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Study of the Relationship Between Uric Acid and Severity of Non-alcoholic Fatty Liver among Patients Referred in Kermanshah University of Medical Sciences' Clinics

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Abstract: Fatty liver disease in non-alcoholic patients is among diseases causing changes in the body's metabolism, especially lipid metabolism. Therefore, with changes in the metabolism of fatty liver, uric acid can be expected to rise in the body. This study was conducted to determine the relationship between levels of uric acid and the severity of non-alcoholic fatty liver disease in patients referred to Kermanshah University of Medical Sciences affiliated clinics in 2016. This study was a cross-sectional and analytical research. The subjects included all patients referred to clinics within the city of Kermanshah that their non-alcoholic fatty liver disease diagnosis and grade had been confirmed by ultrasound. By available sampling method, 215 subjects were selected. In a single laboratory, using the same assay kit their uric acid and other blood biochemical tests were evaluated and the resulted data were analyzed using SPSS Version 18. The results showed that the mean blood uric acid level of samples was equal to 6.44±1.55 mg dL^{-1}. The mean values in men and women were as 6.95 and 5.88 mg dL^{-1}, respectively that the difference was statistically significant ($p<0.05$). The mean value of blood uric acid of the samples would rise according to the non-alcoholic fatty liver grade. The ANOVA and Spearman ranking test showed no significant difference and relationship. The study results showed that high levels of uric acid in patients with fatty liver disease can be strong evidence on the severity of patients' fatty liver. Therefore, to find out the situation and severity of fatty liver of patients they should be examined and followed up with more accurate methods like ultrasound, biopsy or advanced imaging methods.

Key words: Acid uric, nonalcoholic fatty liver, Kermanshah, metabolism, sciences-affiliated clinics

INTRODUCTION

Liver tissue is seen on ultrasound as an accumulation of uniform echoes with a special tissue (Savadkouhi *et al*., 2003). When lipids form >5% of the liver weight, it is referred to as fatty liver (Gahan and Barry, 1998). In the process of fatty liver, the liver parenchymal tissue is accumulated with fat cells. In non-alcoholic fatty liver, fat accumulates in the liver cells in the absence of alcohol consumption or other hepatic diseases. Nonalcoholic fatty liver is more common in adults due to obesity, hyperlipidemia, diabetes type II, pregnancy, prolonged starvations and prolonged use of some of drug (Cai *et al*., 2014). Ultrasound or sonography is the most common method used to assess the fatty liver condition in clinics and studies on individuals (Hernaez *et al*., 2011). Today, some restrictions are argued on the use of ultrasound that the most important ones are as follows: assessment of fatty liver status subjectively, results dependence on the skill of the sonographer as well as limitation in determining the amount of fat accumulated in liver cells (Adams and Talwalkar, 2006).

Today, the hypothesis of a relationship between non-alcoholic fatty liver and high levels of uric acid has been considered on many studies (Cardoso *et al*., 2013; Ryu *et al*., 2011; Sertoglu *et al*., 2014; Shih *et al*., 2015). Many studies have been done in this regard (Sertoglu *et al*., 2014; Shih *et al*., 2015). Normal levels of uric acid have been introduced in many studies as a protector of neurotic system. High levels of uric acid in addition to causing a high risk condition of cardiovascular problems occurrence for patients can cause insulin resistance, type II diabetes as well as metabolic syndrome. Fatty liver disease in non-alcoholic patients is also among those diseases that cause changes in the body metabolism, especially lipid metabolism and the fatty liver can lead to insulin resistance, type II diabetes, hypertension, etc. (Cardoso *et al*., 2013). Xanthine oxidase

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Table 1: Normality test of variables (Uric Acid, Wight, Age, High, FBS, TG, Chol, LDL, HDL)

Index/variables	Mean	SD	Z Kolmogorov-Smirnov	Sig.
Uric acid	6.44	1.51	0.900	0.392
Weight	81.98	12.36	1.280	0.076
High	170.00	9.85	1.340	0.055
Age	44.87	11.59	0.972	0.302
FBS	94.86	17.62	1.360	0.045
TG	210.44	94.48	2.530	0.000
Cholesterol	207.18	41.15	0.940	0.335
HDL	44.94	15.49	2.130	0.000
LDL	120.58	34.34	0.755	0.620

enzyme causes the formation of uric acid from xanthine oxidase and hypo xanthine oxidase in the body. In the human body, uric acid is produced from purine metabolism and excreted in the urine. Therefore, with occurring changes in the metabolism of body in fatty liver condition, uric acid levels can be expected to increase in the body (Sertoglu *et al*., 2014). According to various studies and conflicting results in this regard where some studies have confirmed the relationship between blood uric acid levels and fatty liver and others have rejected it, finding the association between uric acid levels and non-alcoholic fatty liver can then be very useful in the treatment and care of these patients. In addition, lack of similar studies in Iran convinced the researcher to perform a study to determine the association between blood uric acid levels and the severity of non-alcoholic fatty liver disease in Kermanshah (Table 1).

MATERIALS AND METHODS

This was a cross-sectional and analytical study conducted to examine the relationship between uric acid levels and grade levels of fatty liver in patients with non-alcoholic fatty liver disease. The study population included all patients referred to internal medicine clinics of Imam Khomeini (RA) hospital and Doctor Nawabi internal medicine clinic in the city of Kermanshah which had the inclusion criteria (no use of alcohol, absence of liver disease or any malignancy, absence of diabetes type 1 and 2, no history of high levels of blood uric acid) and interested in participating in the study that were selected by available sampling method. After sampling, first, a demographic information form was used to gather data. The form included demographic characteristics questions (age, gender, marital status, weight and occupation). Then, blood samples were taken from all patients willing to participate in the study for whom the non-alcoholic fatty liver diagnosis had been confirmed by ultrasound to measure uric acid levels and do other biochemical tests (fasting plasma glucose, triglycerides and cholesterol, liver enzymes (SGOT, SGPT and ALK-ph., HDL, LDL)). Also, for detection of the fatty liver severity, the patients were sent to understand clinic of Imam Khomeini hospital. Sonography was performed with a single device by a specialist in the unit. Blood tests (level of uric acid and other tests) weredone by a laboratory with calibrated devices. All tests were performed in the laboratory of Imam Khomeini (RA) hospital with a single device by using Pars Azmoon kits (Table 2).

Table 2: Mean of sample's uric acid based nonalcoholic fatty liver

Index/fatty.liver	Mead	SD	F-value	Sig.
Grade 1	6.360	1.60	0.829	0.438
Grade 2	6.500	1.35		
Grade 3	7.014	1.75		

RESULTS AND DISCUSSION

Form a total of 226 subjects with respect to non-completion of some information, only 215 cases could be investigated. Doing Kolmogorov-Smirnov test, the variables such as age, weight, height, blood uric acid levels, blood cholesterol and LDL levels of the subjects appeared to be normal but fasting blood glucose, triglycerides and HDL levels of the subjects did not follow a normal distribution.

The status of fatty liver of the subjects and other demographic variables are given in Table 3. In relation to the average blood uric acid levels based on non-alcoholic fatty liver grade, uric acid levels in patients with fatty liver grade I-III were equal to 6.36±1.6, 6.5±1.35 and 7.014±1.78, respectively. Doing analysis of variance no differences were seen between the means values of uric acid in the three groups of subjects.

In this study, the blood uric acid levels higher than 7 mg dL^{-1} in men and 6 mg dL^{-1} in women were considered as hyperuricemia. In men, the highest rate of hyperuricemia was seen in grade III; thus, 100% of patients in this grade had hyperuricemia. In women, 57.1% of patients in grade II and 60% of patients in grade III had hyperuricemia.

The Spearman ranking coefficient between the grades of non-alcoholic fatty liver and the average blood uric acid levels of subjects was equal to 0.109 which had no significant relationship.

The results showed that 55.8% of patients had fatty liver grade I while 40.9% and only 3.3% had fatty liver grade II and III, respectively. The results a study by Ardakani *et al*. (2015) on children with non-alcoholic fatty liver showed 91.5% grade I and 8.5% grade II. In a study by Seebu and Junise conducted in the state of Kerala in India, the patients were in three categories of grade I-III . Taghavi study had been conducted on children. It is therefore expected that the majority of patients have non-alcoholic fatty liver disease grade I. But in our study,

Table 3: Frequency of hyperuricemia among samples based sex

Hyperuricemia fatty liver	Hyperuricemia G1	Hyperuricemia G2	Hyperuricemia G3	Normal G1	Normal G2	Normal G3	No (%) hyperuricemia
Male	41.4	41.5	100	58.6	58.5	0	43 (42.6)
Female	41.2	57.1	60	58.5	42.9	40	44 (48.4)

the average age was over 44 years; thus, the presence of fatty liver grade II and II as well as variation in the rate and percentage of grades seems to be probable. The results showed that mean value of blood uric acid levels of the subjects was equal to 6.44±1.51 mg dL^{-1} which was respectively equal to 6.95 and 5.88 mg dL^{-1} in men and women with a statistically significant difference. The results of Seebu and Junise study also reported serum levels of uric acid in men and in women as 5.7 and 4 mg dL^{-1}, respectively (Ardakani *et al*., 2015). The levels of uric acid by Kucukazman *et al.* (2014) study were also reported about 6 mg dL^{-1} with a significant difference in men and women. Yong-Jae study had also reported the levels of uric acid in men as 339 and 237.9 μmol L^{-1} in women (Lee *et al*., 2010). The results of Ryu *et al.* (2011) study had also reported the mean uric acid levels in non-alcoholic fatty liver patients as 5.6 mg dL^{-1} in men (Ryu *et al*., 2011). The study results indicated that the mean value of blood uric acid of the subjects rises according to the grade of non-alcoholic fatty liver disease. In this study, the mean value of uric acid in patients with fatty liver grades I-III were respectively as 6.36, 6.5 and 7 mg dL^{-1}. Analysis of variance showed no significant differences. As can be seen with increasing fatty liver grade, the uric acid level also rises. The results of Sirota *et al.* (2013) also suggested increased levels of uric acid with an increase in the fatty liver grade. In their study, the difference had been reported significant (Sirota *et al*., 2013). The results of different studies showed that with increased level of serum uric acid, the incidence of fatty liver would also increase (Sertoglu *et al*., 2014; Xu *et al*., 2010; Lonardo *et al*., 2015). Lanespa *et al.* (2012) also emphasized that increased intensity of non-alcoholic fatty liver can be an important factor for increased level of blood uric acid. In some of these studies, this increase in blood uric acid levels with fatty liver severity was significant (Lee *et al*., 2010; Lanaspa *et al*., 2012; Jookar *et al*., 2015; Li *et al*., 2009). However, in our study, the difference of uric acid levels due to the severity of fatty liver was not significant which could possibly be related to the limitations of our study; since, we conducted the studies only in one group and the samples also included only about 200 subjects. If the research was done as a case-control study in two groups or with a higher number of samples, the results could be more different. In this study, we considered the uric acid levels greater than 7 mg dL^{-1} in men and 6 mg dL^{-1} in women as hyperuricemia that in men, 100% of subjects with fatty liver had hyperuricemia. In case of grades I and II, the rate was as 41% among men but in women with increased fatty liver grade, the rate of hyperuricemia also increased with about 41, 57 and 60% in subjects with grades I-III, respectively. The results of Lee *et al.* (2010) also suggested an increase in uric acid levels and occurrence of severe hyperuricemia in patients with fatty liver (Lee *et al*., 2010). The results of other studies also indicated the incidence of hyperuricemia in severe non-alcoholic fatty liver (Ryu *et al*., 2011; Sirota *et al*., 2013; Xu *et al*., 2010).

The results showed that doing the Spearman ranking test, no significant relationship were observed between the fatty liver grade of the subjects and the average level of blood uric acid. However, this relationship was significant in several studies (Shih *et al*., 2015; Sirota *et al*., 2013; Xu *et al*., 2010; Jookar *et al*., 2015; Petta *et al*., 2009, 2011). But Cardoso *et al.* (2013) study results also demonstrated the relationship insignificant.

CONCLUSION

The study results showed that high levels of blood uric acid in patients with fatty liver cannot be a strong evidence of the severity of fatty liver in patients. Then, to understand the situation and the severity of fatty liver, the patients should be examined and followed up with more accurate methods like ultrasound, biopsy or advanced imaging approaches.

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