

Research Article

Association of serum uric acid level and body mass index between non-alcoholic fatty liver disease patients and healthy volunteers

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ABSTRACT

Background: Non-alcoholic fatty liver disease (NAFLD) is considered as a hepatic manifestation of the metabolic syndrome. Worldwide prevalence of NAFLD is 38%. Serum uric acid level has 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 level and body mass index (BMI) with NAFLD.

Methods: This observational study was conducted in subjects, who attended the master health checkup clinic of PSG Hospitals, Coimbatore, on 50 patients with NAFLD and 50 non fatty liver subjects. NAFLD was diagnosed based on the abdominal ultrasonographic findings. BMI and serum uric acid level 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.

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

After obtaining clearance from the Institute Ethics Committee, the present study was conducted on patients undergoing master health checkup at PSG Hospitals, Coimbatore. After getting informed written consent 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 fast for at least 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 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/m^2) for cases (NAFLD) was 27.01 ± 3.53 and the same for controls (no fatty liver) was 23.91 ± 3.11 . The mean uric acid concentration (mg/dl) for cases was 5.730 ± 1.571 , 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 15% of cases come under 1st quartile as compared to 66% 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 11% in controls that is shown in Figure 2. This shows that

Table 1: The association of BMI between NAFLD (cases) and non-fatty liver (controls).

Parameters	Cases (n=50)	Controls (n=50)	Chi-square value	p value
BMI>25	31	17	7.853	<0.05*
BMI<25	19	33		

*Statistically significant. BMI: Body mass index, NAFLD: Non-alcoholic fatty liver disease

Table 2: The association of serum uric acid levels between NAFLD (cases) and non-fatty liver (controls).

Parameters	Cases (n=50)	Controls (n=50)	Chi-square value	p value
Hyperuricemia	26	12	7.173	<0.05*
Normal uric acid	24	38		

*Statistically significant. NAFLD: Non-alcoholic fatty liver disease

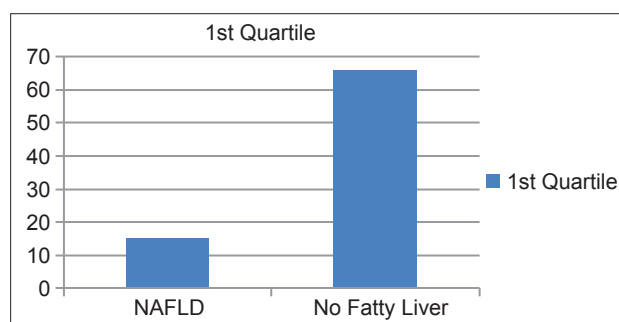


Figure 1: The percentage of subjects in 1st quartile (low) of serum uric acid level in non-alcoholic fatty liver disease (cases) and non-fatty liver (controls).

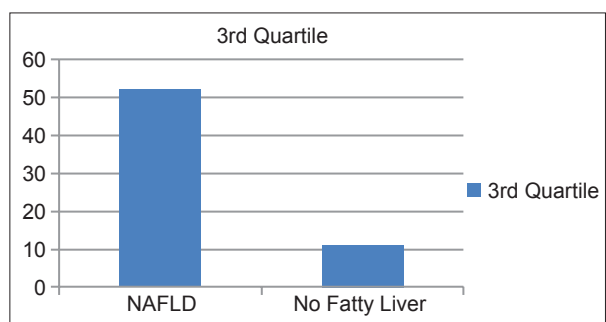


Figure 2: The percentage of subjects in 3rd quartile (high) of serum uric acid level in non-alcoholic fatty liver disease (cases) and non-fatty liver (controls).

higher the uric acid levels higher the chances of developing NAFLD. The percentage of subjects in 4th quartile for cases and controls were 16% and 5% respectively. There was not much difference in percentage (17% and 18% respectively) of study participants in 2nd quartile in both groups.

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 Shi¹¹ and Li et al.¹² 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.¹¹ Li et al.¹² also reported similar results in a study of 8925 apparently healthy Chinese.

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.”¹³ 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,¹⁴ 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.

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.

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- α ,¹⁵ all of which are pro-inflammatory molecules and stimulate production of C-reactive protein in the liver.¹⁶ 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.¹⁷

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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