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Evaluation of Renal Function in Liver Cirrhosis in a Tertiary care Teaching Hospital at Agartala

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Abstract

Introduction: *Liver disease accounts for approximately 2 million deaths per year worldwide, 1 million due to complications of cirrhosis. About 2 billion people consume alcohol worldwide and upwards of 75 million are diagnosed with alcohol-use disorders and are at risk of alcohol-associated liver disease. Current epidemiological trends of the most common liver diseases in Asia–Pacific countries reveals that alcohol consumption, non-alcoholic fatty liver disease (NAFLD), hepatitis B virus (HBV) remains the primary cause of cirrhosis. Renal dysfunction is one of the most common complication of cirrhosis with high morbidity and mortality. The prevalence of chronic kidney disease (CKD) among patients with cirrhosis has increased due to the increased prevalence of CKD-associated comorbidities, such as diabetes [12]. Wong F et al. in 2019 observed 46.8% of chronic kidney disease (CKD) among cirrhosis patients.*

Aims and Objectives: *To evaluate renal function in patients of liver cirrhosis attending A.G.M.C & G.B.P. Hospital, Agartala.*

Materials and Methods: *Cross Sectional hospital based study conducted in Department of Medicine, AGMC & GBP Hospital, Agartala within a period of one and half year. Data was analysed by SPSS software ver. 15 using appropriate statistical tests*

Results: *male preponderance 72 % (n=144) observed out of 200 patients of cirrhosis of liver. The mean age of liver cirrhosis was 52.28 +/- 8.983 years. Female preponderance 70% (n=28) and 30% (n=12) males among 40 non-alcoholic liver cirrhosis patients. The commonest profile of liver cirrhosis in this current study was alcohol induced liver cirrhosis 67% (n=134) out of 200 patients.58% (n=116) were found to be diabetic and 42% (n=84) were found to be nondiabetic. 76% (n=152) was found to be only liver cirrhosis, 24% (n=48) were found to be liver cirrhosis along with chronic kidney disease. Among 24% chronic kidney disease patients, 4% (n=08) were found to be stage 3a chronic kidney disease, 2% (n=04) were found to be stage 3b chronic kidney disease, 5% (n=10) were found to be stage 4 chronic kidney disease, 13% (n=26) were found to be stage 5 chronic kidney disease. So this study revealed that end stage renal disease was most common among liver cirrhosis patients compared to other stages of chronic kidney disease. Prevalence of chronic kidney disease among non-alcoholic liver cirrhosis was more compare to alcohol related liver cirrhosis. Pearson Chi-Square test revealed strong association between non-alcoholic liver cirrhosis and chronic kidney disease with a p value of 0.003 (<0.05).Pearson Chi-Square test showed strong association with a p value of 0.039(<0.05) between diabetes and chronic kidney disease. Pearson Chi-Square test showed a strong association between serum potassium and encephalopathy with a p value of 0.003(<0.05). Pearson Chi-Square test showed a p value of 0.002(<0.05) between serum sodium and minimal encephalopathy, which showed that they have a strong association.*

Conclusion: *Prevalence of 24% (n=48) were found to be liver cirrhosis along with chronic kidney disease among 200 liver cirrhosis patients and 13% (n=26) were found to be stage 5 chronic kidney disease. Wong F et al study which revealed 46.8% chronic kidney disease among liver cirrhosis patients.*

Introduction

Cirrhosis is a condition that is defined histopathologically and has a variety of clinical manifestations and complications, some of which can be life threatening. In the past, it has been thought that cirrhosis was never reversible; however, it has become apparent that when the underlying insult that has caused the cirrhosis has been removed, there can be reversal of fibrosis. The pathologic features of cirrhosis consists of architectural distortion with the formation of regenerative nodules. This results in a decrease in hepatocellular mass and alteration of blood flow. This leads to induction of fibrosis with activation of hepatic stellate cells[1]. Liver disease accounts for approximately 2 million deaths per year worldwide. Cirrhosis is currently the 11th most common cause of death globally and liver cancer is the 16th leading cause of death; combined, they account for 3.5% of all deaths worldwide. Cirrhosis is within the top 20 causes of disability-adjusted life years and years of life lost, accounting for 1.6% and 2.1% of the worldwide burden. According to the WHO, alcohol consumption accounts for 3.8% of the global mortality[2]. Regarding hepatitis B as of 2016, 27 million people (10.5% of all people estimated to be living with hepatitis B) were aware of their infection, while 4.5 million (16.7%) of the people diagnosed were on treatment[4]. Globally, an estimated 71 million people have chronic hepatitis C virus infection. A significant number of those who are chronically infected will develop cirrhosis or liver cancer. WHO estimated that in 2016, approximately 3,99000 people died from hepatitis C, mostly from cirrhosis and hepatocellular carcinoma[5].

Current epidemiological trends of the most common liver diseases in Asia–Pacific countries reveals that alcohol consumption, non-alcoholic fatty liver disease (NAFLD), hepatitis B virus (HBV) remains the primary cause of cirrhosis. The expanding implementation of HBV vaccination has been effective in reducing the incidence of liver cancer, especially in countries like India, China and other countries[3]. Non-alcoholic fatty liver disease (NAFLD) prevalence is increasing owing to increasingly urbanized lifestyles and dietary changes; as a result, the rising trend of NAFLD is becoming comparable to that of Western countries. NAFLD is associated with the development of cardiovascular and kidney diseases, patients with this disease should receive tailor-made advice and continuous support for lifestyle modification [3,16,17].

Cirrhosis is described as either compensated or decompensated. Decompensation means one or more of the following: ascites, bleeding varices, hepatic encephalopathy, jaundice. Acute kidney injury, chronic kidney injury, hyponatraemia and spontaneous bacterial peritonitis are also features of decompensation. Child-Pugh-Turcotte staging (CTP) and Model of End Stage Liver Disease (MELD) score used for prognosticating cirrhotic patients. However, Child Turcotte Pugh (CTP) is clinically convenient and easy to use[6].

Renal dysfunction is one of the most common complication of cirrhosis with high morbidity and mortality[7,8,9,13,14]. Renal dysfunction in this population may present acutely, or may be a result of underlying chronic kidney disease (CKD). An accurate assessment of renal function is recommended in all patients with cirrhosis. Indeed, the renal function assessment guides the management of patients, helps to refine prognosis and to define transplant strategies. Despite its limitations, serum creatinine is still the most used biomarker for the estimation of glomerular filtration rate (GFR) in patients with cirrhosis [10,13,14,20]. The most important chronic liver diseases associated with chronic renal disease are alcohol intake, nonalcoholic fatty liver disease hepatitis B and C[11]. The prevalence of chronic kidney disease (CKD) among patients with cirrhosis has increased due to the increased prevalence of CKD-associated comorbidities, such as diabetes[12]. Wong F et al. in 2019 observed that the prevalence of chronic kidney disease (CKD)

among patients with cirrhosis has increased due to the increased prevalence of CKD-associated comorbidities, such as diabetes. There were 46.8% CKD patients who had significantly higher serum creatinine & higher prevalence in nonalcoholic steatohepatitis cirrhosis[89].

Lee WC study revealed that Compared with cirrhotic patients with ascites had a significantly higher serum uric acid level (6.7+/-1.6 mg/dL vs. 5.6+/-1.7 mg/dL, $p < 0.05$) and lower effective renal plasma flow (396+/-125 mL/min vs. 445+/-149 mL/min, $p < 0.05$) [94].

So valuation of renal function is of immense value in the management of cirrhosis of liver and outcome of intervention have definite role with variations in renal function.

This study is designed and proposed to be conducted for the first time at AGMC & GBP Hospital with a view to generate baseline data on evaluation of renal function and cirrhosis of liver as this kind of study has never been conducted earlier in any tertiary care hospitals of Tripura.

Aim

To evaluate renal function in patients of liver cirrhosis attending A.G.M.C & G.B.P. Hospital, Agartala.

Objectives

1. To assess renal function by estimating serum urea, serum creatinine, serum uric acid, urine analysis, serum cystatin, estimated glomerular filtration rate among the patients of cirrhosis of liver admitted in medicine department.
2. To study the association of risk factors namely alcohol, Hepatitis B infection, Hepatitis C infection and Non Alcoholic Fatty Liver Disease causing liver cirrhosis.

Methodology

A cross sectional study hospital based study (IPD) at department of medicine, AGMC and study duration (one and half years for data collection and 6 months for data management).

Study Population

Patient those will be diagnosed to have cirrhosis of liver admitted at Agartala Government Medical College & GBP Hospital during this study duration, will be included in the study.

Sample Size

All the patients suffering from liver cirrhosis admitted in Agartala Government Medical College & GBP Hospital following exclusion and inclusion criteria will be included in the study and their renal function will be estimated. From previous records it is found that in one year approximately 150 patients was admitted at medicine department. So in one and half year it will be approximately 200 patients. So the sample size in this study will be approximately 200.

Sample Technique

No sampling technique is required as approximately all the patients, diagnosed with cirrhosis of liver has been included in te study.

Operational Definitions:

Cirrhosis of Liver: Cirrhosis is defined anatomically as a diffuse process with fibrosis and nodule formation. It is the end result of the fibrogenesis that occurs with chronic liver injury. The most common causes include alcohol excess, viral hepatitis, non-alcoholic steatohepatitis (NASH) and autoimmune diseases[6].

Chronic kidney disease: chronic kidney disease encompasses a spectrum of pathophysiologic process associated with abnormal kidney function and a progressive decline in glomerular filtration rate (GFR). The risk of CKD progression is closely linked to both the GFR and the amount of albuminuria[1]. The Kidney Disease Improving Global Outcome (KDIGO) definition and classification were accepted, with clarifications. CKD is defined as kidney damage or glomerular filtration rate (GFR) <60 mL/min/1.73 m(2) for 3 months or more, irrespective of cause[88].

Criteria for Chronic Kidney Disease

A. Duration for > 3 months: kidney disease lasts for > 3 months.

B. Decreased GFR: GFR < 60ml/min/1.73 m2 for > 3 months, preferably CKD-EPI CREATININE-CYSTATIN EQUATION 2012 i.e eGFR=$135\times\min(S_{Cr}/\kappa,1)^{\alpha}\times\max(S_{Cr}/\kappa,1)^{-0.601}\times\min(S_{cys}/0.8,1)^{-0.375}\times\max(S_{cys}/0.8,1)^{-0.711}\times 0.995^{Age}\times 0.969$[if female]×1.08 [if black].

C. Urine protein: persistence proteinuria for 3 months.

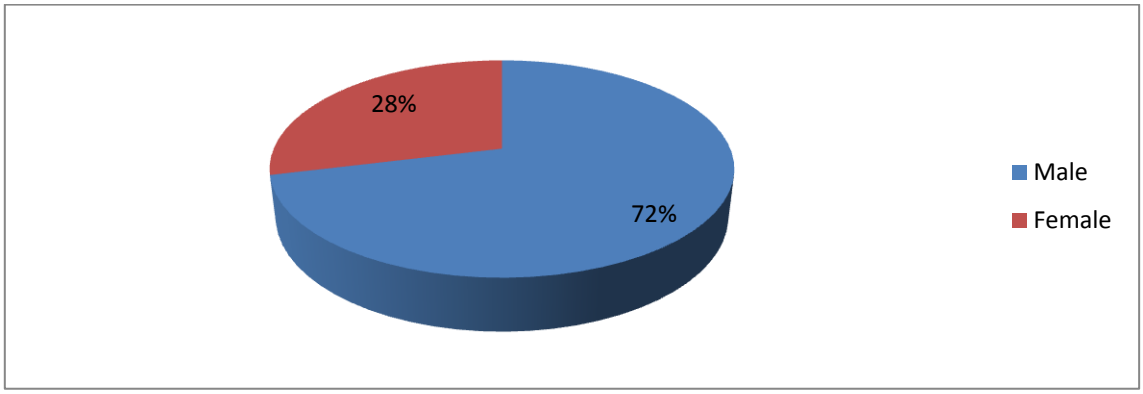
D. Urine casts: Broad waxy casts indicate chronic kidney disease.

E. Ultrasonography of whole abdomen: reduced renal cortical thickness <6 mm, more reliable than length, increased renal cortical echogenicity, poor visibility of the renal pyramids and the renal sinus, marginal irregularities[93].

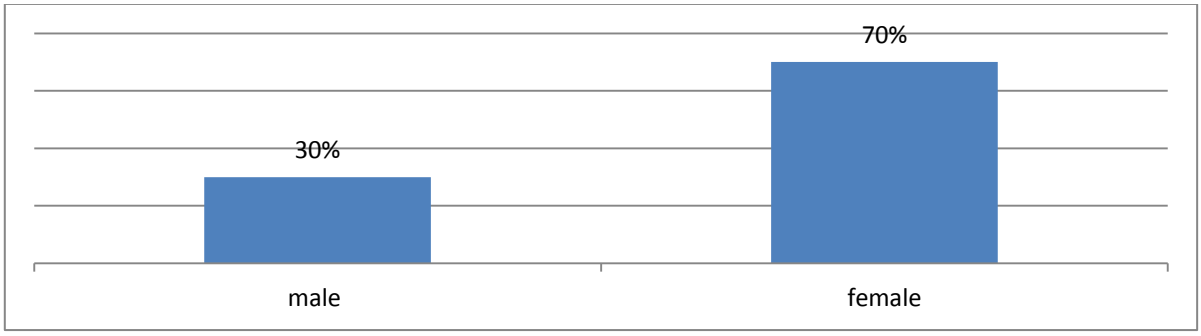
Results and Analysis

A total of 200 patients were worked up according to the procedure detailed in the methodology and Annexure 1 and data obtained thereby was presented and analysed below

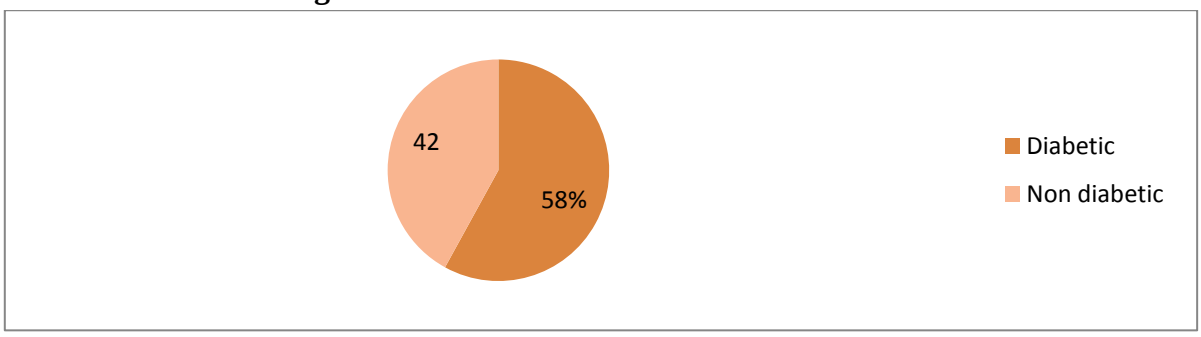
Gender distribution



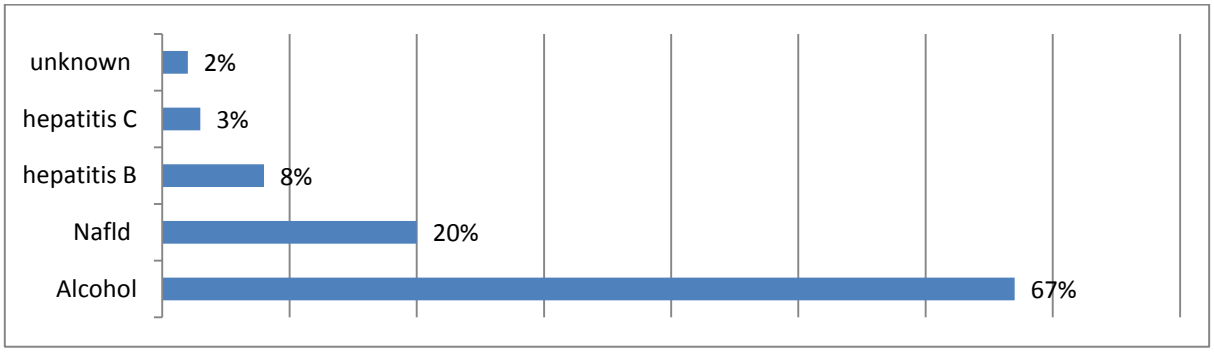
Gender distribution in non-alcoholic liver cirrhosis



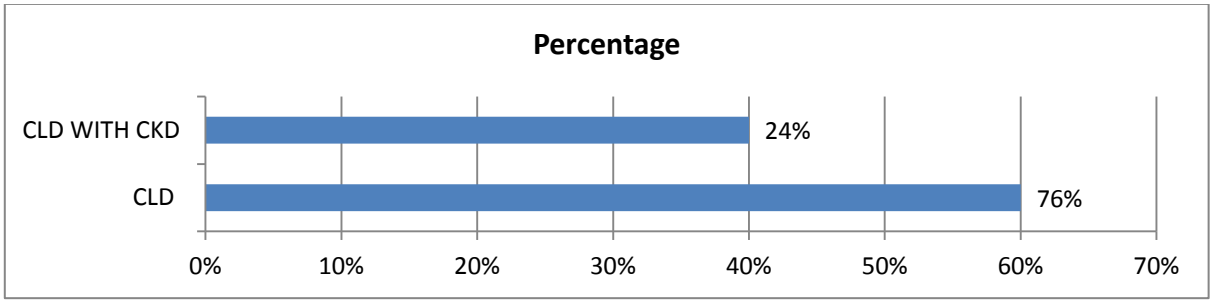
Distribution of Diabetes among liver cirrhosis



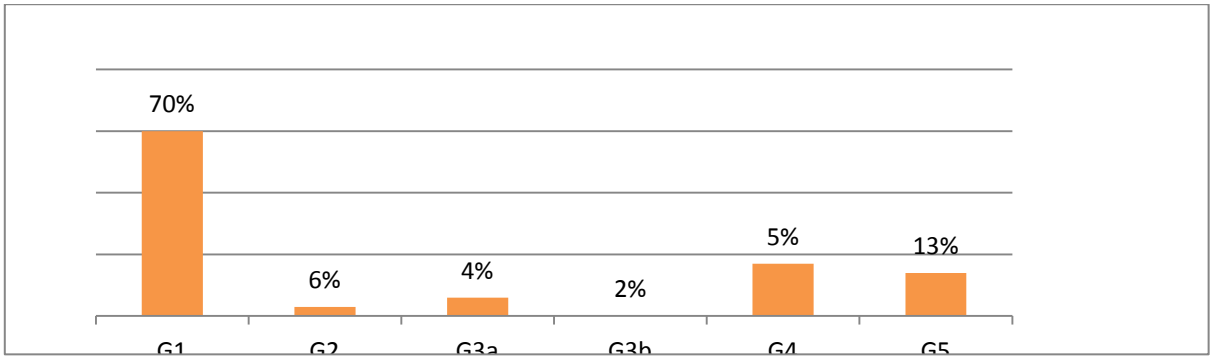
Distribution of different causes of liver cirrhosis



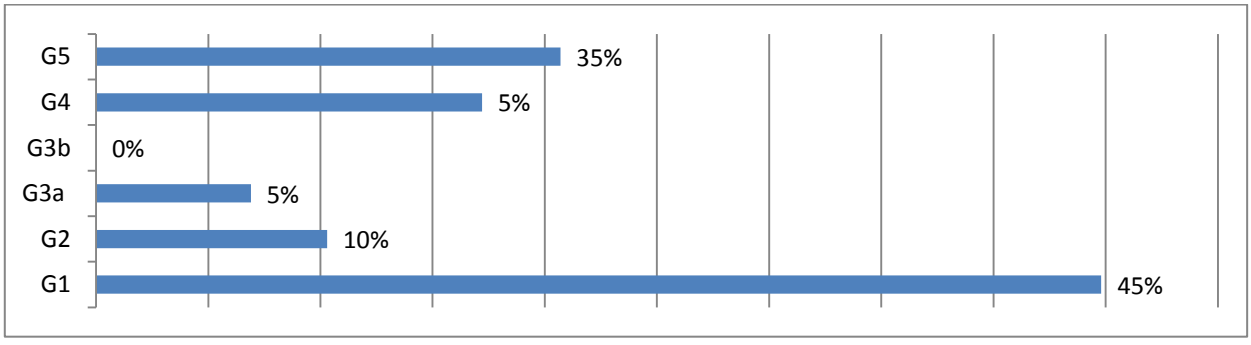
Distribution of chronic kidney disease among liver cirrhosis patients



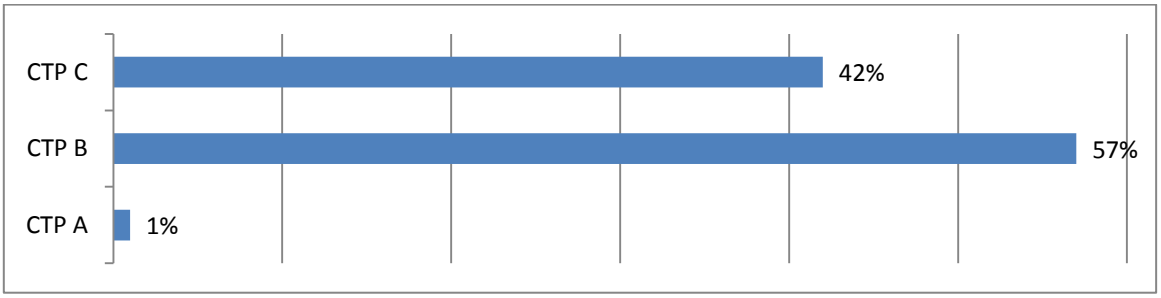
Glomerular filtration rates among liver cirrhosis patients



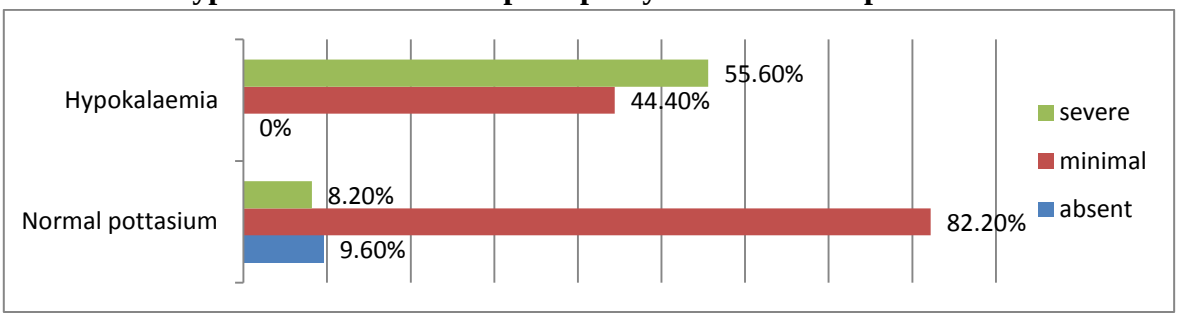
Glomerular filtration rate among non-alcoholic liver cirrhosis patients



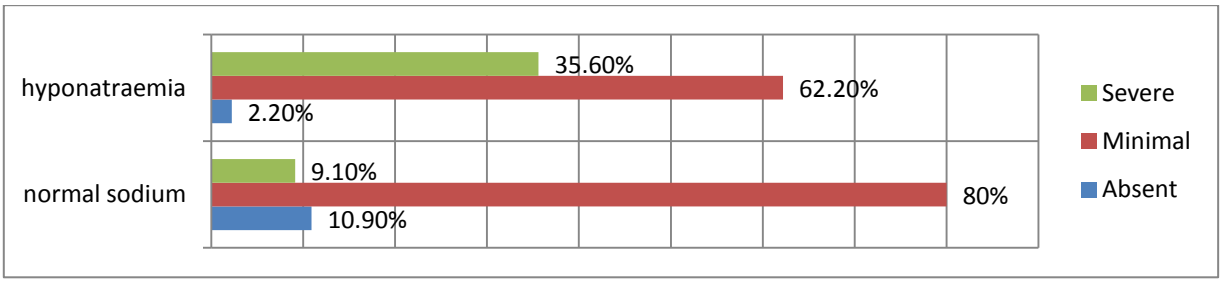
CTP scoring among liver cirrhosis patients



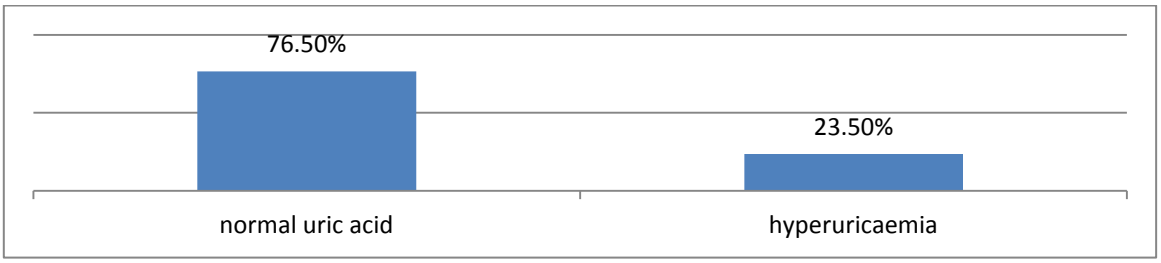
Association between hypokalaemia with encephalopathy liver cirrhosis patients



Association between hyponatraemia with encephalopathy liver cirrhosis patients



Association between serum uric acid with liver cirrhosis



Discussion

This cross sectional study was conducted in a Tertiary care centre of North – Eastern Region, to see the Renal function of liver cirrhotic patients and to see the association of risk factors namely alcohol, Hepatitis B infection, Hepatitis C infection and Non Alcoholic Fatty Liver Disease causing liver cirrhosis. IPD patients who had diagnosed liver cirrhosis were screened by inclusion and exclusion criteria. 200 of such liver cirrhosis patients were taken as samples for this study. 72 % (n=144) were male and 28% (n=56) were female. This study showed male preponderance among liver cirrhosis patients. Florence et al conducted a Cross-sectional study with 2346 patients, which also showed male preponderance (63.2%).The mean age of all liver cirrhosis patients were 52.28 years. And it was 50.4 years in that study conducted by Florence et al.

Among 20% (n=40) of non-alcoholic steatohepatitis liver cirrhosis patients 70% (n=28) females and 30% (n=12) males. So there was female preponderance among non-alcoholic steatohepatitis liver cirrhosis. Florence et al also showed female preponderance (72.7%). Among 200 patients of liver cirrhosis, 58% (n=116) was found to be diabetic and 42% (n=84) was found to be nondiabetic. And it was 61% to be diabetic in that study conducted by Florence et al. 67% (n=134) was found to be alcohol induced liver cirrhosis, 20% (n=40) were found to be non-alcohol liver cirrhosis and 8% (n=16) were found to be hepatitis B related cirrhosis, 3% (n=6) were found to be hepatitis C related cirrhosis, unknown 2%(n=4) cases. So this study showed that alcohol intake was the leading cause of liver cirrhosis & non-alcoholic fatty liver disease was the second most common cause. Florence et al also showed alcohol consumption was the leading cause with prevalence of 63%.

24% (n=48) were found to be liver cirrhosis along with chronic kidney disease. Florence et alstudy showed 46.8% (n=1099) liver cirrhosis with chronic kidney disease patients among 2346 patients.

Among 200 liver cirrhosis patients 4% (n=08) were found to be stage 3a chronic kidney disease, 2% (n=04) were found to be stage 3b chronic kidney disease, 5% (n=10) were found to be stage 4 chronic kidney disease, 13% (n=26) were found to be stage 5 chronic kidney disease. So this study revealed that end stage renal disease was most common among liver cirrhosis patients compared to other stages of chronic kidney disease.

Out of 24% (n=48) chronic kidney disease patients, 40% (n=18) patients were suffering from non-alcoholic liver cirrhosis with chronic kidney disease . Pearson Chi-Square test is applied to find out the association between non-alcoholic liver cirrhosis and chronic kidney disease, which shows that they have a strong association with a p value of 0.003 (<0.05), that is patients with non-alcoholic liver cirrhosis are more prone to develop chronic kidney disease than alcohol related liver cirrhosis. Pearson Chi-Square test is applied to find out the association between diabetes and chronic kidney disease, which shows that they have a strong association with a p value of 0.039(<0.05). So prevalence of chronic kidney disease among non-alcoholic liver cirrhosis was more common than alcohol related liver cirrhosis.

This study revealed that hypokalaemia precipitates severe encephalopathy. Among 47 hyperuricaemic patients, 40.4% (n=19) were liver cirrhosis only and 59.6.% (n=28) were liver cirrhosis with chronic kidney disease. Lee et al conducted study showed that liver cirrhosis with chronic kidney disease patients had raised serum uric acid.

Overall, these findings might have possible clinical and public health implications. Our results indicate that the 24% liver cirrhosis patients are suffering from chronic kidney disease Florence et al study which was 46.8%. This study reveals that prevalence of chronic kidney disease is most common in those who are suffering from non-alcoholic liver cirrhosis and females are more prone to develop non-alcoholic liver cirrhosis compared to males.We should look for NAFLD in diabetics, especially in the presence of metabolic syndrome. Once found, aggressive management of cardiovascular and renal morbidity should be the primary goal. It has only recently been appreciated that chronic kidney disease represents an important burden of disease for patients with non-alcoholic liver cirrhosis.

The present study was carried out over a period of only one and half year and included a modest sample size of two hundred subjects. Other studies on larger scales including those from general population conducted over longer time periods are required to properly validate the findings of this study. Few numbers of studies are available across various parts of India as well as here in Tripura on this topic. On this point the current study will be considered as a foundation stone for further studies which can be conducted over long period of time, which could yield more accurate results.

Conclusion

This study was conducted over two hundred (200) liver cirrhosis patients attending AGMC & GBP Hospital This particular study has revealed some interesting facts about liver and renal disease occurrence in this region and its various clinico-biochemical associations. This study showed that though alcohol was the most common cause of liver cirrhosis and male were more prone to develop compared to female.

Prevalence of 24% (n=48) were found to be liver cirrhosis along with chronic kidney disease among 200 liver cirrhosis patients and 13% (n=26) were found to be stage 5 chronic kidney disease. Wong F et al study which revealed 46.8% chronic kidney disease among liver cirrhosis patients. Few number of Indian studies had shown mixed results. The prevalence of chronic kidney disease among non-alcoholic liver cirrhosis was more compare to alcohol related liver cirrhosis and pearson chi-square test revealed strong association between non-alcoholic liver cirrhosis and chronic kidney disease with a p value of 0.003 (<0.05).Wong F et al study had shown similar results .

Females were having a higher prevalence of non alcoholic liver cirrhosis than males in this study, diabetes was the most common cause non-alcoholic liver cirrhosis. Most of the studies across the various parts of the world had shown similar results.

Most of the patients were in decompensated phase of liver cirrhosis. 80% of liver cirrhosis patients were in minimal hepatic encephalopathy state. Hyperuricaemia were detected more in liver cirrhosis with chronic kidney patients.

In the course of the study, various literatures from different authors across the globe were referred to. Since, it was a cross-sectional study, these results need to be validated by further long-term prospective studies with more number of study sample. Further experimental and follow-up studies are needed to elucidate the pathomechanism of renal dysfunction in liver cirrhosis patients.

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