

RESEARCH ARTICLE



A study on serum uric acid levels and insulin resistance in type-2 diabetic subjects

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Abstract

Insulin resistance (IR) is the principle etiological factor for development and progression of type-2 diabetes mellitus (T2DM) and decreased insulin function. Independently, increased serum uric acid (SUA) is known to play a critical role in the development of T2DM as well as in progression of its complications. To assess the correlation between SUA levels and IR in diabetic patients, data with lab investigations of HbA1c, fasting levels of serum glucose, UA, TAG, HDL-C of confirmed and known cases of T2DM were collected from the Hospital Biochemistry Laboratory, DMWIMS Hospital, Wayanad, Kerala. Fasting ratio of TAG to HDL-C was used as an index for IR. A significant increase in fasting serum glucose, SUA, HBA1C, TAG, TAG/HDL-C ratio (IR) and a significant decrease in HDL-C were observed in data of cases when compared with the data of normal healthy subjects. This study shows a positive correlation between SUA levels and IR in known cases of T2DM.

Keywords: type2 diabetes mellitus; serum uric acid; insulin resistance

Introduction

Insulin resistance (IR) is the principle etiological factor for development and progression of type-2 diabetes mellitus (T2DM) and decreased insulin function. Independently, increased serum uric acid (SUA) is known to play a critical role in the development of T2DM as well as in progression of its complications⁽¹⁾. How-

ever, hyperuricemia is not always found in diabetic individuals. Conflicting data exist about UA levels in T2DM, as low levels were found in diabetic patients, while elevated SUA is a feature of hyperinsulinemia and impaired glucose tolerance⁽²⁾. The present study was undertaken to assess the correlation between SUA levels and IR in known cases of T2DM.

Materials and Methods

Study Setting & Data Source

A retrospective observational case control study was conducted in DM WIMS Hospital, Wayanad, Kerala, in collaboration with Department of Medical Biochemistry, School of Health Sciences, Palayad, Kannur University, Kerala, during the period from May 2019 to July 2019. Institutional Research Committee approval has been taken for conducting this study. A year data (from Jan 2018-Jan 2019) of confirmed and known cases of T2DM were collected along with the normal subjects' data, from the Hospital Biochemistry Laboratory.

Study Subjects & Groups

The present study included data of total of 107 subjects out of whom 52 were of healthy normal individuals and 55 were of known cases of T2DM and were grouped as Group-1 and Group-2 respectively. The normal subjects had a mean age of 43.13 ± 5.98 years of which 23 were males and 29 were female and diabetic subjects had mean age of 61.06 ± 13.19 years of which 31 were males and 24 were females.

Inclusion criteria: Both male and female patients >35 years of age with known case of T2DM were included in this study.

Exclusion criteria: Patients with Type-1 DM, patients with acute complications of DM, those with a history of acute infections and other ailments like gross congestive heart failure, tuberculosis, gout, rheumatoid arthritis and skeletal muscle injury, those with serum creatinine levels of >1.5 mg/dl, renal failure, diabetic nephropathy, uric acid lowering drugs, were excluded from the study.

Study Parameters

Data of fasting serum levels of glucose (FBS), uric acid (UA), Triacylglycerol (TAG), High density lipoprotein- Cholesterol (HDL-C) and Glycated Hb (HbA1c), of both type-2 diabetic and normal subjects were assessed for the present study. Estimation principles of the studied parameters were as follows: Glucose by hexokinase method^(3,4), HbA1c by HPLC method⁽⁵⁾ TAG by enzymatic colorimetric test⁽⁶⁾, HDL-C by homogenous enzymatic colorimetric assay^(7,8), UA by enzymatic colorimetric test^(9,10). Data of serum TAG and serum HDL-C were used to calculate IR. There are many limitations to establish direct methods for measuring insulin resistance *in vivo*. So, an indirect method is used for calculating IR index. TAG to HDL-C ratio is the indirect method⁽¹¹⁻¹³⁾, that has been reported to be closely related to IR in adults. All the parameters were estimated using Roche

Cobas Integra 400 -Plus fully automated analyzer.

Statistical Evaluation

Data analysis was done using SPSS software version 24 (IBM, Armonk, NY, USA). The data were expressed as their Mean \pm SD and the statistical significance was calculated using Mann Whitney U test. $p < 0.05$ was considered as significant and $p < 0.001$ was considered to be statistically highly significant. Pearson correlation 'r' was used to assess the correlation between serum uric acid levels and insulin resistance

Results

The results of the present study are depicted in Table 1 and Figure 1.

Figure 1: Showing Pearson's correlation co-efficient for the correlation between SUA levels and TG/HDL -C ratio (IR) among Group-2 subjects

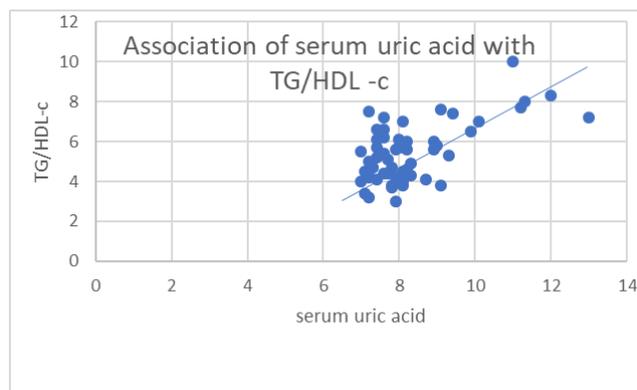


Fig 1. Pearson's correlation co-efficient $r=0.6$ Insulin resistance (IR) was indirectly calculated as TAG/HDL-C ratio

Discussion

The association of hyperuricemia and development of T2DM have been observed by various researchers^(1,14). Many studies have also shown that elevated levels of SUA may lead to progression of chronic complications such as CVD and CKD in diabetic patients⁽¹⁵⁻¹⁷⁾. Hyperuricemia & hypertriglyceridemia are suggested to be associated with insulin resistance syndrome⁽¹⁸⁻²⁰⁾.

The results of the present study show a positive correlation ($r = 0.605$) between SUA & IR (calculated indirectly by measuring the ratio of TAG/HDL-C) [refer Table 1 & Figure 1]. This is consistent with the recent meta-analysis by Xu et al⁽²¹⁾. The mechanism for uric acid-induced insulin resistance appears to be mediated by the development of mitochondrial oxidative stress and impairment of insulin-dependent stimulation of nitric oxide in endothelial cells, mediated by the expression of CRP⁽²²⁾. Pilot studies in

Table 1. Showing fasting levels of serum glucose, SUA, HbA1c, serum TAG, serum HDL-C & IR as ratio of TAG/HDL-C, in both Group-1 & Group-2 subjects

Parameters	FBS mg/dL	HbA1C %	SUA mg/dL	TAG mg/dL	HDL-C mg/dL	IR [TAG/HDL-C ratio]
Group-1 (52)	87.15±6.94	5.01±0.36	4.63±1.14	99.32±22.95	47.18±11.66	2.22±0.66
Group-2 (55)	198.34±65.79	9.50±2.04	8.30±1.30	213.05±47.19	40.07±9.79	5.47±1.47
P value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.002	< 0.001

p value of < 0.05 was considered significant. Insulin resistance was indirectly calculated as TAG/HDL-C ratio. Ratios of >3 in men and >2 in females are considered as abnormal /elevated IR.

Normal ranges of parameters: FBS- 70-100 mg/dL, TAG- M:50-200 mg/dL, F: 40-150, SUA – M:3.5-7 mg/dL, F: 2.5-5 mg/dL, HDL-C- 30-60 mg/dL, HbA1c- <5.7%

Number in parentheses shows the number of subjects.

humans have reported a potential benefit of lowering SUA on IR (23).

Limitations of the study

This study may come short of generalizability and authenticity due to small sample size, not analyzing sufficient dependent and independent variables, and fails to account for any confounders effect.

Conclusion

The present study shows a positive correlation between SUA and IR in type-2 diabetic patients suggesting that SUA may serves as a better risk indicator of IR status. Lowering SUA may prove to be a simple and inexpensive strategy to help prevent the development of diabetes and/or its complications and to slow down the epidemic. Large clinical trials with SUA lowering drugs are recommended.

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