

# Study of Serum Uric Acid Levels and BMI in Patients with Nafld, a Observational Study at a Tertiary Care Centre of Central India.

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## ABSTRACT

**Introduction:** Nonalcoholic fatty liver disease (NAFLD) represents a spectrum of conditions from simple steatosis to nonalcoholic steatohepatitis (NASH) and cirrhosis, NAFLD has been considered as the hepatic manifestation of metabolic syndrome. The association between serum uric acid concentration and metabolic syndrome has been demonstrated in previous studies, which leads us to speculate that there might be a relationship between uric acid concentrations and NAFLD. The aim of the present study was to investigate the association of serum uric acid level and body mass index (BMI) with NAFLD.

**Material and Methods:** A total of 120 subjects including 60 known cases of NAFLD attending outdoor clinics of MY Hospital and 60 age and sex matched healthy controls. Fasting venous blood sample was analysed for uric acid by uricase/peroxidase method. Statistical analysis was performed using SPSS software.

**Results:** In our study there were 26 women and 34 men as cases and 21 females & 39 males in control group. Mean BMI of NAFLD cases were  $32 \pm 3.48$  and that of control group was  $27 \pm 2.56$ . Difference between the two groups were statistically significant. Mean serum uric acid in case group were 6.78mg/dl and that of control group it was 4.28. The difference in uric acid levels between cases and control were statistically significant.

**Conclusion:** Study concluded that increased serum uric acid concentrations are a risk factor in NAFLD. The possible pathogenetic role of uric acid in NAFLD and the metabolic syndrome deserves to be further studied.

**Keywords:** BMI, NAFLD, Uric Acid

## INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) represents a spectrum of conditions from simple steatosis to nonalcoholic steatohepatitis (NASH) and cirrhosis. Non-alcoholic fatty liver disease (NAFLD) is defined as a diffuse accumulation of fat in the liver, after excluding excessive alcohol intake and other causes of liver disease. Along with the “obesity epidemic”, the worldwide prevalence of NAFLD, based on imaging studies, is increasing rapidly and now includes 14%–31% of the general population.<sup>1</sup> NAFLD is an emerging problem in the Asia-Pacific region and the prevalence is likely to increase in the future.<sup>2,3</sup> It is generally attributed to obesity-induced insulin resistance. Uric acid is the major end product of purine metabolism and is formed from xanthine by the action of xanthine oxidoreductase.<sup>4</sup> Serum uric acid concentrations have long been considered a marker of gout or urolithiasis. However, emerging evidence suggests that increased uric acid, despite being a major antioxidant in the human plasma<sup>5</sup>, is associated with the prevalence and incidence of cardiovascular disease (CVD)<sup>2</sup>, diabetes<sup>3</sup> and metabolic syndrome<sup>6,7</sup> conditions linked to increased oxidative stress, chronic low-grade inflammation, and insulin resistance.<sup>8,9</sup>

Identifying risk factors is essential for prevention of NAFLD but the exact risk factors for NAFLD have not been fully clarified. Recent studies showed that NAFLD is closely associated with obesity, hypertension, dyslipidemia, and glucose intolerance, a cluster of metabolic disorders that is now recognized as metabolic syndrome.<sup>10,11</sup> For this reason, NAFLD has been considered as the hepatic manifestation of metabolic syndrome.<sup>10</sup> The association between serum uric acid concentration and metabolic syndrome has been demonstrated in previous studies<sup>12</sup>, which lead us to speculate that there might be a relationship between uric acid concentrations and NAFLD. Although several laboratory parameters, such as alanine aminotransferase (ALT), and C-reactive protein (CRP) have been reported as useful markers for the diagnosis of NAFLD<sup>13</sup>, little has been written regarding the association between uric acid and NAFLD. Therefore, we performed a cross-sectional study to examine whether serum uric acid concentrations are related to NAFLD.

## MATERIAL AND METHODS

For the present cross-sectional study, 60 newly diagnosed cases of NAFLD and 60 normal control subjects aged 30-65years were included in the study. The patients and controls were matched by ethnic group. They were taken from the outdoor clinics of Maharaja Yashwant Rao Hospital, Indore (M.P). 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 study protocol was approved by the local ethical committee and a verbal informed consent was taken by all the subjects.

### Collection and preparation of sample

Taking all aseptic precautions, about 5 ml fasting venous blood was drawn from a peripheral vein without anticoagulant and allowed to clot. Clotted blood was centrifuged and clear serum was collected. Fresh serum samples were taken. Serum was checked for hemolysis and if hemolyzed then that serum was discarded. Serum was analysed for Uric acid.

### Analytical methods

Serum uric acid was assessed by automated analyzer

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enzymatically by uricase/peroxidase method.

## STATISTICAL ANALYSIS

Data was maintained on excel spread sheet. Analysis was performed using SPSS software. Descriptive data were expressed as mean, standard deviation, and range of all variables. Results were presented as mean  $\pm$  S.D. Means of data in patients and controls were compared using the independent t-test. Differences were considered statistically significant at  $p < 0.05$ .

## RESULT

120 subjects, 60 patients of nafld and 60 healthy volunteers controls, were included in this study. There were 26 women and 34 men as cases and 21 females & 39 males in control group. Mean BMI of NAFLD cases were  $32 \pm 3.48$  and that of control group was  $27 \pm 2.56$  (table-1). Difference between the two groups were statistically significant. Mean serum uric acid in case group were 6.78mg/dl and that of control group it was 4.28. The difference in uric acid levels between cases and control were statistically significant (table-2).

## 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<sup>14</sup> and Li et al.<sup>15</sup> 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.<sup>14</sup> Li et al.<sup>15</sup> also reported similar results in a study of 8925 apparently healthy Chinese. The biochemical role of uric acid in NAFLD is poorly understood, and current data on this subject seem at least partially conflicting. Increased systemic oxidative stress in patients with NAFLD has long been recognized both in animal experiments and clinical studies<sup>16</sup>, and uric acid has been proposed to act as an antioxidant of peroxynitrite and peroxynitrite-derived radicals.<sup>17,18</sup> A recent study showed that treatment with uric acid in obese ob/ob mice resulted in a nearly complete resolution of fatty liver.<sup>19</sup> Thus, elevated SUA levels may reflect a compensatory mechanism counteracting the increased oxidative stress associated with NAFLD. On the contrary, uric acid becomes a strong oxidant in the environment of metabolic syndrome.<sup>20</sup> Indeed, some have proposed using allopurinol<sup>21</sup> or dietary measures, such as reduced intake of fructose, which is associated with increased uric acid levels<sup>22,23</sup> in the treatment of the metabolic syndrome and NAFLD. It must be appreciated, though, that serum uric acid may be only a marker of the metabolic syndrome and not etiologically important in the disease.

Current understanding of the progression of NAFLD involves the "2-hit hypothesis."<sup>24</sup> 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,<sup>25</sup> 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.

| Parameters   | Cases (n=60) | Controls (n=60) | p value |
|--|--------------|-----------------|---------|
| BMI >25  | 34           | 16              | P<0.05* |
| BMI <25  | 26           | 44              |         |
| *Statistically significant. BMI: Body mass index, NAFLD: Non-alcoholic fatty liver disease   |              |                 |         |
| <b>Table-1:</b> The association of BMI between NAFLD (cases) and non-fatty liver (controls). |              |                 |         |

| Parameters  | Cases (n=60) | Controls (n=60) | p value |
|---|--------------|-----------------|---------|
| Hyperuricemia   | 36           | 14              | P<0.05* |
| Normal uric acid  | 24           | 46              |         |
| *Statistically significant. NAFLD: Non-alcoholic fatty liver disease  |              |                 |         |
| <b>Table-2:</b> The association of serum uric acid levels between NAFLD (cases) and non-fatty liver (controls). |              |                 |         |

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- $\alpha$ ,<sup>26</sup> all of which are pro-inflammatory molecules and stimulate production of C-reactive protein in the liver.<sup>27</sup> 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.<sup>28</sup>

## CONCLUSION

Study concluded that increased serum uric acid concentrations are a risk factor in NAFLD. The possible pathogenetic role of uric acid in NAFLD and the metabolic syndrome deserves to be further studied.

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