Level of Serum Uric Acid in Patients with Cirrhosis of Liver.

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ABSTRACT… Objectives: To determine the serum uric acid levels among the patients of liver cirrhosis. Study Design: Cross Sectional, Descriptive study. Setting: Department of Medicine, Indus Medical College, Tando Muhammad Khan. Period: 6 months (23 April 2019 to 23 October 2019). Material & Methods: Patients of liver cirrhosis attending the medical OPD or admitted in the Medicine ward, meeting selection criteria included in this study. Any diseases other than liver disease, disturbing uric acid levels were excluded from the study. Other exclusion criteria were type 2 and 1 Diabetes mellitus, drugs altering serum uric acid levels, gout, pregnancy and chronic kidney disease. Results: In this study, the causes of liver cirrhosis revealed were hepatitis B 5 (5.15%), hepatitis C 44 (45.36%), both hepatitis B and C 4 (4.12%), NAFLD 34 (34.05%) and alcohol 10 (10.31%) respectively. Mean of the serum uric acid (mg/dl) compared in liver cirrhosis due to different etiologies Mean ±SD of uric acid levels due to hepatitis B, hepatitis C, both hepatitis B and C, NAFLD and alcohol were 2.66±1.4, 2.22±0.3, 2.34±1.0, 7.70±0.9 and 6.69±2.0 respectively; these all compared by one way ANOVA, (p value <0.01) with df (degree of freedom) 4. Serum uric acid levels are raised among the NAFLD patients in this study that is warning factor for cardiovascular disease. In this research hypouricemia has been observed among the patients of liver cirrhosis due to hepatitis B, hepatitis C, both hepatitis B and C, NAFLD and alcohol as 5.15%, 45.36%, 4.12%, 2.06% and 8.25% respectively while hyperuricemia has been observed among the cirrhotic patients due to NAFLD. Conclusion: Serum uric acid levels are raised among the liver cirrhosis patients with NAFLD while decreased among cirrhotic patients with viral hepatitis. Further the area is open for further research to determine the underlying mechanisms.

Key words: Hepatitis B, Hepatitis C, Liver Cirrhosis, NAFLD, Uric Acid.

INTRODUCTION
Uric acid is formed as the end-product after the metabolism of purine nucleotides. It accounts about 60 % of the antioxidant capability in plasma.¹ Cirrhosis is a grave and irreparable disease and fundamental cause of death and also ill health globally. It develops as the result of worsening of chronic liver disease (CLD). It is characterized by fibrosis and generation of regenerative nodules in hepatic tissue, leading to advanced loss of normal hepatic architecture as well as liver functions. Cirrhosis has been identified as the most leading cause of mortality amongst the Pakistan population and also the frequent reason for admission in the hospitals and visiting outpatient department.² Liver cirrhosis remains in a silent stage until decompensating. Decompensation is determined by ascites, bleeding from esophageal varices or hepatic encephalopathy. There are chances of evolving to hepatocellular carcinoma among the almost 15% of cirrhotic patients.³ Hepatitis C virus (HCV), hepatitis B virus (HBV) and hepatocellular carcinoma has been observed as the key reasons for severe liver disease and also the cirrhosis-related end-stage liver disease. According to World Health Organization (WHO) estimations, 350 million individuals are suffering from hepatitis B as well as 170 million patients has been found infected with HCV at global level.⁴ Setiawan et al has shown in his study about non-alcoholic fatty liver disease (NAFLD) as the highest source of cirrhosis in the entire cohort (29.3%).⁵ Prevalence of NAFLD among Sindhis was 35.3%
according to a study conducted by Shah AS and his coworkers.\(^6\) Independent of their etiologies, all chronic liver disease patients eventually lead to hepatic cirrhosis, that is the major health concern throughout world.\(^7\) There are adequate suggestions that raised serum uric acid has been allied with cardiovascular complications that may lead to death.\(^8\) It has been hypothesized that levels of the serum uric acid may be amplified in liver cirrhosis; with this background the current study was piloted to assess the serum uric acid levels among liver cirrhosis patients.

**OBJECTIVE**
To determine the serum uric acid levels among the patients of liver cirrhosis.

**MATERIAL & METHODS**
This cross sectional study was conducted. Medicine Department of Indus Medical College, Tando Muhammad Khan for 6 months (23 April 2019 to 23 October 2019).

The Sampling technique was nonprobability purposive sampling.

Inclusion Criteria
Patients of liver cirrhosis attending the medical OPD or admitted in the Medicine ward included in the study.

Exclusion Criteria
Any diseases other than liver disease, disturbing uric acid levels were excluded from the study. Other exclusion criteria were type 2 and 1 Diabetes mellitus, drugs altering serum uric acid levels, gout, pregnancy and chronic kidney disease.

After thorough history, taking informed consent, explaining the purpose of study, confirmation of liver cirrhosis on abdominal ultrasound, all the patients meeting the selection criteria were recruited in the study. After all aseptic measures their i/v blood samples were taken to determine serum uric acid levels. Hyperuricemia considered when serum uric acid levels were found > 7 mg/dl among male and > 6.0 mg/dl in female individuals.

**RESULTS**
Mean age in this study is 44.56 years ±5.7 in males and 44.50 years ±6.0 in females. Mean serum uric acid in mg/dl among males is 5.52±2.8 and among females is 3.71±2.4 (p value 0.009).

In this study, the causes of liver cirrhosis revealed were hepatitis B 5 (5.15%), hepatitis C 44(45.36%), both hepatitis B and C 4(4.12%), NAFLD 34 (34.05%) and alcohol 10(10.31%) respectively. Figure-1

Mean of the serum uric acid (mg/dl) compared in liver cirrhosis due to different etiologies Mean ±SD of uric acid levels due to hepatitis B, hepatitis C, both hepatitis B and C, NAFLD and alcohol were 2.66±1.4, 2.22±0.3, 2.34±1.0, 7.70±0.9 and 6.69±2.0 respectively; theses all compared by one way ANOVA, (p value <0.01) with df (degree of freedom) 4. Serum uric acid levels are raised among the NAFLD patients in this study that is warning factor for cardiovascular disease. Table-I

In this research hypouricemia has been observed among the patients of liver cirrhosis due to hepatitis B, hepatitis C, both hepatitis B and C, NAFLD and alcohol as 5.15%, 45.36%, 4.12 %, 2.06% and 8.25% respectively while hyperuricemia has been observed among the cirrhotic patients due to NAFLD. Figure-2

**DISCUSSION**
Different uric acid levels has been observed by diverse research studies among the patients of liver cirrhosis. Among the CLD patients, raised serum uric acid levels are found to be linked to more severe disease condition.\(^9\) Nevertheless, there are limited numbers of studies showing the trends of uric acid levels in liver cirrhosis due to different etiologic factors. Most common cause of liver cirrhosis in this study (n=97) is hepatitis C, that is similar to various studies that also reveal hepatitis C as the extreme frequent basis of liver cirrhosis amongst the developing nations\(^10,11,12\), and this is probable that more than 185 million publics exist anti-HCV seropositive generally.\(^12\)
Next to the hepatitis C, NAFLD has been found to be the utmost widespread ground for advancement towards liver cirrhosis. NAFLD leads to steatohepatitis and ultimately hepatocellular carcinoma. This finding is in contrast to other Pakistani studies that reveal NAFLD most prevalent in European countries.

Blood uric acid was detected in 223 patients with hepatitis B cirrhosis and 106 normal controls by some researcher and results showed that the level of serum uric acid in patients with cirrhosis were significantly lower than normal. Similarly, in this study also, decreased uric acid levels has been revealed in patients with cirrhosis due to hepatitis B as well as in the patients suffering from both hepatitis B and C. In this study, uric acid levels are raised among the patients of NAFLD, this finding is similar to research studies by Millic S et al., Khosla UM, et al. and Sertoglu E et al.

Table-I. Descriptive statistics of study population (n=97)

|                | Gender | N  | Mean | Std. Deviation | Std. Error Mean | P-Value |
|----------------|--------|----|------|----------------|-----------------|---------|
| Age            | Male   | 49 | 44.69| 5.702          | .815            | 0.376   |
|                | Female | 48 | 44.50| 6.049          | .873            |         |
| Serum uric acid (mg/dl) | Male   | 49 | 5.5282| 2.85277       | .40754          | 0.009   |
|                | Female | 48 | 3.7159| 2.40704       | .34743          |         |

Table-II. Mean of the serum uric acid levels (mg/dl) among patients of liver cirrhosis (n=97)
P value <0.01 with df =4
**highly significant
Serum uric acid in liver cirrhosis

who revealed that hyperuricemia is a common finding in patients with NAFLD. Mean serum uric acid levels observed in this study are 7.7 mg/dl. A higher mean ±standard deviation of serum uric acid level observed among patients with NAFLD (7.04±1.61) in one of the research study similarly. Elevated serum uric acid levels intensely reflect and might lead to the oxidative stress, insulin resistance as well as the progression to metabolic syndrome and these all are well known risk factors for poor prognosis of CLD patients.17

CONCLUSION
Serum uric acid levels are raised among the liver cirrhosis patients with NAFLD while decreased among cirrhotic patients with viral hepatitis. Further, the area is open for further research to determine the underlying mechanisms.

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| 1     | Ramesh Kumar Suthar     | Data collection, concept and drafting.                        |                     |
| 2     | Kavita Bai              | Statics and Data analysis.                                    |                     |
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