

**CORRELATION BETWEEN SERUM URIC ACID LEVELS AND LDL/HDL RATIO IN TYPE II DIABETES MELLITUS – AN OBSERVATIONAL STUDY****DR.KALAISELVI.V.S^{*1}, DR.GUNANITHI.K², DR.MANJULA DEVI.A.J¹,
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*2*post graduate,department of biochemistry,sree balaji medical college and hospital,Chennai**ABSTRACT**

Serum uric acid level is associated with the individual components of diabetic metabolic syndrome such as obesity, dyslipidemia. Various components of diabetic dyslipidemia including raised LDL cholesterol, low HDL cholesterol and raised triglycerides were independently associated with hyperuricemia in type II diabetes mellitus. Uric acid increase is observed in individuals with insulin resistance, probably because hyperinsulinemia would cause lower renal uric acid excretion¹ Additionally, insulin could indirectly act on uric acid, since there is an association between hyperinsulinemia and hyper triglyceridemia. The association between serum uric acid levels and LDL/HDL cholesterol ratio could pave way for newer therapeutic strategies aimed at serum uric acid levels. This study was done in 60 individuals aged 40-60 years, cases including 30 diabetic individuals, and controls 30 healthy individuals. The study showed that serum uric acid levels were significantly higher in patients with type II diabetes mellitus than in normal healthy controls. LDL/HDL cholesterol ratio was significantly higher in patients with type II diabetes mellitus.

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INTRODUCTION

Diabetes mellitus type 2 is a common condition among the Indian population. The prevalence of type 2 diabetes mellitus is 2.4% in rural population and 11.6% in urban population. Serum uric acid level is associated with the individual components of metabolic syndrome such as obesity, dyslipidemia. Several studies shows that various components of diabetic dyslipidemia including raised LDL cholesterol, low HDL cholesterol and raised triglycerides were independently associated with hyperuricemia in type II diabetes mellitus. There are studies which show a positive correlation between LDL cholesterol and serum uric acid levels. Many studies show negative correlation between HDL cholesterol and serum uric acid levels in which the likely mechanism is the relationship between decreased HDL-C and insulin resistance. LDL cholesterol plays a major role in atherogenesis thereby contributing to its pathogenic role in various complications of type II diabetes mellitus. The association between serum uric acid levels and the ratio of LDL/HDL cholesterol in type II diabetes mellitus would make way for better understanding of the pathogenic role. Hence physicians might not only aim at reducing LDL cholesterol as their primary target in reducing the morbidity but also altering its ratio with HDL cholesterol and also serum uric acid levels in type II diabetes mellitus.

MATERIALS & METHODS

The ground work for the study was started after getting clearance from the research committee and the Institutional human ethical committee of sree balaji medical college and hospital, Chennai. Blood sample (5 ml) , serum separated is obtained from 60 individuals aged 40-60 years, cases including 30 diabetic individuals ,and controls 30 healthy individuals attending medicine / diabetology OPD of our institute Sree Balaji Medical College And Hospital , Chromepet , Chennai , India .

INCLUSION CRITERION

Type 2 diabetes mellitus patients of both sexes (40–60 years of age) and normal healthy controls of both sexes (40 – 60 years of age).

EXCLUSION CRITERION

Patients with chronic kidney disease, liver dysfunction, history of cancer, and patients on treatment with systemic steroids were excluded from the study.

INVESTIGATIONS

1. FBS , PPBS by GOD – POD method , Diatek Kit , Fully Automated Analyser
2. Fasting serum lipid profile Total cholesterol by CHOD-POD method
HDL cholesterol by CHOD-POD method after precipitation
VLDL cholesterol, calculated value [triglycerides / 5]
LDL cholesterol, by friedwald equation [Total cholesterol-(VLDL+HDL)]
Non HDL cholesterol, calculated value [total cholesterol-HDL cholesterol]
3. Serum uric acid by uricase method
4. Serum Creatinine By Jaffes Kinetic Method , Erba Biochem
5. 12 lead ECG

The association of serum uric acid levels with a ratio of LDL/HDL cholesterol was evaluated by using pearsons correlation co efficient. Statistical analysis was performed using SPSS data editor version20 with the help of a statistician. The study was approved by the institutional ethical committee of Sree Balaji Medical College Ansd Hospital . An informed consent was obtained from all the study participants both in English and in vernacular languages.

RESULTS OF THE STUDY

The tests of significance for comparison of serum uric acid levels among type II diabetic patients and controls showed (t value = 6.68) using an Independent sample t test. The level

of significance , p value significant at 0.000 level .The tests of significance for comparison of serum LDL/HDL ratio among cases and controls showed (t value = 5.82) using Independent sample t test. The level of significance , p value significant at 0.000 level . The tests of correlation showed by Pearsons correlation coefficient between serum uric acid levels and ratio of LDL/HDL cholesterol [r value = 0.284] showing positive correlation.

DISCUSSION

URIC ACID & TYPE II DIABETES MELLITUS

Uric acid increase is observed in individuals with insulin resistance, probably because hyperinsulinemia would cause lower renal uric acid excretion¹ Additionally, insulin could indirectly act on uric acid, since there is an association between hyperinsulinemia and hyper triglyceridemia. Some studies show that high concentrations of plasma triglycerides are related to hyperuricemia²⁻⁴. There are some explanations for such relation, and one of them is that during triglycerides (TG) synthesis there would be a greater need for NADPH. The synthesis of fatty acids in the liver is associated with the de novo synthesis of purine, thus accelerating uric acid production⁵ Chen *et al.* (2007) observed a negative correlation between HDL-c and uric acid. The likely mechanism is the relationship between decreased HDL-C and insulin resistance⁶. In the adipose tissue, there is adipokine production, including that of leptin. One possible explanation for the association between higher waist circumference and hyperuricemia were suggested by Bedir *et al.* (2003)⁷ and Fruehwald-Schultes *et al.* (1999)⁸ which studies found that uric acid serum concentrations are independently related to leptin concentration, thus suggesting that would be a pathogenic factor responsible for the uric acid increase in obese patients. Some authors report uric acid to be responsible for blood pressure increase, and others show arterial hypertension to be a risk factor for hyperuricemia. Uric acid inhibits the bioavailability of nitric oxide, which is a

vasodilator⁹ and, on the other hand, hypertension would lead to vascular disease and increase renal vascular resistance. Both of these processes reduce renal flow, thus increasing urate resorption¹⁰

URIC ACID & DYSLIPIDEMIA

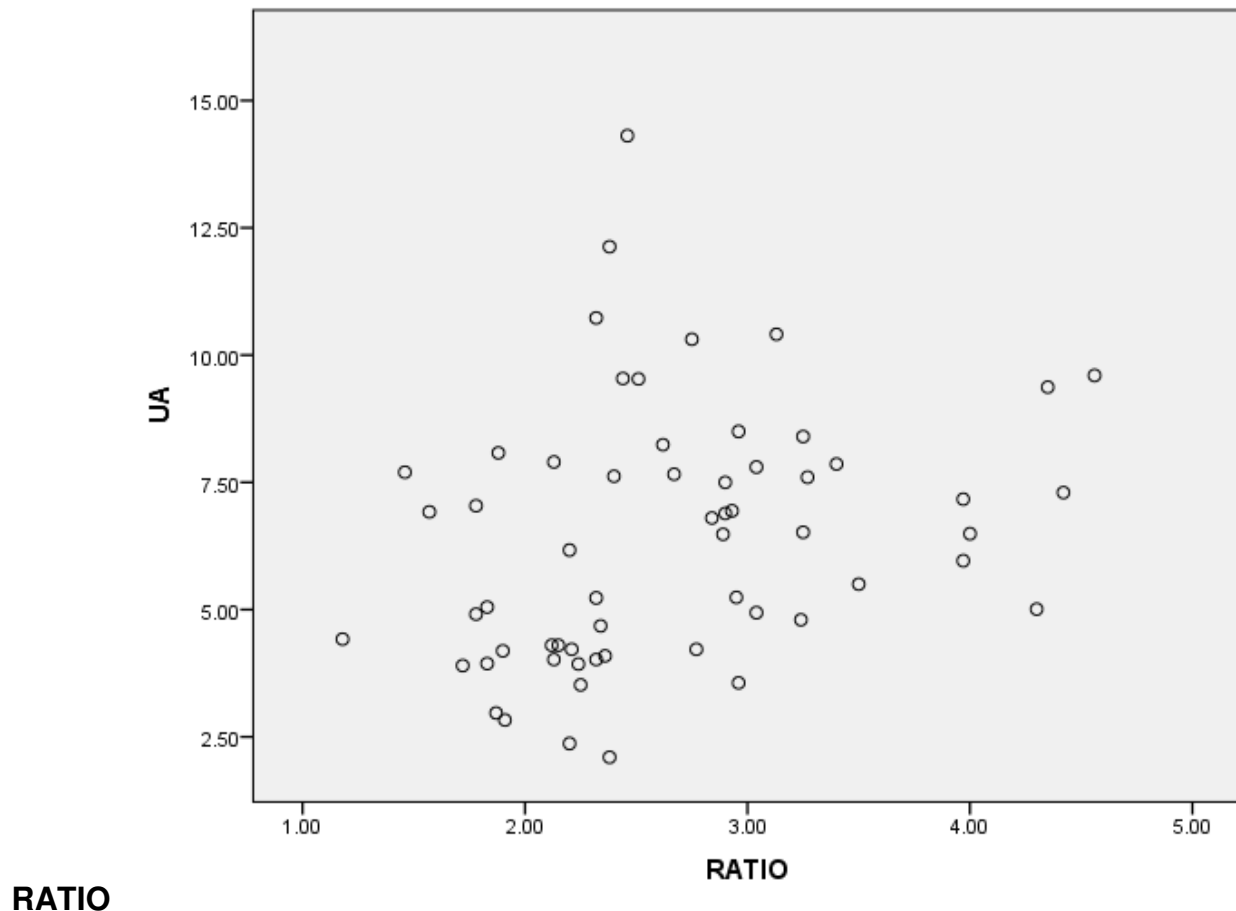
In 1993 Reaven and colleagues suggested that hyperuricemia is commonly part of the cluster of metabolic and hemodynamic abnormalities along with abdominal obesity, glucose intolerance, insulin resistance, dyslipidemia, and hypertension¹¹. Recent studies, however, have suggested a potential contributory role of uric acid to metabolic syndrome. For example, an elevated serum uric acid has been reported to be an independent predictor of obesity and hyperinsulinemia and thus if it precedes the development of hyperinsulinemia, it is difficult to attribute it solely to the effects of elevated insulin levels. Lowering uric acid also ameliorates the elevation in blood pressure, serum triglycerides, and insulin resistance in the fructose-induced metabolic syndrome in rats¹². Additionally, obesity and muscle mass reduction are associated with low-intensity chronic inflammation, and uric acid levels can increase in order to protect the organism against the moderate oxidative stress resulting from this situation. Low muscle mass (sarcopenia) is negatively associated with uric acid, However, what the cause or effect is. Probably, oxidative stress produced by excessive uric acid can influence muscle mass reduction.. The main mechanism of excretion of urate concentrations occurs by means of renal excretion; hence, glomerular function markers (urea and creatinine) are positively associated with uric acid. Zheng fang *et al* shows that elevated waist circumference and high triglyceride were statistically significantly associated with higher uric acid concentration in both men and women. Men with high blood pressure and low HDL-cholesterol had higher uric acid concentrations than those without such conditions.. Phosphoribosylpyrophosphate (PRPP) is an important metabolite in this respect. Its availability depends on ribose-5-phosphate (R-

5-P), the production of which is governed by glycolytic flux.

Diversion of glycolytic intermediates toward R-5-P, PRPP, and uric acid will follow if there is diminished activity of GA3PDH (glyceraldehyde-3-phosphate dehydrogenase), which is regulated by insulin. The importance of hyperuricemia and the clustering phenomenon of the metabolic syndrome were first described by Kylin in 1923 when he described the clustering of three clinical syndromes: hypertension, hyperglycemia, and hyperuricemia. Hyperuricemia might be partially responsible for the proinflammatory endocrine imbalance in the adipose tissue, which is an underlying mechanism of the low-grade inflammation and insulin resistance in subjects with the metabolic syndrome. The

increase in the prevalence of type 2 diabetes is closely linked to the augmentation in obesity¹⁵. The adipose tissue is now accepted to be an endocrine organ that secretes numerous hormones, growth factors, matrix proteins, enzymes, cytokines, and complement factors that exert multiple effects at both the local and the systemic level¹⁵. Elevated blood levels of uric acid, the final product of the purine degradation in humans, is strongly associated with cardiovascular and kidney disease, hypertension, and overall risk of mortality. It is also commonly present in metabolic syndrome. Serum levels of uric acid are positively correlated with individual components of the metabolic syndrome, in particular visceral obesity, and this correlation is stronger when other components are also present¹⁶.

STATISTICS :SCATTER PLOT – CORRELATION BETWEEN SERUM URIC ACID AND LDL/HDL



CONCLUSION

The study showed that serum uric acid levels were significantly higher in patients with type II diabetes mellitus than in normal healthy controls . LDL/HDL cholesterol ratio was significantly higher in patients with type II diabetes mellitus. It could further be concluded that serum uric acid levels were significantly higher and positively correlated with ratio of LDL/HDL cholesterol in patients with type II diabetes mellitus. Thereby, serum uric acid also could be done as a routine in screening of type II diabetic patients with raised LDL/HDL cholesterol ratio and along with other parameters.

CONFLICT OF INTEREST

The authors declare no conflict of interest

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LIMITATIONS

A variety of limitations of this study needs however also to be addressed . The sample size is small which did not allow a multivariate approach for incorporating additional , potentially meaningful factors for modifying the levels of serum uric acid levels and serum LDL/HDL ratio levels. Nevertheless ,it seems reasonable that routine screening for serum uric acid levels among diabetics provide additional information and so might also be included as one of the therapeutic targets apart from other primary targets like reducing LDL cholesterol.

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