Gender differences in relation to hyperuricemia and nonalcoholic fatty liver disease among Type 2 diabetics in Telangana, India

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ABSTRACT

Background: Scarcity of data in relationship between hyperuricemia and nonalcoholic fatty liver disease (NAFLD) in Type 2 diabetics (T2DM), particularly in terms of gender differences. Hence, the study was aimed to investigate the gender difference in association between hyperuricemia, and NAFLD in the Indian population.

Methodology: A cross-sectional study was conducted with 134 Indian adults, of which 93 males and 41 were females. Among them hyperuricemics are 66 (71%) males and 26 (63%) are females. The sample was collected at the department of gastroenterology. The student t-test was applied to assess the risk of hyper and non-hyperuricemia among the NAFLD in Type-2 diabetics. Pearson correlation was used to assess link between serum uric acid and other biochemical parameters.

Results: The BMI, SGOT, ALP and LDL levels are significantly elevated in hyperuricemia male subjects ($P < 0.05$). Triglyceride levels had a weak negative correlation with serum uric acid (SUA) levels, which was significant in male NAFLD subjects ($P 0.01$). The overall prevalence of hyperuricemia was more in males as compared with females ($P < 0.05$).

Conclusion: Our results reveal that the dyslipidemia is more closely associated with hyperuricemia in men than women with NAFLD. Total cholesterol and Triglycerides showed significant weak negative correlation with SUA in males. Further longitudinal studies are required to prove these findings.

1. Introduction

Non-alcoholic fatty liver disease (NAFLD) is a divergent hepatobiliary disorder that is one of the leading causes of chronic liver disease worldwide. The disease's prevalence in the general Indian population is estimated to be 9–32%¹ with obese and diabetic patients having a higher incidence rate. Metabolic syndrome and associated co-morbidities such as type 2 diabetes (T2DM), obesity, and dyslipidemia are risk factors for NAFLD, and the prevalence of NAFLD has risen in tandem with these epidemics.^{2,3}

Serum uric acid (SUA) level greater than 7.0 mg/dL in men and greater than 5.7 mg/dL in women was considered to be hyperuricemia and it is an independent risk factor for hypertension, diabetes, metabolic syndrome, CKD, and cardiovascular events.^{4,5} The rising prevalence of

hyperuricemia is regarded as a new public health concern. Many factors, including dietary and lifestyle changes, excess weight, population ageing, and increased antihypertensive drug prescription, may increase the risk of hyperuricemia. A number of studies have found a link between hyperuricemia and NAFLD, with elevated UA levels increasing the prevalence of NAFLD.^{6,7} However, the link between gender-specific hyperuricemia in NAFLD and Type 2 diabetes were not well understood. Hence, were aimed to explore the link between the hyperuricemia in NAFLD with Type-2 diabetes.

2. Materials and methods

A cross-sectional study conducted at department of gastroenterology, Bhargavi gastro and surgical clinic Warangal, between January 2020

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and March 2021 with eligible criteria. To the study subjects were included based on the inclusion and exclusion criteria.

2.1. Inclusion of subjects with NAFLD

Patients with history of type 2 diabetes mellitus and were subjected to ultrasonography. NAFLD was diagnosed based on histological or imaging findings, and subjects with no history of alcohol consumption were included in the study.

2.2. Exclusion criteria

Subjects were excluded based on the following criteria were excluded: alcohol consumption >140 g/week for men and 70 g/week for women, lipid-lowering, or anti hyperuricemic agents, any other known potential causes of chronic liver disease such as viral or autoimmune hepatitis and those using hepatotoxic medications; subjects with history of cancer, respiratory, renal, or hepatobiliary disease, gout, and other rheumatologic diseases. Type 1 diabetes, gestational diabetes, or acute complications of diabetes. All study participants provided informed written consent prior to participate in the study.

2.3. Laboratory examinations

Fasting blood samples obtained from each subject were used for the analysis of biochemical parameters. The parameters assessed include fasting plasma glucose (FBS), serum uric acid (SUA), total proteins, albumin (A), globulin (G), A/G ratio, serum glutamate pyruvate transaminase (SGPT), serum glutamate oxaloacetate transaminase ((SGOT), SGOT:SGPT ratio, alkaline phosphates, nitrogenous end product-blood urea nitrogen (BUN), serum creatinine (Cr), and fasting lipid profiles that comprise of triglyceride (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol. All the biochemical parameters were analyzed through standard protocols with the aid of automated immunochemical analyzer (Abbott AxSYM).

2.4. Statistical analysis

All statistical analyses were performed using IBM SPSS 20 (SPSS, Chicago, Illinois, USA) statistical package for windows. Continuous variables were compared using the Student's *t*-test or the Mann-Whitney *U* test, depending on the normality of distribution, whereas the relationships between SUA and other metabolic risk variables were assessed using Pearson's correlations. Any value of $p < 0.05$ was considered statistically significant.

3. Results

The study included 134 subjects with Type 2 diabetes who had NAFLD, of which 93 males (69%) and 41 females (31%). The data were collected at the outpatient department of Bhargavi gastro and surgical clinic, Hanamkonda, Warangal, Telangana. The study was conducted during the period of 2019 and 2021. Table 1 show that male subjects have a higher BMI, higher levels of liver enzymes (SGOT and SGPT) than females, which is statistically significant ($P < 0.05$). The remaining demographic and biochemical parameters are not significant among the subjects. Table 2 illustrated the association between gender and hyperuricemia among the Type-2 NAFLD subjects. The mean and SD values of BMI, SGOT, ALP and LDL levels are higher in male NAFLD subjects compared to females. The mean difference was statistically significant.

The male subjects were having higher mean values for body weight, FBS, liver enzymes, and serum uric acids. Despite all are having NAFLD, male subjects SUA levels were borderline elevated. SUA are normal in female subjects with NAFLD. These findings suggest that SUA levels play no role in the development of NAFLD in Type 2 diabetics (Table 3). The

Table 1

Gender wise distribution of demographic and clinical characteristics of study subjects.

Variables	Male (n = 93, 69%)	Female (n = 41,31%)	p value
	Mean $\pm$ SD	Mean $\pm$ SD	
Age	46.6 $\pm$ 7.605	47.46 $\pm$ 8.24	0.753
Marital status†			
Married (n,%)	60 (87)	38 (93)	0.311
Unmarried (n,%)	09 (13)	03(07)	
Level of study†			
Illiterates (n,%)	15 (16)	09 (22)	0.404
10 + 2 and above (n,%)	78 (84)	32 (78)	
Duration of Diabetes (yrs)	4.57 $\pm$ 2.35	4.58 $\pm$ 1.99	0.882
Height (mts)	1.637 $\pm$ 0.08	1.621 $\pm$ 0.09	0.245
Body Weight(kg)	61.69 $\pm$ 8.41	54.73 $\pm$ 6.5	<0.0001***
BMI (Kg/m ²)	22.51 $\pm$ 3.03	21.21 $\pm$ 2.38	0.0163*
Waist Circumference (cm)	90.56 $\pm$ 4.99	90.84 $\pm$ 7.96	0.804
FBS (mg/dl)	111.8 $\pm$ 26.98	108 $\pm$ 27.88	0.183
SGOT (u/l)	48.15 $\pm$ 41.34	30.09 $\pm$ 13.76	0.0003 ***
SGPT (u/l)	69.72 $\pm$ 62.7	46.11 $\pm$ 23.73	0.0055 **
SGOT:SGPT	0.76 $\pm$ 0.36	0.77 $\pm$ 0.62	0.204
ALP mg/dl	88.53 $\pm$ 32.27	80.07 $\pm$ 26.9	0.0384*
Total Proteins(gm/dl)	6.99 $\pm$ 0.83	6.99 $\pm$ 0.48	0.746
Albumin(gm/dl)	3.62 $\pm$ 0.42	3.62 $\pm$ 0.50	0.874
Globulin(gm/dl)	3.438 $\pm$ 0.43	3.33 $\pm$ 0.40	0.181
A/g ratio	1.072 $\pm$ 0.22	1.09 $\pm$ 0.24	0.869
Serum Creatinine (mg/dl)	0.94 $\pm$ 0.36	0.89 $\pm$ 0.31	0.248
Blood urea(mg/dl)	23.77 $\pm$ 6.29	22.57 $\pm$ 4.57	0.068
SUA (mg/dl)	7.53 $\pm$ 1.16	7.056 $\pm$ 1.76	0.067
TC (mg/dl)	205.6 $\pm$ 43.91	197.3 $\pm$ 33.98	0.206
LDL (mg/dl)	145.6 $\pm$ 32.29	136.4 $\pm$ 27.55	0.062
HDL (mg/dl)	45.97 $\pm$ 22.99	47.37 $\pm$ 26.11	0.933
TG (mg/dl)	176.9 $\pm$ 30.46	175.3 $\pm$ 21.62	0.801

P value < 0.05 was considered to be statistically significant.

Table 2

Association of hyperuricemia among the study the subjects.

Variables	Hyperuricemic subjects (N = 92)		p value
	Male(n = 66)	Female (n = 26)	
	Mean $\pm$ SD	Mean $\pm$ SD	
Age	47.71 $\pm$ 7.88	47.88 $\pm$ 9	0.898
Height (mts)	1.64 $\pm$ 0.07	1.63 $\pm$ 0.07	0.527
Body Weight(kg)	65.18 $\pm$ 7.193	58.69 $\pm$ 7.16	0.0017**
BMI (Kg/m ²)	24.38 $\pm$ 4.01	22.19 $\pm$ 3.81	0.0468*
Waist Circumference (cm)	91.02 $\pm$ 4.7	90.52 $\pm$ 7.98	0.456
Duration of Diabetes (yrs)	4.86 $\pm$ 2.36	4.55 $\pm$ 1.95	0.735
FBS (mg/dl)	116.85 $\pm$ 35.19	115.19 $\pm$ 31.38	0.864
SGOT (u/l)	51.1 $\pm$ 46.09	33.16 $\pm$ 16.4	0.0101*
SGPT (u/l)	73.3 $\pm$ 71.18	49.27 $\pm$ 29.23	0.107
ALP (u/l)	91.11 $\pm$ 31.8	83.06 $\pm$ 33.68	0.0388*
Total Proteins(gm/dl)	7.08 $\pm$ 0.56	6.95 $\pm$ 0.51	0.309
Albumin(gm/dl)	3.57 $\pm$ 0.42	3.55 $\pm$ 0.51	0.973
Globulin(gm/dl)	3.49 $\pm$ 0.39	3.37 $\pm$ 0.39	0.147
A/g ratio	1.04 $\pm$ 0.19	1.06 $\pm$ 0.23	0.900
Serum Creatinine (mg/dl)	0.94 $\pm$ 0.38	0.89 $\pm$ 0.35	0.419
Blood urea(mg/dl)	24.21 $\pm$ 6.87	22.92 $\pm$ 4.73	0.140
SUA (mg/dl)	8.08 $\pm$ 0.79	8.15 $\pm$ 1.18	0.440
TC (mg/dl)	209.68 $\pm$ 42.89	201.84 $\pm$ 36.87	0.379
LDL (mg/dl)	149.12 $\pm$ 31.93	134.5 $\pm$ 29.11	0.0386*
HDL (mg/dl)	46.63 $\pm$ 24.11	51.65 $\pm$ 25.8	0.438
TG (mg/dl)	179.07 $\pm$ 32.26	174.5 $\pm$ 26.14	0.413

P value < 0.05 was considered to be statistically significant.

proportion of hyperuricemia was high (N = 66, 71%) in male subjects as compared to females and which was statistically significant ($P < 0.05$) (Table 4).

Table 5 shows the relationship between SUA and other variables. According to the findings in Table 5, nearly all variables are negatively

Table 3

Gender wise association of Non-hyperuricemia among the study the subjects.

Variables	Non-Hyperuricemic subjects (N = 42)		p value
	Male (n = 27)	Female (n = 15)	
	Mean $\pm$ SD	Mean $\pm$ SD	
Age	44.62 $\pm$ 5.42	46.73 $\pm$ 6.94	0.316
Height (mts)	1.62 $\pm$ 0.09	1.59 $\pm$ 0.10	0.298
Body Weight(kg)	61.96 $\pm$ 7.48	53.4 $\pm$ 6.10	0.0003***
BMI (Kg/m ²)	23.61 $\pm$ 3.44	21.49 $\pm$ 1.38	0.120
Waist Circumference (cm)	89.45 $\pm$ 5.57	91.38 $\pm$ 8.18	0.627
Duration of Diabetes (yrs)	3.88 $\pm$ 2.2	4.63 $\pm$ 2.14	0.269
FBS (mg/dl)	114.65 $\pm$ 40.26	94.61 $\pm$ 11.82	0.0108*
SGOT (u/l)	38.93 $\pm$ 23.94	24.74 $\pm$ 3.46	0.0462*
SGPT (u/l)	57.55 $\pm$ 31.22	40.62 $\pm$ 5.62	0.0211*
ALP (u/l)	81.96 $\pm$ 33.14	75.08 $\pm$ 5.31	0.752
Total Proteins(gm/dl)	6.8 $\pm$ 1.26	7.06 $\pm$ 0.45	0.356
Albumin(gm/dl)	3.73 $\pm$ 0.43	3.76 $\pm$ 0.48	0.921
Globulin(gm/dl)	3.29 $\pm$ 0.48	3.26 $\pm$ 0.42	0.963
A/G ratio	1.14 $\pm$ 0.27	1.15 $\pm$ 0.24	0.974
Serum Creatinine (mg/dl)	0.96 $\pm$ 0.31	0.88 $\pm$ 0.21	0.369
Blood urea(mg/dl)	22.68 $\pm$ 4.49	21.89 $\pm$ 4.35	0.263
SUA (mg/dl)	6.2 $\pm$ 0.77	5.14 $\pm$ 0.51	<0.0001****
TC (mg/dl)	195.77 $\pm$ 45.6	189.46 $\pm$ 27.69	0.470
LDL (mg/dl)	137.11 $\pm$ 32.14	139.6 $\pm$ 25.24	0.691
HDL (mg/dl)	44.33 $\pm$ 20.28	39.93 $\pm$ 25.78	0.478
TG (mg/dl)	171.7 $\pm$ 25.28	176.8 $\pm$ 10.56	0.202

P value < 0.05 was considered to be statistically significant.

Table 4

Association of Hyperuricemia among the male and female gender with NAFLD.

Parameter	Male (N = 93) (%)	Female (N = 41) (%)	p value
Hyperuricemia	66 (71)	26 (63)	<0.0001***
Non- Hyperuricemia	27 (29)	15 (37)	0.0193

P value < 0.05 was considered to be statistically significant.

Table 5

Pearson bivariate correlations between serum uric acid and other variables in male and female subjects.

Variables	Males		Females	
	r	p	r	P
Height (mts)	-0.078	0.534	-0.35	0.08
Body Weight(kg)	-0.085	0.567	-0.159	0.437
BMI (Kg/m ²)	0.019	0.877	0.085	0.68
Waist Circumference (cm)	-0.036	0.778	-0.24	0.248
FBS (mg/dl)	-0.033	0.791	-0.176	0.389
SGOT (u/l)	-0.068	0.588	-0.112	0.585
SGPT (u/l)	-0.105	0.401	-0.111	0.591
TC (mg/dl)	-0.245*	0.048	-0.346	0.084
LDL (mg/dl)	-0.193	0.121	-0.317	0.114
HDL (mg/dl)	-0.151	0.225	-0.191	0.351
TG (mg/dl)	-.315**	0.01	-0.267	0.187

P value < 0.05 was considered to be statistically significant.

correlated with SUA, particularly the weak negative correlation. Triglyceride levels had a weak negative correlation with SUA levels, which was significant in male NAFLD patients (P 0.01).

4. Discussion

In our study, we noticed that the prevalence of hyperuricemia is high in male NAFLD patients with Type 2 diabetes. The findings also revealed that the link between hyperuricemia and NAFLD was significantly stronger in men than in women. In contrast, obesity or being overweight is one of the factors that cause of hyperuricemia in men.^{8,9} The onset of NAFLD is complicated and still poorly understood. Many risk factors, including genetic, metabolic, and dietary factors, are thought to play a

role in the development of NAFLD.¹⁰ Liver cell damage was observed in NAFLD, particularly in Type-2 diabetics. Liver enzymes such as SGOT were found to be impaired.¹¹ In this study, males had significantly higher mean values of liver enzymes than females. Similarly, an association was observed with alkaline phosphatase. ALP is found in various body tissues and has varying physiochemical properties. ALP is an enzyme that is elevated by a variety of hepatobiliary diseases or bone disorders.¹² In our study, male subjects had significantly higher ALP levels. Similarly, Chen et al. were confirmed in a prospective study, stating that increased levels of ALP are one of the risk factors in Type 2 diabetics.¹³ In NAFLD hyperuricemic diabetic patients, an elevated BMI is also a risk factor. Males have a higher BMI than females in our study. Increased BMI may likely to cause depression.¹⁴ Dyslipidemia is a major contributor to the development of NAFLD.¹⁵ A 20–80% of NAFLD cases were having, hypertriglyceridemia, low HDL-C levels, and high low-density lipoprotein cholesterol (LDL-C) levels respectively. According to Marchesini et al., hypertriglyceridemia is also present in 64% of patients with hepatic steatosis, with low HDL-C levels reported in 30–42% of cases.¹⁶

In our study, hyperuricemic subjects had elevated TG and LDL cholesterol. A significant association with high lipid levels and hyperuricemia was noticed in male subjects. Non-hyperuricemic subjects had borderline LDL cholesterol and high TG levels. These findings clearly demonstrated that elevated triglycerides were strongly associated with NAFLD. Our Pearson bivariate analysis confirmed that, the serum uric acid levels and triglyceride levels were found to have a significant negative weak correlation among Type-2 diabetic NAFLD subjects.

4.1. Strengths and limitations

The current research has both benefits and weaknesses. To our knowledge, this is the first research in Telangana, India, to investigate the relationship between hyperuricemia and NAFLD in Type-2 diabetics. In terms of gender, our results support the links between hyperuricemia and NAFLD. Additionally, in our study, we have not seen any confounders; hence, we have not adjusted for confounding variables in our analyses. As a result, further longitudinal research is required to prove these findings. Hence, the conclusions may not be generalized to the population in the whole India.

5. Conclusion

Our findings demonstrate, dyslipidemia is more closely associated with hyperuricemia in men than women with NAFLD. Particularly, total cholesterol and triglycerides are showed significant weak negative correlation with SUA in males. Further longitudinal studies are needed to confirm these findings to establish the role of uric acid in the pathogenesis of NAFLD in Type-2 diabetics.

Author contributions

Concept- VR.N; Design-SR.R VS.M; Supervision-VS.M; Materials Data Collection and/or Processing-US.P; Analysis and/or Interpretation-VR.N., US.P., VS.M; Literature Search-US.P.; Writing-US.P., VR.N.; Critical Reviews-VR.N, SR.K,VS.M.

Source of funding

Self funded study.

Compliance with ethical standards

The study procedure was approved by the Institutional Ethics Committee, Dated:10.12.2019 (IEC/19/Nov/71/10) of Sri Ramachandra Institute of Higher Education and Research (Deemed to be University), Chennai and has affiliation with Bhargavi gastro and surgical clinic

Warangal, Telangana, India, and the research was carried out in conjunction with Good clinical practice guidelines.

Declaration of competing interest

Authors declare that they have no conflict of interest.

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