



Journal Homepage: - www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/16719

DOI URL: <http://dx.doi.org/10.21474/IJAR01/16719>



RESEARCH ARTICLE

STUDY OF SERUM URIC ACID LEVELS IN CIRRHOSIS OF LIVER AND IT'S CORRELATION WITH CHILD PUGH SCORE

Dr. Kotule Pradnya Ashokrao¹, Dr. Ganesh U. Jadhao² and Dr. Baba S. Yelke³

1. Junior Resident, MD General Medicine.
2. Associate Professor, MD General Medicine.
3. Professor and HOD, MD General Medicine.

Manuscript Info

Manuscript History

Received: 20 February 2023

Final Accepted: 24 March 2023

Published: April 2023

Key words:-

Liver Cirrhosis, Uric Acid, Child Pugh Score, Alcoholic, Hematological, Biochemical

Abstract

Background: Liver cirrhosis is one of the most common causes of morbidity and mortality. Elevated serum uric acid (UA) levels strongly reflect progression of liver disease. Child Pugh Score used to assess the severity of cirrhosis of liver. The present study was undertaken to estimate the level of serum UA in liver cirrhosis patients and its association with the child Pugh score.

Method: A total 70 patients diagnosed with cirrhosis of liver, aged above 20 years were included in the study. For each patient, a modified Child Pugh Score were calculated. Blood samples were collected, and hematological and biochemical tests were performed.

Results: The mean serum UA level was 7.53mg/dl, and it was raised in patients with liver cirrhosis disease in relation to its severity. Alcoholic liver disease was the most common etiology for liver cirrhosis (80%). The mean serum AST and ALT level was 72.8mg/dl and 42.07mg/dl respectively, they were not increasing with increase in serum UA level. Whereas mean serum total bilirubin level and INR value was 2.73mg/dl and 2.02mg/dl respectively, they increased with increase in serum UA level. The mean serum albumin level was 2.6mg/dl and it decreased with increase in serum UA level. Serum UA levels increased as CTP score increased. Maximum UA levels were found in CTP class C (Mean 9.23mg/dl) and maximum mean UA levels (6.6mg/dl) were noted in alcoholic liver disease.

Conclusions: Serum UA level is an important part of spectrum of liver cirrhosis disease. UA is a mediator of inflammation and tissue damage; thus, it may be considered as a marker of severity of liver cirrhosis disease.

Copy Right, IJAR, 2023, All rights reserved.

Introduction:-

Liver diseases affect millions of people worldwide [1]. The Global Burden of Disease reported that over 1 million people died due to cirrhosis in 2010 [2]. Cirrhosis is defined as a diffuse process affecting the liver characterized by fibrosis and nodule formation. The common causes include excess alcohol intake, viral hepatitis, Non-Alcoholic Steatohepatitis (NASH) and autoimmune diseases. Alcoholism accounts for >50% of cases and Viral 30-70% [3]. In many patients of liver cirrhosis many hematological parameters are altered as hemoglobin, total leukocyte counts

Corresponding Author:- Dr. Kotule Pradnya Ashokrao

Address:- Junior Resident, MD General Medicine.

and platelets count, MCV. Raised or decreased total leukocytes count in case of spontaneous infections due to low immunity, Thrombocytopenia due to hypersplenism or sepsis. Other biochemical changes as hyponatremia, hypoalbuminemia, hypocalcemia or hypokalemia are also common in liver cirrhosis patient [4].

For predicting the prognosis of end stage liver disease and severity, various prognostic models are recommended. Child Pugh (CP) score is one such universally accepted prognostic score. Based on the CP score, chronic liver disease (CLD) patients can be categorized according to the severity of the disease. CP score is calculated by the five factors including ascites, encephalopathy, serum bilirubin, albumin, and prothrombin time. The score can range from the 5 to 15 points and is classified into three classes. Class A, B and C. Class A (5-6 points), Class B (7-9 points) and Class C (10 or above points) correspond to the disease severity [5].

In chronic liver disease of different etiologies, uric acid levels are found to be high. In human blood plasma, the reference range of uric acid is normally 3.4-7.2 mg/dL for men and 2.4 -6.1 mg/dL for women. In cases of non-alcoholic fatty liver disease (NAFLD), high uric acid levels are considered as independent etiological risk factors [6]. Also, a high uric acid level is known effect of alcohol metabolism and thus, hyperuricemia may be found in alcoholic liver disease [7]. Compared to the serum levels, the tissue levels of uric acid may be even better predictors of tissue injury [8]. Thus, serum uric acid may be considered as a marker of tissue damage. Although elevated serum uric acid levels strongly reflect and may even cause oxidative stress, insulin resistance, and metabolic syndrome, which are risk factors for the progression of liver disease. Serum UA levels are associated with the development of cirrhosis or the presence of elevated serum liver enzymes. A few studies are available in published literature and articles that focused on serum uric acid and its correlation with CTP Score. This study aims at the correlation of serum uric acid levels with Child Turcotte Pugh Score in CLD patients.

Materials and Methods:-

After obtaining Institutional Ethical Committee approval and written informed consent from all the patients, this cross sectional, observational study was conducted in the Department of Medicine, at Tertiary Health Center during a period from December 2020 – November 2022. A total 70 outpatients and inpatients diagnosed with cirrhosis of liver, aged above 20 years were included in the study. Patients with hematological malignancy (Leukemias and Lymphomas), gout, chronic kidney disease, sepsis, trauma, recent surgery, patients on chemotherapy and patients taking drugs (Frusemide, Thiazide, Allopurinol and Febuxostat) were excluded from the study.

We selected CLD patients of any etiology coming to medical OPD and admitted in tertiary health center. Hematological and biochemical workup includes measurement of hemoglobin, total leukocyte count, platelet count, prothrombin time, serum concentration of bilirubin (Total and Conjugated), serum albumin, SGOT and SGPT. For each patient, a modified Child Pugh Score were calculated. All patients were tested for HBsAg and antibodies to Hepatitis C virus to determine the cause of Liver Cirrhosis. Blood samples were collected, and Hematological and biochemical tests were performed by the following methods:

1. Hemoglobin, Total Leucocyte Count and Platelet Count by Ms4s2 Ms4se Auto analyzer based on spectrophotometric method.
2. Prothrombin Time by using semiautomatic coagulometer cysmex ca 50 by using rabbit brain liquid thromboplastin reagent.
3. Serum bilirubin level was calculated by calorimetric assay by Roche/Hitachi 911 analyzer: CAN.
4. SGOT /SGPT were measured turbo chem.
5. Serum albumin level was measured by turbo chem.
6. Other routine tests including Kidney Function Test, Fasting Plasma Glucose, ECG, Urine Examination and Chest X-ray were performed.

Statistical Analysis

Data was analysed using SPSS software Version 21.0. Qualitative data was analysed in terms of percentage (%) and proportions and Chi-square test was used as the test of significance. Quantitative data was analysed in terms of mean, standard deviation (SD) & standard error (SE). T-test was used as the test of significance. P value less than 0.05 was considered statistically significant.

Observations and Results:-

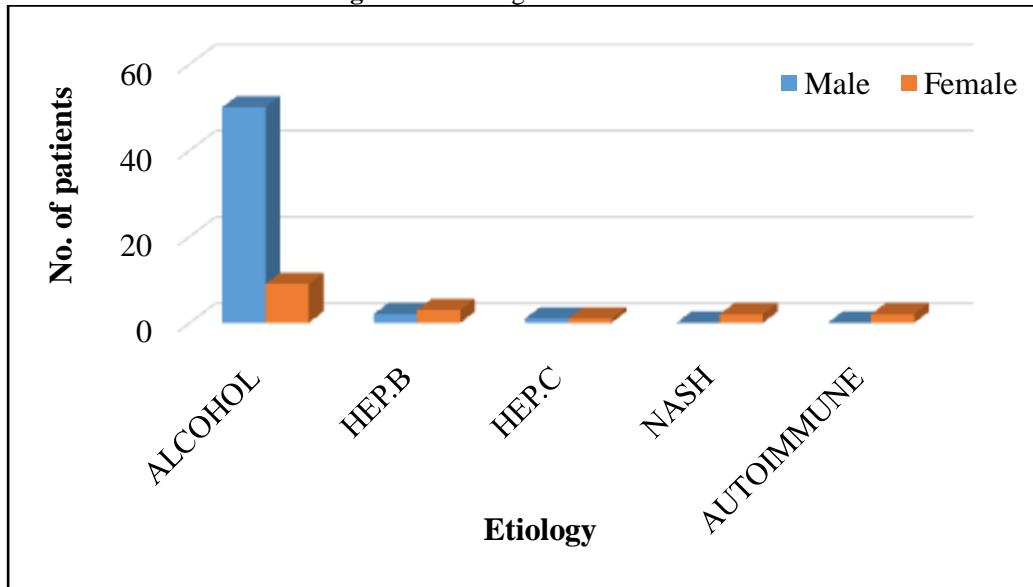
A total of 70 patients with cirrhosis of liver in the age group of above 20 years were enrolled in the study. Maximum number of cases were in the age group of 31 to 50 years (58.57%) with male predominance (75.72%) and maximum patients from rural area (71.42%) as shown in table 1.

Table 1:- Socio-demographic profile of the patients.

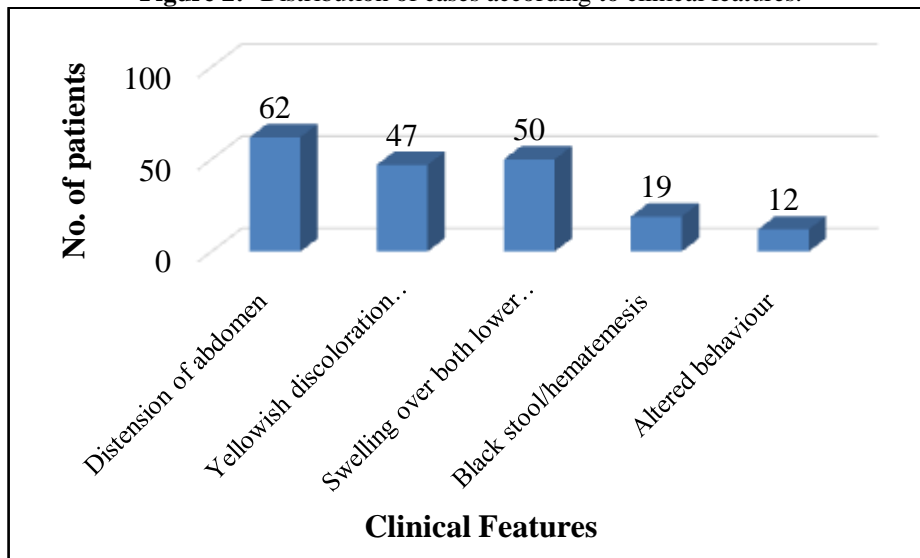
Demographic data		Frequency	Percentage
Age group in years	21 to 30	09	12.85
	31 to 40	27	38.57
	41 to 50	14	20.0
	51 to 60	10	14.28
	61 to 70	08	11.42
	71 to 80	02	2.85
	>80	00	0.0
Gender	Male	53	75.72
	Female	17	24.28
Residence	Urban	20	28.57
	Rural	50	71.42

Alcoholic liver disease was the most common etiology for CLD (80%) as depicted in figure 1.

Figure 1:- Etiological Classification.



The most common clinical feature was distension of abdomen (62) followed by swelling over both lower limbs (50) as depicted in figure 2.

Figure 2:- Distribution of cases according to clinical features.

Maximum cases had grade III ascites (54.28%), icterus present in 67.47%, pedal oedema in 71.42%, encephalopathy in 17.14% and anemia present in 95.71% of cases as shown in table 2.

Table 2:- Associated disease conditions.

Parameters		Frequency	Percentage
Ascites	GRADE I	08	11.42
	GRADE II	24	34.38
	GRADE III	38	54.28
Icterus	Present	47	67.47
	Absent	23	32.53
Pedal Oedema	Present	50	71.42
	Absent	20	29.28
Encephalopathy(N=12)	Grade I	03	4.28
	Grade II	03	4.28
	Grade III	04	5.7
	Grade IV	02	2.86
Anemia	Present	67	95.71
	Absent	03	4.28

Most of the patients had normal TLC count (62.85%). Platelet count, Sr sodium, Sr potassium were decreased in 61.42%, 41.43%, and 40% of patients respectively. Whereas Sr, bilirubin, SGOT, SGPT, prothrombin time (11-16sec) and level of PT/INR were raised in 52.85%, 74.28%, 61.43%, 55.71% and 55.72% of patients respectively. The maximum patients (51.42%) had serum albumin level<2.8, (Table 3).

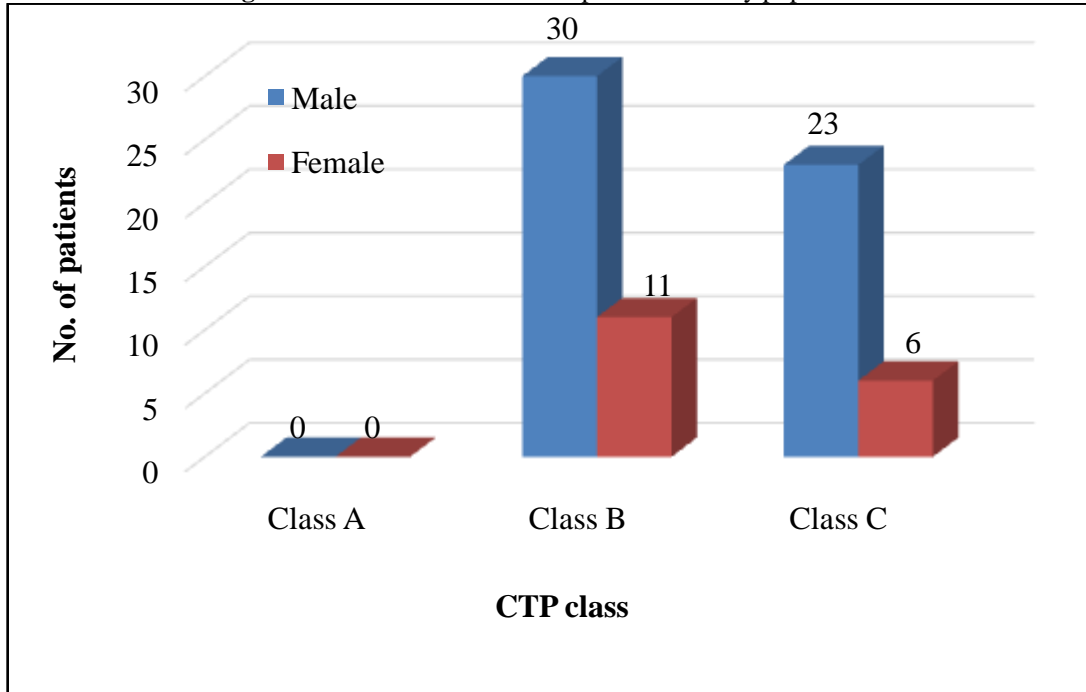
Table 3:- Laboratory parameters.

Parameters		Frequency	Percentage
TLC count	Normal (4-11000)	44	62.85
	Decreased<4000	06	8.57
	Raised>11000	20	28.57
Platelet count	Normal	27	38.57
	Decreased	43	61.42
SR. Sodium	Normal (135-145)	41	58.57
	Decreased<135	29	41.43
SR. Potassium	Normal (3.5-5.5)	42	60.0
	Decreased<3.5	18	40.0

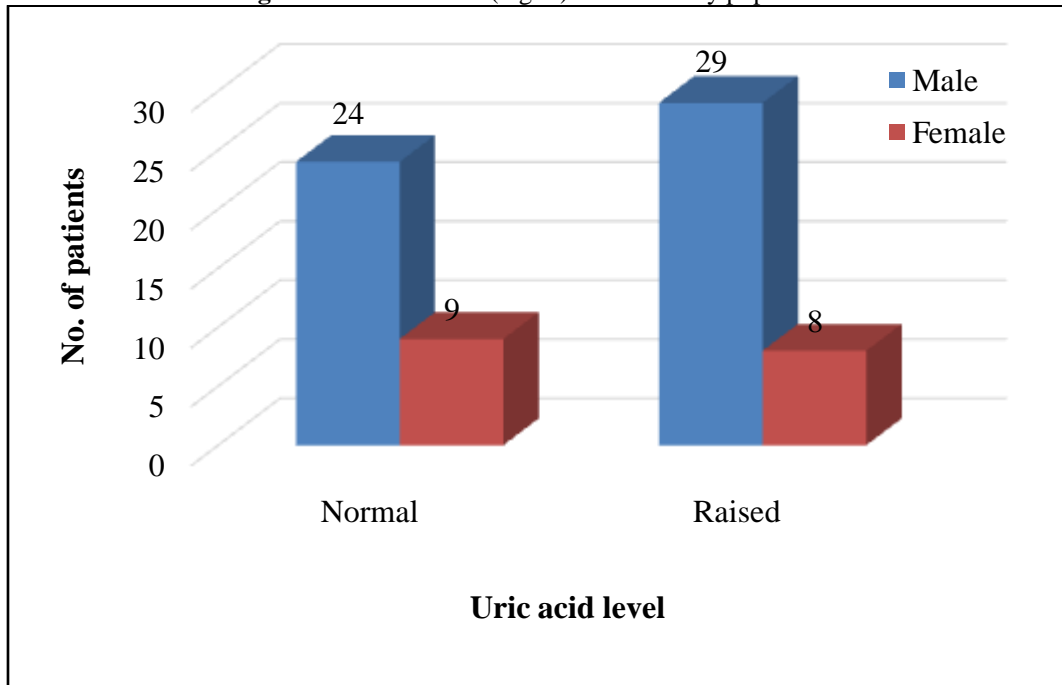
SR. Bilirubin	Normal <2	33	47.14
	Elevated 2-3	04	5.72
	Elevated>3	33	47.14
SGOT	Normal	18	25.72
	Raised>40	52	74.28
SGPT	Normal	27	38.57
	Raised>35	43	61.43
Prothrombin time (11-16sec)	Normal	31	44.29
	Raised>16	39	55.71
Level of PT/INR	Normal	31	44.28
	Raised>1.7	39	55.72
Serum albumin level	>3.5	02	2.85
	2.8-3.5	32	45.71
	<2.8	36	51.42

In class B there were 55.55% i.e., 41 out of which 30 were males and 11 females while in class C there were 44.55% i.e., 29 out of which 23 were male and 6 females, (Figure 3).

Figure 3:- CTP classes and no of patients in study population.



Sr Uric acid level was raised in 37 patients of them 29 were male and 8 were female as depicted in figure 4. Percentage of patients with serum uric acid levels increased with increasing severity of Chronic Liver Disease as assessed by Child Pugh Scoring

Figure 4:- Sr Uric acid (mg/dl) level in study population.

Various parameters like serum total bilirubin, INR, albumin, and grades of ascites were significantly associated with serum uric acid levels in liver cirrhosis disease patients. While liver enzymes like AST, ALT not that much associated with the severity of liver cirrhosis as shown in table 4.

Table 4:- Correlation of Sr. uric acid value and various study parameters.

Parameters		Normal uric acid (<7mg%)	Raised uric acid >7	P value
SR. Billirubin	Normal	17	16	0.03
	Raised >2	16	21	
SGOT	Normal	10	08	3.008
	Raised	19	33	
SGPT	Normal	14	13	2.06
	Raised	19	24	
Sr. Albumin	Normal >3.5	01	01	0.008
	<3.5	32	36	
Grades of ascites	Grade I	07	01	0.028
	Grade II	13	11	
	Grade III	13	25	
PT/INR	Normal	17	14	0.028
	>1.7	16	23	
CTP Class	Class A	00	00	-
	Class B	25	16	
	Class C	08	21	

Discussion:-

In the present study, serum uric acid levels were studied in relation to liver cirrhosis and various haematological and biochemical parameters. Total 70 patients of liver cirrhosis were enrolled in this study with mean age of presentation was 42.66 years (from above 12-yrs) with male predominance (75.72%) which is comparable with the previous studies [9-11]. Most of the cases were in 31-50 years age group and minimum cases in above 80 years age group and no patients in 12-20 years of age group. This may be due to the fact that it takes minimum 10-20 years of alcoholism to develop liver cirrhosis. So, on average if a person starts to drink alcohol at the age of 18-20 years the disease will manifest at the age of 28- 30 years and above. This also depends upon the content of alcohol, frequency of drinking

and associated co morbidities. The male predominance in the population of the patients with alcoholic liver cirrhosis can be due to the cultural and religious influence which prevails that prohibits woman from alcoholism.

In the present study most of the patients were having alcoholic liver disease (ALD) (84.28%) followed by Hepatitis-B (7.14%) and Hepatitis-C (2.86%) and Autoimmune Hepatitis (2.8%) and about (2%) NASH. These findings are correlated with the study conducted by Ray et al [12] and Jain et al [13]. However, according to study of Indian journal study of etiology most common cause of liver cirrhosis is alcohol [14]. ALD patients had higher S. UA levels (mean 6.6 mg/dl) as compared to Hep-B (mean 6.2 mg/dl) and Hep-C (mean 6.18 mg/dl) and in NASH mean 6.12 which is comparable with the study done by Raut SE et al [15].

Among 70 patients, the most common clinical finding was ascites with 88.57% of total population in which 54.28% having grade III and 34.38% having grade II ascites. This is in accordance with the study done by Behera BP et al [11] and Hegde S et al [16]. Majority of population shows no encephalopathy or low grades of encephalopathy, few patients in grade 3-4 were having CTP class b and c classification. Majority of population was having pallor i.e., 67(95%) out of 70 having anemia, out of which females were more than male population. These findings are correlated with the other studies [6, 10, 17].

Most of the cases (62.85%) had normal WBC count, 28.57% had leukocytosis, 8.57% had leucopenia. There was no significant relationship could be established between total WBC count and liver cirrhosis. There are only limited data available regarding the relationship between total WBC count and liver cirrhosis. This is because in patients with liver cirrhosis the total leucocyte count may be altered by the presence of co-existing sepsis, spontaneous bacterial peritonitis, and other super added infections. 61.42% having thrombocytopenia, this finding is consistent with the previous studies [11, 18]. 47.14% of patients having bilirubin level <2 mg/dl 5.72% having 2-3 mg/dl and 47.14% > 3 mg/dl. Mean total bilirubin level was 2.73 mg/dl which is comparable with the study done by Kumar R et al [19]. In our study population having sr. uric acid >7 and raised bilirubin were 23 i.e., 32% and normal bilirubin with raised sr. uric acid 27% it shows that raised bilirubin correlates with raised uric acid levels (P value <0.05) than normal sr. bilirubin level. Similar findings are reported in study conducted by Gupta PK et al [9] and Prakash BC et al [17]. The serum AST level (Mean 72.8 mg/dl, P value >0.05) and serum ALT level (Mean 42.07 mg/dl, P value >0.05) were not higher in patients with high serum uric acid levels as compared to patients with normal serum uric acid levels. In many studies [9, 20] there is trend of increasing sr. uric acid with raising AST and ALT, but in my study, there is rise in both uric acid and AST, ALT but their correlation is not significant with p values of >0.05. It may be due to less sample size. Serum albumin levels (Mean 2.8 mg/dl, P value <0.05) were low in patients with high serum uric acid levels as compared to patients with normal serum uric acid levels. Other studies demonstrated low serum albumin levels in CLD patients [6,10,12,17]. INR values (Mean 1.513 mg/dl, P value <0.05) were higher in patients with high serum uric acid levels as compared to patients with normal serum uric acid levels. Previous study by Siddiqui SA et al demonstrated coagulation abnormalities were profound in CLD patients [21].

The maximum UA levels were present in CTP Class C patients. In CTP Class C, Sr. UA level mean value was 9.23mg/dl. Both these conditions are associated with progression of chronic liver disease. Percentage of patients with serum uric acid levels increased with increasing severity of chronic liver disease as assessed by Child Pugh Scoring. Similar findings are reported in study conducted by Afzali, Weiss NS et al [22]. The mean sr. uric acid level in class B is 7.32 and class C is 9.23 it shows raise in uric acid level with child Pugh Turcotte score. Other studies also reported similar findings [6, 9, 10, 17].

Conclusions:-

In conclusion, serum uric acid level is an important part of spectrum of Liver cirrhosis Disease. Uric acid in tissues may be a major activator of inflammasomes and thus, it may promote damage to surrounding tissue. It is a mediator of inflammation and tissue damage. Serum uric acid may thus be considered as a marker of severity of Liver cirrhosis Disease.

References:-

1. Xiao J, Wang F, Wong NK, He J, Zhang R, Sun R, et al. Global liver disease burdens and research trends: analysis from a china perspective. *J Hepatol*, 2019;71(1):212-21.
2. Wong MC, Huang J. The growing burden of liver cirrhosis: implications for preventive measures. *Hepato Inter*. May 2018;12(3):201-3.

3. Upadhyay R. Alcoholic Liver Disease. In: Munjal Y P, Sharma S K, eds. API Textbook of Medicine. 9 th ed. New Delhi: Jaypee Brothers; 2012: 873-882.
4. Song JX, Zhu L, Zhu CL, Hu JH, Sun ZJ, Xu X et al. Main Complications of AECHB and Severe Hepatitis B (Liver Failure). Acute Exacerbation of Chronic Hepatitis B. 2019:91–226.
5. Tsois A, Marlar CA. Use of The Child Pugh Score In Liver Disease. [Updated 2023 Mar 13]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK542308/>
6. **Choudhary J, Fiza B, Sinha M. Serum uric acid level and its association with child pugh score in chronic liver disease.** Int J Med Res Prof 2019; 5:13-5
7. Lieber CS, Jones DP, Losowsky MS, Davidson CS. Interrelation of uric acid and ethanol metabolism in man. The Journal of clinical investigation. 1962;41(10):1863-70.
8. Matsumoto I, Moriya S, Kurozumi M, Namba T, Takagi Y. Relationship between serum uric acid levels and the incidence of cardiovascular events after percutaneous coronary intervention. Journal of Cardiology. 2021;78(6):550-7.
9. Gupta PK, Agarwal H, Singhal S, Manocha K. Study of association between serum uric acid levels and chronic liver disease. European Journal of Molecular & Clinical Medicine. 2021 Oct 11;8(4):1169-73.
10. Hasan R, Roy PK, Khan MM, Ahmed F, Alam MR, Gain G. Relation of Serum Uric Acid Concentrations with Etiology and Severity in Patients with Cirrhosis of Liver. Bangladesh Medical Journal. 2021;50(1):46-51.
11. Behera BP, Dash M. An observational study of clinical and hematological profile of cirrhosis of liver. Asian J Pharm Clin Res. 2020;13(4):149-52.
12. Ray et al: Trends of Chronic Liver Disease in a Tertiary Care Referral Hospital in Eastern India J pub Health, 2010: 58.
13. Jain et al, Agarwal S, Tamhankar P, Verma P et al: Lack of association of primary iron overload and common HFE gene mutation with liver cirrhosis in adult's Indian population. Indian j Gastroenterology 2011, 30: 161-5.
14. Ray G. Trends of chronic liver disease in a tertiary care referral hospital in Eastern India. Indian Journal of Public Health. 2014 ;58(3):186.
15. Raut SE, Pagar AB, Kowale AN. Effect of alcohol consumption on serum uric acid level. National Journal of Basic Medical Sciences.2(4):369-373.
16. Hegde S, Vishnar A, Ramteke GB. Study of clinical and laboratory profile in alcoholic liver disease with emphasis on renal function. Int J Res Med Sci 2015; 3:446-50.
17. Prakash BC & Rai SK. Study of serum uric acid in liver cirrhosis and its correlation with Child Turcotte Pugh, MELD and UKELD score. International Journal of Research in Medical Sciences, 2020;8(2):450–454.
18. Aswathi S and Vikranth V. Clinical Profile of Alcoholic Liver Disease in Saveetha Medical College and Hospital and Its Association with Type, Amount and duration of Alcohol Consumption. Journal of Pharmaceutical Research International, 2021;33(48B):132–138.
19. Kumar R, Rastogi A, Maras JS, Sarin SK. Unconjugated hyperbilirubinemia in patients with non-alcoholic fatty liver disease: a favorable endogenous response. Clinical biochemistry. 2012;45(3):272-4.
20. Molla NH, Kathak RR, Sumon AH, Barman Z, Mou AD, Hasan A, Mahmud F, Fariha KA, Ali N. Assessment of the relationship between serum uric acid levels and liver enzymes activity in Bangladeshi adults. Scientific Reports. 2021;11(1):20114.
21. Siddiqui SA, Ahmad M et al. Coagulation abnormalities in patients with Chronic Liver Disease; Eng. J Med. 2005;34 (231-34).
22. Afzali, Weiss NS et al: Hepatology.2010;52 (2): 578- 89.