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Original Article

A Study on levels of Uric acid, liver enzymes and lipid profile variations in patients with Non-alcoholic fatty liver disease and Healthy volunteers in rural areas

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ABSTRACT

Background: Non-alcoholic fatty liver disease (NAFLD) is considered as a hepatic manifestation of the metabolic syndrome. The prevalence of NAFLD is ranging from 38-48%. Serum uric acid, LFT levels have been suggested to be associated with factors that contribute to insulin resistance and metabolic syndrome. The aim of this study is to investigate the association of serum uric acid, LFT levels and body mass index (BMI) with NAFLD compared to healthy volunteers. **Methods:** A total number of 100 subjects, who attended for the General check up in GEMS Hospitals, Srikakulam, 50 patients with NAFLD and 50 healthy subjects. NAFLD was diagnosed based on the abdominal ultrasonographic findings. BMI and serum uric acid, liver enzymes, lipid profile were also measured in all the study participants. Uric acid quartiles were categorized into four groups, and the number of subjects, who came under each group, was noted. 57% of NAFLD patients had normal ALT between 25 and 40 U/L, 53% of NAFLD subjects had normal GGT between 15 and 30 U/L. ALT <25 U/L and GGT <15 U/L had highest negative predictivity whereas ALT >40 U/L and GGT > 30 U/L had highest positive predictivity for presence of NAFLD in our study sample. **Results:** The mean BMI (kg/m²) for cases was 27.01 ± 3.53 and the same for controls was 23.91 ± 3.11. Elevated BMI was associated with an increased incidence of NAFLD with a statistical significance ($p < 0.05$).The mean uric acid concentration (mg/dl) for cases was 5.73 ± 1.57, and for controls was 4.69 ± 0.91. Increased serum uric acid concentration was associated with an increased incidence of NAFLD with a statistical significance ($p < 0.05$). **Conclusion:** This study showed that elevated BMI is associated with an increased incidence of NAFLD. Serum uric acid levels are significantly associated with NAFLD, and high uric acid levels showed a high incidence of NAFLD compared to low serum uric acid level.

Keywords: Non-alcoholic fatty liver disease, Uric acid, Body mass index

INTRODUCTION

Uric acid is the major end product of purine metabolism and is formed from xanthine by the action of xanthine Oxidoreductase[1]. Serum uric acid level is maintained by the balance between uric acid production and excretion[2]. Non-alcoholic fatty liver disease (NAFLD) is defined as a diffuse accumulation of fat in the liver, after excluding alcohol intake and other causes of liver disease. NAFLD has clinical importance because of its increasing prevalence and its potential to become advanced cirrhosis and hepatic failure[3]. Identifying risk factors is essential for the prevention of NAFLD. The exact risk factors for NAFLD have not been fully clarified. Recent studies showed that NAFLD is almost associated with obesity, hypertension, dyslipidemia, and glucose intolerance, a cluster of disorders now recognized as metabolic syndrome[4-7]. For this reason, NAFLD has been considered as the hepatic manifestation of metabolic syndrome.5,8 In previous studies, an association between serum uric levels and metabolic syndrome has been reported[9]. The association between serum uric acid and chronic liver disease has also been reported in United States[10], which leads us to investigate the possibility of the same among the Indians. In view of the above background, the present study was planned to evaluate the serum uric acid levels with NAFLD in comparison to normal body mass index (BMI) and elevated BMI.

METHODS

The present study was conducted on patients undergoing health checkup at GEMS Hospitals, Srikakulam. After getting informed written consent

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from all the participants, 50 patients (cases) of both sex (22 men and 28 women) in the age group of 31-60 with NAFLD and 50 healthy volunteers with non fatty liver (controls) of both sex (21 men and 29 women) were included in our study. Subjects with a history of smoking, alcohol consumption, diabetes mellitus, hypertension, history of liver disease such as hepatitis and participants on hepatotoxic drugs were excluded from the study. The subjects were instructed to be in fasting for 12 h prior to the examination, refrain from exercise the day before the examination. Standing height and body weight were measured without shoes. Baseline ultrasound abdomen (FNAC to be added) examination was carried out by a radiologist. Hepatic steatosis was diagnosed by characteristic echo patterns, such as evidence of diffuse hyperechogenicity of the liver and poor visualization of intra-hepatic structures. To explore the association between serum uric acid level and NAFLD, subjects were divided according to their serum uric acid levels. Serum uric acid quartiles were defined = 5.0, 5.1-6.0, 6.1-7.0, > 7 mg/dl for men and = 4.0, 4.1-5.0, 5.1, 6.0, > 6.0 mg/dl for women.

RESULTS

The mean BMI (kg/m²) for cases (NAFLD) was 24.01 ± 3.03 and the same for controls (no fatty liver) was 21.91 ± 2.91. The mean uric acid concentration (mg/dl) for cases was 5.930 ± 1.271, and that of controls was 4.696 ± 0.914. The results are given in Table 1, which shows the comparison of BMI between cases and controls and Table 2 shows the comparison of serum uric acid level between cases and controls which is higher in cases with a $p < 0.05$, which is also statistically significant than controls. This proves higher the uric acid level the greater the chances of developing NAFLD. As already mentioned about uric acid quartiles for better association, only 14% of cases come under 1 quartile as compared to 65% in controls, which indicates that the low uric acid level in the control group (controls) which is depicted in Figure 1. 52% of cases come under 3rd quartile as compared to 10% in controls that is shown in Figure 2. This shows that higher the uric acid levels higher the chances of developing NAFLD. The percentage of subjects in 4 quartile for cases and controls were 15% and 4% respectively. There was not much difference in percentage (17% and 18% respectively) of study participants in 2nd quartile in both groups.

Table 1: Comparison of BMI between NAFLD (cases) and healthycontrols.

Parameter s	Cases (n=50)	Controls (n=50)	P Value
BMI >25	30	18	<0.05
BMI<25	18	34	

Table 2: The association of serum uric acid levels between NAFLD (cases) and controls

Parameter s	Cases (n=50)	Controls (n=50)	P Value
Hyperuricemia	25	13	<0.05
Normal Uric acid	23	27	

Figure 1: The percentage of subjects in 1 quartile (low) of serum uric acid level in non-alcoholic fatty liver disease (cases) and controls.

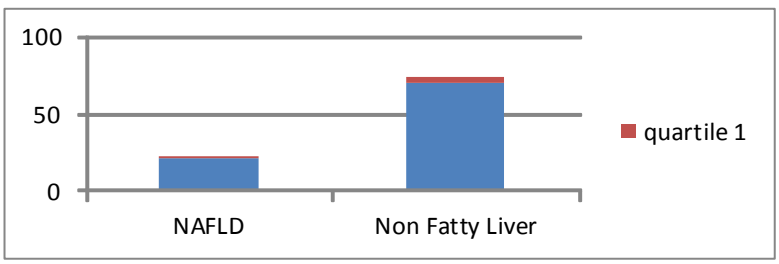

Table 3: Comparison of lipid profile in non-alcoholic fatty liver disease (cases) and Controls

Parameter	Control	NAFLD
Cholesterol	128.79±70.42	300.57±167.98
TGL	121.60±61.11	431.61±48.76
HDL	54.05±25.38	70.62±35.67
LDL	25.93±16.50	80.40±13.65
VLDL	101.81±39.67	123.35±39.39

Table 4: Comparison of ALT, AST, ALP & GGT in non-alcoholic fatty liver disease (cases) and controls.

Parameters	Controls	NAFL
ALT	20.8 ± 14	44.2 ± 22
AST	26 ± 13	33.6 ± 16
GGT	16 ± 13	37.4 ± 15
AST: ALT	1.18 ±0.3	0.78 ± 0.2
ALP	137 ± 54	143 ± 72

DISCUSSION

NAFLD is now recognized worldwide as an important cause of chronic liver disease. We observed independent association between serum uric acid concentrations and the presence of NAFLD. Our results are in agreement with previous studies conducted by and Shi 11and Li et al. serum uric acid was independently associated with biopsy-proven hepatic steatosis in a study of 1915 Chinese patients aged 12-80 years with chronic hepatitis B infection. Also reported similar results in a study of 8925 apparently healthy Chinese.11 Same mechanism could explain the significant relationship between serum uric acid and NAFLD, current understanding of the progression of NAFLD involves the "2-hit hypothesis."1312 Li et al. The "first hit" is excessive fat accumulation in hepatocytes, which is closely linked to insulin resistance. Numerous studies have introduced significant association between serum uric acid concentration and the metabolic syndrome and its components, where insulin resistance is the primary problem. The significant association between serum uric acid and NAFLD suggest that insulin resistance is a possible mechanism linking serum uric acid with NAFLD.14 The "second hit" is a process from oxidative stress to hepatocyte injury, inflammation and fibrosis. Excessive free fatty acids in hepatocytes of patients with NAFLD generate an excess of reactive oxygen species leading to lipid peroxidation of hepatocytes, cytokine production and hepatic inflammation as shown in table 3 in our study. An experimental study has shown that serum uric acid stimulates the synthesis of microcyte chemo-attractant protein, interleukin-1, interleukin-6 and tumor necrosis factor-a, all of which are pro-inflammatory molecules and stimulate production of C-reactive protein in the liver.15 So major factors connecting increased serum uric acid concentration with NAFLD may be due to oxidative stress and chronic low-grade inflammation. In this study, we included BMI to show a strong association between BMI and NAFLD because BMI has already been shown to be associated with NAFLD in previous studies. Loannou *et al.* demonstrated classical cardiovascular disease (CVD) risk (by Framingham risk score) with elevated ALT. The population-based Hoorn study showed that high normal ALT levels were associated with an increased 10-year risk of coronary heart disease independent of CVD risk factors indicating that ALT may be a useful marker in assessment of CVD risk in patients who may have NAFLD. Asian-Indian men may be genetically predisposed to develop hepatic steatosis, hepatic insulin resistance and T2DM at a lower BMI with greater central obesity than other ethnic groups suggesting significant ethnic differences in the pathogenesis of insulin resistance. A study showed that GGT and ALT even within the "normal" range, but not AST were significantly associated as shown in table 4 with BMI and WC, HOMA-IR, triglycerides, HDL-C, glucose even after further adjustment for BMI.

Liver ultrasonography and assessment of the severity of NAFLD using more specific severity scoring, serological assessment of fibrosis, or measurement of liver stiffness (transient elastography or acoustic radiation force imaging), can be performed in a secondary care setting. Liver biopsy may be required to clarify the severity of the underlying liver disease but even this "definitive" investigation is subject to considerable variability. Recognition of those patients with more advanced liver disease or at risk of progressive liver damage allows appropriate monitoring; in particular patients with cirrhosis can be entered into surveillance programmes for hepatocellular carcinoma and the presence of oesophagogastric varices.

CONCLUSION

This study clearly demonstrates that serum uric acid is a significant factor associated with the development of NAFLD. It is necessary to analyze serum uric acid, when a person is incidentally diagnosed to have NAFLD because recent studies have proved hypouricemic therapy clinically lowers serum uric acid levels, which significantly ameliorated hepatic steatosis.

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