



# A CORRELATIVE STUDY OF URIC ACID WITH LIPID PROFILE

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<sup>1</sup>Devajit Sarmah, <sup>2</sup>Boooloo Sharma. <sup>1,2</sup> Assistant Professor, Department of Biochemistry, R D Gardi Medical College, Ujjain. India

## ABSTRACT

### CORRESPONDENCE:

Dr. Devajit Sarmah,  
Assistant Professor,  
Department of Biochemistry,  
R D Gardi Medical College,  
Ujjain. India  
Email: [dr.devajit@gmail.com](mailto:dr.devajit@gmail.com)  
Contact no. +91 8120926967

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*“The study shows how at risk are hyperuricemic Assamese populations for developing CVD due to dyslipidemia accompanying hyperuricemia, which is mostly unnoticed by hyperuricemic Assamese people.”*

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**Objective:** the study was conducted to verify the association of hyperuricemia with lipid profile in a group of Assamese people so as to take necessary precautions from developing future cardiovascular disease (CVD).

**Methods:** lipid profile (total cholesterol, triglycerides, HDL and LDL) were estimated in sixty hyperuricemic Assamese people who had no previous history of CVD to ascertain the pattern of their association between uric acid and lipid profile if any.

**Results:** The study proves a significant positive correlation ( $p < 0.005$ ) between uric acid and TC, TG and LDL, and a significant negative correlation ( $p < 0.005$ ) between uric acid and HDL.

**Conclusion:** The study thus shows that hyperuricemia is associated with dyslipidemia which may predispose to future CVD. So treating such subject for hyperuricemia and dyslipidemia can very well reduce cardiovascular morbidity.

**Keywords:** Uric acid, Total cholesterol, Triglycerides, HDL, LDL, Cardiovascular disease.

## INTRODUCTION

It was Alfred Baring Garrod who first showed that subjects with gout had high concentrations of uric acid in their blood and demonstrated that their serum could crystallize on a thread previously dipped in acetic acid<sup>1</sup>. Hyperuricemia is a metabolic consequence originating with a wide range of etiology concerned with production and excretion of uric acid and also as a combination of both. By definition, hyperuricemia is the increase in urate concentration  $>420\mu\text{mol/L}$  ( $7.0\text{ mg/dl}$ ) in blood<sup>2</sup>. It was since 1950s when cardiovascular diseases such as stroke or ischemic heart disease was thought to be associated with serum uric acid and has been confirmed by numerous epidemiological studies conducted after that<sup>3-9</sup>. Elevated serum uric acid levels have been linked to hypertension, hyperinsulinemia, reduced physical activity, increased body mass index (BMI), increased alcohol consumption and decreased HDL cholesterol<sup>6, 10-13</sup>. Hyperuricemia is said to be a mediator of proinflammatory endocrine imbalance in the adipose tissue which may be one of the factors for dyslipidemia and the inflammatory process leading to atherogenesis<sup>14</sup>. The association of uric acid with almost all risk factors for CVD has made it very difficult to determine whether uric acid has a causal role in these conditions or whether it is simply a marker for individuals at increased risk.

Although there are several studies showing the association of lipid profile namely serum total cholesterol (TC), triglycerides (TG), high density lipoprotein (HDL) and low density lipoprotein (LDL) and serum uric acid level, there are very few studies showing this association from India and there are no such studies from North east India. As hyperuricemia is often associated with dyslipidemia which in turn is associated with CVD, indentifying hyperuricemic subjects and treating the condition can prevent CVD in such hyperuricemic subjects. With this background the present study was

conducted to estimate the lipid profile in hyperuricemic Assamese population of North east India so as to verify whether hyperuricemia is associated with abnormal lipid profile among Assamese population.

## MATERIALS AND METHODS

The present study was conducted in the Department of Biochemistry, Gauhati Medical College and Hospital in collaboration with the Out Patient Department of Orthopedics and Medicine of Gauhati Medical College and Hospital for a period of one year from December 2008 to December 2009. The clinical material comprises of 60 adult patients of either sex having symptoms of Gout / asymptomatic hyperuricemia and 60 normal healthy controls. Clearance from the ethical committee and written consent from all the participants of the study were obtained.

### Selection of cases

**Patient group:** A group of sixty (60) patients with asymptomatic hyperuricemia / Gout in the age group of 20 - 60 of either sex were selected for the study. The selected patients had no history of any cardiovascular events and were not on lipid lowering drugs. Out of the 60 patients considered for the study 27 were recently diagnosed to be diabetic (less than six month) and are either on oral hypoglycemic or on diet restriction and none were on Insulin. These recently diagnosed diabetics were considered because various studies have shown that uric acid is a predictor of diabetes but diabetes does not lead to hyperuricemia<sup>15, 16-19</sup>. Those who had a history of diabetes for more than six months were excluded from the study. Alcoholics and subjects with renal disorders, hepatic disorders and those on drugs that may affect uric acid levels were excluded from the study.

**Controls:** This group consists of normal healthy individual selected randomly among people from different sectors of the society and

belonging to diverse occupation and socio-economic status. Among the subjects selected, healthy individuals, of either sex and within the age group of 20 and 60 years were included as normal controls.

A proper smoking and alcoholic history were taken from the subjects of the study. Blood pressure (BP) was measured three times consecutively on the right arm with a standard sphygmomanometer, the subject being in a sitting position after at least 30 minutes of rest<sup>20</sup>.

#### Test included

- Fasting blood sugar
- Serum creatinine.
- Blood urea
- Serum uric acid.
- Total cholesterol (TC)
- Triglyceride (TG)
- HDL cholesterol
- LDL cholesterol

#### Procedure

A proper 12 hours fasting sample were used for estimation of serum total cholesterol (TC), triglyceride (TG), High Density Lipoprotein cholesterol (HDL), Low Density Lipoprotein cholesterol (LDL), fasting blood sugar and serum uric acid. For rest of the test non fasting sample were used. All the tests done in the present study were performed using Vitros 350 dry chemistry analyser manufactured by Ortho Clinical Diagnostics of Jhonson & Jhonson, USA. LDL Cholesterol was calculated using Friedewald's formula.

#### Statistical analysis

The statistical analysis was done manually. The results of the study were expressed as mean  $\pm$  standard deviation (SD). The statistical significance of difference between the various groups was determined by using the student's t-

test, and a p value of  $< 0.005$  is considered significant.

## RESULTS AND OBSERVATIONS

The study was conducted with 60 subjects as controls with 41 male and 19 female. While in the Patient group out of 60 hyperuricemic patients 45 were male and 15 were females.

Table 1 and Figure 1 shows the statistical value for serum uric acid in both the Control and the patient group. The mean level of serum uric acid in the control and the patient group are  $4.6 \pm 0.74$  mg/dl and  $8.0 \pm 0.65$  mg/dl respectively ( $p < 0.005$ ). Figure 1 shows the bar-diagram depicting the mean values of the two groups.

Table 1.

Comparison of mean uric acid between patient group and control group

TEST	CONTROL (mean $\pm$ SD)	PATIENT GROUP (mean $\pm$ SD)
Serum Uric acid	$4.6 \pm 0.74$	$8.0 \pm 0.65$

Figure 1

Bar showing comparison of mean Uric acid levels in the controls and hyperuricemic patient group

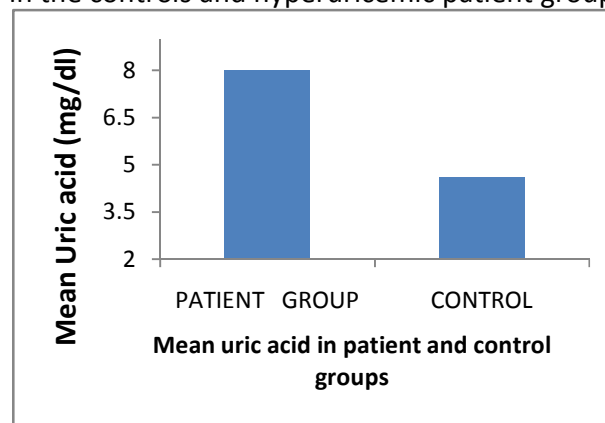


Table 2 shows that there is no significant correlation of serum urea and creatinine among the patient group and the control group which signifies a normal renal profile in both the

control and the patient group. Table 2 represents the mean ± SD for serum creatinine and serum urea among the patients and the control subjects.

Table 2.

Comparison of mean serum creatinine and urea between patient group and control group

Tests	Patient Group (mean ± SD)	Control (mean ± SD)
Serum Creatinine	0.77 ± 0.13	0.75 ± 0.14
Serum Urea	25.87 ± 4.29	24.9 ± 4.27

The study reveals a definite relation between hyperuricemia and dyslipidemia. The study shows a significant correlation ( $p < 0.005$ ) in the levels of TC, TG, HDL and LDL between hyperuricemic patient group and normal healthy control group. Though TC is only slightly raised above the upper normal permitted level according to National Cholesterol Education Programme Adult Treatment Panel III (NCEP ATP III) guideline in the patient group, there is a significant correlation ( $p < 0.005$ ) between the patient and the control groups, the mean ± SD being  $203 \pm 22.8$  and  $140.6 \pm 12$  respectively. Table 3 shows the mean ± SD values for TC, TG, HDL and LDL for both the patient and control group.

Table 3.

Comparison of lipid profile parameters between test and control

TESTS	PATIENT GROUP (mean ± SD)	CONTROL (mean ± SD)
TC	$203 \pm 22.8$	$140.6 \pm 12$
TG	$191 \pm 17$	$116 \pm 10.7$
HDL	$36.6 \pm 3.4$	$42 \pm 2.4$
LDL	$128.1 \pm 24.4$	$75 \pm 12$

Figure II, III, IV and V shows Pearson's correlation plot between uric acid and TC, TG, HDL and LDL levels respectively in patient group.

HDL and LDL levels respectively in patient group.

Figure II

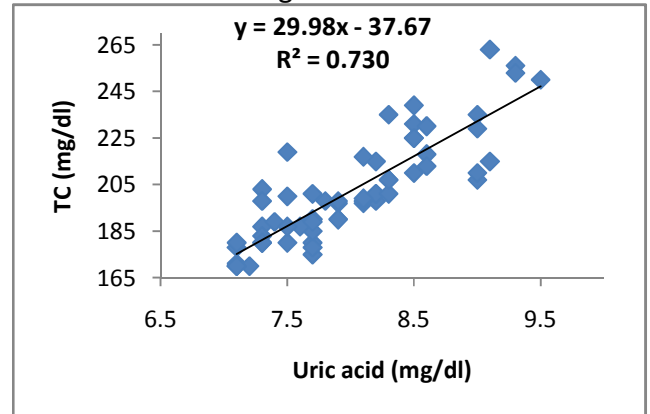


Figure III

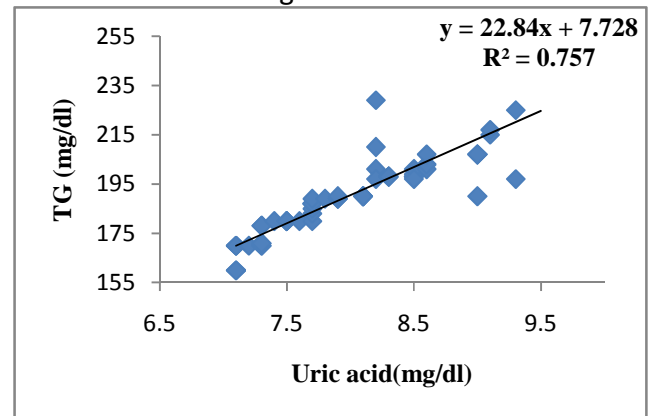


Figure IV

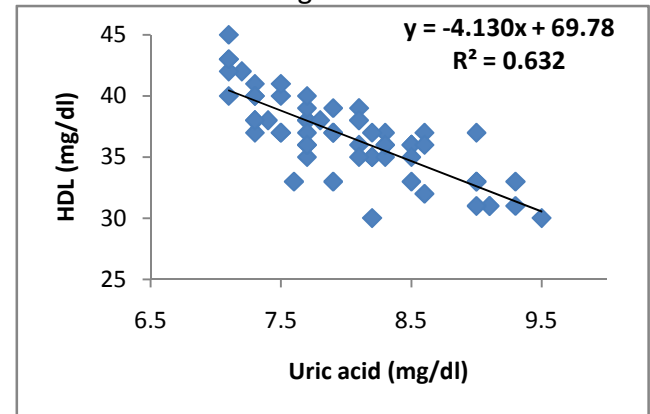
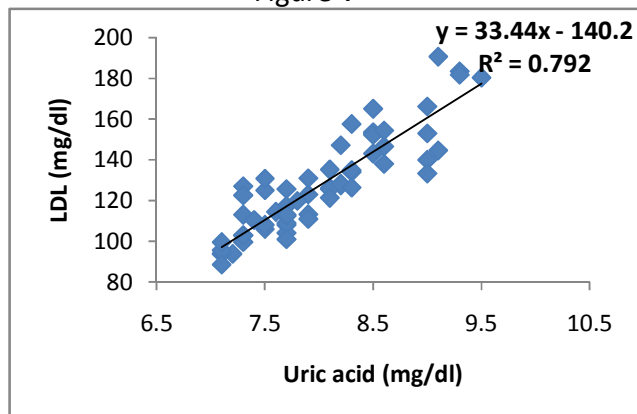


Figure V



## DISCUSSION

The study was conducted to verify whether hyperuricemia without a known cardiovascular disease is associated with dyslipidemia, so that identifying and treating such person can prevent development of CVD. Therefore only hyperuricemic people without a known CVD and who are not diabetic for more than six months were considered for the study. Hyperuricemia is a metabolic consequence originating with a wide range of etiology concerned with increase production or decrease excretion of uric acid and also as a combination of both<sup>1</sup>. The study shows a normal renal profile in the patient and the control group, which signifies that the hyperuricemia under study is not due to decrease excretion of uric acid.

There are enough evidence that hyperuricemia has been linked with cardiovascular diseases<sup>3-9</sup>. Hyperuricemia predispose to the development of hypertension and is also thought to result in increase oxidative stress and generation of free radicals, which eventually can be the nidus of future cardiovascular disease<sup>14, 21</sup>. Animal model study have proved that uric acid causes dramatic increase in the expression and release of MCP-1, infiltration of macrophages and expression of proinflammatory cytokine TNF- $\alpha$  in the vascular

smooth muscles, and thus can eventually lead to atherosclerosis<sup>14</sup>. This is not the only cause of increase risk of CVD in hyperuricemic patients. One of the earliest studies documenting hypertriglyceridemia in hyperuricemic patients is shown by Bendek and later various studies have proved this association<sup>22</sup>. Various studies have shown an inverse relationship between HDL and uric acid. The negative correlation of HDL in hyperuricemia resulted in decrease in good cholesterol (HDL) and consequently and increase in atherosclerosis and eventually predisposes to CVD. LDL cholesterol is always considered to be bad cholesterol and increase in LDL results in atherosclerosis which leads to various cardiovascular events ranging from angina to myocardial infarction<sup>10, 11, 23-25</sup>.

According to the latest ATP III guideline the optimal level of TC, TG, HDL and LDL are < 200 mg/dl, < 150 mg/dl, > 40 mg/dl and < 100 mg/dl respectively<sup>26</sup>. Madhumita et al. has shown from a study conducted on 1485 Assamese subjects that an average healthy urban Assamese population has a TC, TG, HDL and LDL value of 170 mg/dl, 110 mg/dl, 40 mg/dl and 103 mg/dl respectively<sup>27</sup>. Considering the ATP III criteria as well as the values provided by study of Madhumita et al., the hyperuricemic cases in the present study are associated with dyslipidemia. The study proves a significant positive correlation ( $p < 0.005$ ) between hyperuricemia and TC, TG and LDL and a significant negative correlation ( $p < 0.005$ ) between hyperuricemia and HDL. Therefore, it is inferred that hyperuricemia is associated with dyslipidemia in Assamese population as is for other ethnic groups and races proved by various studies, and these hyperuricemic are at a high risk for developing CVD.

Metabolic syndrome is associated with insulin resistance and therefore diabetes and

also dyslipidemia, and in turn hyperinsulinemia is associated with hyperuricemia<sup>11</sup>. Our study includes 27 diabetic in whom status of insulin resistance is not taken into accounts; further BMI is not calculated in any of the study population which we consider as the demerits of the study. Consideration of the BMI and taking an account of the metabolic syndrome criteria in the study population could give a more clear understanding of the association of hyperuricemia and dyslipidemia. Also the study included only 60 prospective hyperuricemic subjects and a study conducted in a large population is expected to give a better association between uric acid and lipid profile.

## CONCLUSION

The present study proves that hyperuricemia is often associated with dyslipidemia, which can lead to a possible cardiovascular event. So prevention of hyperuricemia and associated dyslipidemia can reduce the incidence of CVD in such subjects. A large scale study taking into account the metabolic syndrome, diabetes, BMI, life style etc. are however needed to avail a better understanding of this association.

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