

# Association of Serum Uric acid Level and BMI in NAFLD and Healthy Volunteers

Ajoy Tiwari, Vineeta Tewari, Jay Tewari

**Abstract**—A number of studies have reported that exact aetiology of non alcoholic fatty liver disease NAFLD is unknown. Serum uric acid is often incriminated as the etiological agent. Hence this study was taken up explore the role of BMI and serum uric acid in occurrence of NAFLD. A case control study was undertaken to compare the role of serum acid in occurrence of 100 NAFLD cases with 100 healthy volunteers. All the cases and controls were subjected for ultrasound examination and serum uric acid estimation with height and weight. Most of study subjects belonged to 21 – 40 years of age group and females outnumbered males. The Mean BMI among the cases was 25.34 ( $\pm$  4.44) and controls was 25.12 ( $\pm$  4.08). Mean serum uric acid level among the cases was 5.68 mg/dl and 4.14 mg/dl among the controls. BMI was more than 25 in 51% of the cases and 54% of the controls. Hyperurecemia was present in 37% of the NAFLD cases and 16% of the healthy volunteers. The author concludes that, the increased serum uric acid was demonstrated as risk factor for non alcoholic fatty liver disease.

**Index Terms**— Aetiology, BMI, Controls, Serum Uric Acid, NAFLD.

## I. INTRODUCTION

Non alcoholic fatty liver (NAFLD) is an important public health problem due to its high prevalence [1]. It mainly represents a spectrum of conditions varying from steatosis to non-alcoholic steatohepatitis (NASH) and cirrhosis.

The prevalence of NAFLD is often rising due to “Obesity epidemic” varying from 14 – 31% in the general population [2]. It has become an emerging problem in countries like India and often reported to increase in the prevalence in near future [3], [4].

The risk factors resulting in to the NAFLD are not known. The prevention of NAFLD warrants the identification of the risk factors. The studies have shown that, there is a close relationship between the serum uric acid levels (SUA) and risk of NAFLD [5].

The research also reported that, high activity of serum xanthine oxidoreductase in NAFLD patients, which catalyzes the formation of uric acid and then the increased generation of uric acid and then increased generation of uric acid is able to accelerate the development of NAFLD mediated by Xanthine oxidoreductase [6].

Elevated uric acid levels have shown to induce the triglyceride accumulation by promoting the over expression of pro lipogenic enzymes sterol regulatory element binding proteins [7].

Obesity has been shown to be a risk factor for NAFLD. It can also occur in non obese subjects. The estimate shows that, the prevalence varies from 15% to 21% in non – obese Asians with body mass index of less than 25. It is often considered as earliest predictor of metabolic disorders and an important cause of cryptogenic liver disease in normal – weight population.

NAFLD is also known to be associated with metabolic syndrome which bears BMI as an important component. Hence, this study was undertaken to compare and contrast serum uric acid levels and BMI in patients with NAFLD and normal cases.

## II. MATERIAL AND METHODS

A case control study was undertaken in the department of General Medicine of a Medical College for a period of three years between January, 2015 to December, 2018. A total of 100 NAFLD cases and 100 healthy volunteers with non fatty liver constituted the study sample. Clearance from institutional ethics committee was obtained before the study was started. An informed consent was obtained from all the cases and controls.

Patients aged between 18 – 60 years of both the sexes were included in to the study. The patients with history of smoking, alcohol consumption, diabetes mellitus, hypertension, history of liver disease including hepatitis and those who were on hepatotoxic drugs were excluded from the study.

The patients were instructed to come in fasting for not less than 12 hours to the examination and not to exercise one day prior to the examination. The standing height and weight were measured without shoes. A baseline ultrasound examination was carried out on all cases and controls by an experienced radiologist.

Hepatic steatosis was diagnosed by its characteristic echo patterns including evidence of diffuse hyperechogenicity of the liver and poor visualization of intra hepatic structures. The data thus obtained was collected by using a proforma and compiled using Excel sheet.

## III. RESULTS

TABLE I. Distribution of the cases and controls according to age and sex

|           |                    | Cases n (%) | Controls n (%) |
|-----------|--------------------|-------------|----------------|
| Age group | Less than 20 years | 12 (12.0)   | 3 (3.0)        |
|           | 21 – 30 years      | 33 (33.0)   | 25 (25.0)      |
|           | 31 – 40 years      | 35 (35.0)   | 40 (40.0)      |
|           | 41 – 50 years      | 11 (11.0)   | 21 (21.0)      |
|           | 51 – 60 years      | 9 (9.0)     | 11 (11.0)      |
| Sex       | Male               | 45 (45.0)   | 48 (48.0)      |
|           | Female             | 55 (55.0)   | 52 (52.0)      |
| Total     |                    | 100 (100)   | 100 (100)      |

Published on August 7, 2020.

Ajoy Tiwari, Jai Clinic & Diabetes Care Centre, India.

(corresponding e-mail: docajoy@gmail.com)

Vineeta Tewari, ERA's Lucknow Medical College & Hospital, India.

Jay Tewari, King George Medical University, India.

This study had shown that, about 35% of the cases and 40% of the controls were aged between 31 – 40 years. Majority of the cases and controls were females.

TABLE II. Distribution of the cases and controls according to mean BMI & Serum uric acid

| Mean $\pm$ SD   | Cases            | Controls         | T value | P value, Sig |
|-----------------|------------------|------------------|---------|--------------|
| BMI             | 25.34 $\pm$ 4.44 | 25.12 $\pm$ 4.08 | 0.37    | 0.712, NS    |
| Serum-Uric Acid | 5.68 $\pm$ 1.43  | 4.14 $\pm$ 0.46  | 10.25   | 0.000, Sig   |

Mean BMI among the cases was 25.34 ( $\pm$  4.44) and controls was 25.12 ( $\pm$  4.08). Mean serum uric acid level among the cases was 5.68 mg/dl and 4.14 mg/dl among the controls was statistically significant between NAFLD cases and healthy volunteers.

TABLE III. Distribution of the cases and controls according to BMI categories

| BMI          | Cases n (%) | Controls n (%) |
|--------------|-------------|----------------|
| Less than 25 | 49 (49.0)   | 46 (46.0)      |
| More than 25 | 51 (51.0)   | 54 (54.0)      |
| Total        | 100 (100.0) | 100 (100.0)    |

$\chi^2$  Value=0.18, df=1, P value, Sig=0.671, NS

BMI was more than 25 in 51% of the cases and 54% of the controls. This difference in BMI was statistically significant between the NAFLD cases and Healthy volunteers.

TABLE IV. Distribution of the cases and controls according uric acid levels

| Hyperurecemia | Cases n (%) | Controls n (%) |
|---------------|-------------|----------------|
| Absent        | 63 (63.0)   | 84 (84.0)      |
| Present       | 37 (37.0)   | 16 (16.0)      |
| Total         | 100 (100.0) | 100 (100.0)    |

$\chi^2$  Value=11.321, df=1, P value, Sig=0.001, Sig

Hyperurecemia was present in 37% of the NAFLD cases and 16% of the healthy volunteers. This difference was statistically significant between the cases and controls.

#### IV. DISCUSSION

This study was mainly undertaken to compare and contrast serum uric acid levels and BMI in patients with NAFLD and normal cases. This study had shown that, cases were aged around 21–40 years of age. Females outnumbered males in this study. A similar study by Mohan et al, also reported same results [9]. A similar study by Bansal et al had also shown similar findings [10].

The mean BMI among the cases was 25.34 ( $\pm$  4.44) and controls was 25.12 ( $\pm$  4.08). BMI was more than 25 in 51% of the cases and 54% of the controls. In a study by Mohan et al, the mean BMI was 27.01 among the NAFLD cases and 23.91 among the controls [9]. In a study by Bansal et al, The mean BMI of NAFLD cases was 32 and 27 among controls in contrast to this study results [10].

Mean serum uric acid level among the cases was 5.68 mg/dl and 4.14 mg/dl among the controls was statistically significant between NAFLD cases and healthy volunteers.

Hyperurecemia was present in 37% of the NAFLD cases and 16% of the healthy volunteers. This study had shown an independent association of uric acid with NAFLD. A study by Mohan et al had reported that, the mean serum Uric acid levels in NAFLD cases was 5.73 and 4.97 among the controls. Bansal et al had reported that, the mean serum Uric acid levels were 6.78 in the NAFLD cases and 4.28 among the controls [10]. Shi et al had reported that, the serum uric acid was an independent risk factor for the biopsy proven hepatic steatosis cases with chronic hepatitis B infection [11]. An epidemiological study by Li et al also reported the same in apparently healthy Chinese subjects at the beginning and also at the end of 3 years of follow up [12]. A study by Zheng et al had reported a positive association between the elevated serum uric acid levels and the risks of NAFLD in non obese Chinese population [13].

The studies available explains a “two hit hypothesis” where first hit due to excessive accumulation of fat in hepatocytes resulting in insulin resistance. Second hit is due to oxidative stress to hepatocyte injury, inflammation and subsequently fibrosis [9], [14].

#### V. CONCLUSION

From the results of this study, the author concludes that, the increased serum uric acid was demonstrated as risk factor for non alcoholic fatty liver disease. The exact mechanism of the effect of uric acid as a risk factor should explored further.

#### REFERENCES

- [1] E. Hashimoto, M. Tanai, K. Tokushige, “Characteristics and diagnosis of NAFLD/NASH,” *J Gastroenterol Hepatol*, vol. 28, no. (Suppl 4), pp. 64-70, 2013.
- [2] P. Angulo, “GI epidemiology: non-alcoholic fatty liver disease,” *Aliment Pharmacol Ther*, vol. 25, pp. 883–9, 2007.
- [3] M. J. Bos, P. J. Koudstaal, A. Hofman, J. C. Witteman, M. M. Breteler, “Uric acid is a risk factor for myocardial infarction and stroke: the Rotterdam study,” *Stroke*, vol. 37, pp. 1503–7, 2006.
- [4] A. Dehghan, M. van Hoek, E. J. Sijbrands, A. Hofman, J. C. Witteman, “High serum uric acid as a novel risk factor for type 2 diabetes,” *Diabetes Care*, vol. 31, 361–2, 2008.
- [5] C. Xu, C. Yu, L. Xu, M. Miao, Y. Li, “High serum uric acid increases the risk for nonalcoholic fatty liver disease: a prospective observational study,” *PLoS ONE*, vol. 5, no. e, pp. 11578.
- [6] J. Zhang, C. Xu, Y. Zhao, Y. Chen, “The significance of serum xanthine oxidoreductase in patients with nonalcoholic fatty liver disease” *Clin Lab*, vol. 60, pp. 1301–7, 2014.
- [7] Y. J. Choi, H. S. Shin, H. S. Choi, J. W. Park, I. Jo, E. S. Oh, et al, “Uric acid induces fat accumulation via generation of endoplasmic reticulum stress and SREBP-1c activation in hepatocytes,” *Lab Invest*, vol. 94, pp. 1114–25, 2014.
- [8] C. J. Liu, “Prevalence and risk factors for non-alcoholic fatty liver disease in Asian people who are not obese” *J Gastroenterol Hepatol*, vol. 27, pp. 1555–60, 2012.
- [9] J. Mohan, R. Ramanathan, L. Velliangiri, D. Thangavel, V. Rangan, V. Subramaniam, “Association of serum uric acid level and body mass index between non-alcoholic fatty liver disease patients and healthy volunteers,” *Int J Adv Med*, vol. 1, pp. 234-7, 2014.
- [10] A. Bansal, R. Lohokare, P. D. Sarkar, P. Harganekar, “Study of serum uric acid levels and BMI in patients with NAFLD, a observational study at a tertiary care centre of Central India,” *International Journal of Contemporary Medical Research*, vol. 4, no. 5, pp. 1050-1052, 2017.
- [11] J. P. Shi, J. G. Fan, R. Wu, X. Q. Gao, L. Zhang, H. Wang, et al, “Prevalence and risk factors of hepatic steatosis and its impact on liver injury in Chinese patients with chronic hepatitis B infection,” *J Gastroenterol Hepatol*, vol. 23, no. 9, pp. 1419-25, 2008.

- [12] Y. Li, C. Xu, C. Yu, L. Xu, M. Miao, "Association of serum uric acid level with non-alcoholic fatty liver disease: a cross-sectional study," *J Hepatol*, vol. 50, no. 5, pp. 1029-34, 2009.
- [13] X. Zheng, L. Gong, R. Luo, "Serum uric acid and non alcoholic fatty liver disease in non obesity Chinese adults," *Lipids in Health and Disease*, vol. 16, pp. 202, 2017.
- [14] X. Sui, T. S. Church, R. A. Meriwether, F. Lobelo, S. N. Blair, "Uric acid and the development of metabolic syndrome in women and men," *Metabolism*, vol. 57, no. 6, pp. 845-52, 2008.