk for coronary artery

disease and such patients should be repeatedly, periodically evaluated for coronary artery disease. Similar study conducted by Kim SY, Albert DA et al, showed in their study that hyperuricemic patients (in which uric acid is above desirable range) are at risk of coronary artery disease.<sup>13</sup> Therefore the study has shown a significant relation between serum uric acid and dyslipidemia.

## CONCLUSION

This study concludes that, the incidence of dyslipidemia is increasing at a rapid rate in developing and developed countries. Our study and several other studies have shown that uric acid being the important component of dyslipidemia.

From the clinical standpoint, uric acid and if its levels are elevated, it should alert the clinician to an overall increased risk of cardiovascular disease and especially those patients with an increased risk of cardiovascular events. If uric acid levels are elevated it should therefore be regarded as a red flag and appropriate approach should be attempted to obtain the risk reduction. The bottom line is that measuring uric acid is a useful test for a clinician, as it carries important prognostic information. An elevation of uric acid is associated with an increased risk for cardiovascular disease and mortality.

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