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Study of Renal Function in Chronic Liver Disease.

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ABSTRACT

Background: Renal dysfunction is common in chronic liver diseases. The cause of renal dysfunction is either multi-organ involvement in acute conditions or secondary to advanced liver diseases. The present study was undertaken to assess the renal function test in chronic liver diseases and find out the association of alteration of renal function with gradation of liver diseases (assessed by child –pugh criteria) and find out the association of alteration of renal functions among the case of chronic liver disease of different aetiology. **Methods:** This prospective cross sectional study was conducted in the Department of Medicine, Shri. B. M. Patil Medical College, Hospital & Research Centre, Vijayapur during November 2016 to August 2018 with 65 case of chronic liver diseases after considering the exclusion criteria. The patient were interviewed with predesigned and pre tested schedule examined clinically followed by some laboratory investigation relevant to diagnose the aetiology of chronic liver diseases, and to assess the severity of renal dysfunction. Statistical analysis was done by appropriate statistical software including but not restricted to MS Excel, SPSS ver.20 **Results:** Majority of the patients were male(90.8%) and the mean age of the patients was 45.78 ±13.19 years. 72.2% patients suffered from Alcoholic liver diseases while 13.9% and 10.8% patients had chronic hepatitis B and chronic hepatitis C respectively. Two patients had Nonalcoholic steatohepatitis. It was observed that 36.9% patients had renal dysfunction and most. **Conclusion:** This study emphasizes the fact that we should be more vigilant when treating Chronic Liver Disease (CLD) patients, regarding their renal function, as proper screening, prevention and treatment of renal dysfunction can decrease morbidity and mortality.

Keywords: Chronic Liver disease, Renal dysfunction.

INTRODUCTION

Chronic liver disease is common clinical problem in our country. Chronic liver disease involves a process of progressive destruction and regeneration of liver parenchyma leading to fibrosis and cirrhosis.[1] Acute kidney injury, chronic kidney disease and the evaluation of numerous exogenous and endogenous measures of kidney function continue to be the focus of much research different patient population.[2] The presence of renal impairment in both groups is a poor prognostic indicator. Hepato-renal syndrome is a unique form of renal failure associated with advanced liver disease or cirrhosis and is characterized by functional renal impairment without significant changes in renal histology.[3]

Renal failure is a common occurrence in patients with chronic liver disease. Based on etiology, renal failure is divided into prerenal, renal, and postrenal categories. "It is caused by a variety of factors, some specific to chronic liver disease (eg.Hepatorenal syndrome), and others affecting the general patient population. An episode of acute renal failure may be reversible, but renal function may remain diminished over the long term, and patients may develop chronic kidney disease. Patients with chronic liver disease who develop renal failure pose unique diagnostic and therapeutic challenges.

Chronic liver disease and cirrhosis are frequently complicated with renal dysfunction and this combination leads to significant morbidity and mortality.[4] There is considerable evidence that renal failure in patient with cirrhosis primarily related to disturbances in circulatory function-mainly, a reduction in system vascular resistance due to primary arterial vasodilatation in the splanchnic circulation, triggered by portal hypertension.[5] Intrinsic renal diseases may occur in patient with hepatitis B or hepatitis C and alcoholic cirrhosis. Moreover, patients with cirrhosis may develop a specific acute renal failure called type-I hepatorenal syndrome. Independent of event that leads to acute renal failure, patient with cirrhosis may have

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diseases, such as diabetes mellitus or hypertension and atherosclerosis, which may cause chronic renal injury.[6,7]

In clinical practice plasma creatinine level and endogenous creatinine clearance are commonly used as more convenient but less accurate method for glomerular filtration rate" assessment.[8]

Non-alcoholic steato-hepatitis and non-alcoholic fatty liver disease are increasing causes of chronic liver disease in the general population of Western countries with prevalence rates of 1–5% and 10–24%, respectively. Hepatitis C has long been associated with several glomerulopathies, most notably cryoglobulin and noncryoglobulin associated membrano proliferative glomerulonephritis. The prevalence of cryoglobulinemia is around 50%.Hepatitis C has also been associated with an increased risk of albuminuria, progression of diabetic nephropathy, and progression of chronic kidney disease to end stage renal disease.[9]

Renal failure in patient with cirrhosis primarily related to disturbances in circulatory function-mainly, a reduction in system vascular resistance due to primary arterial vasodilatation in the splanchnic circulation, triggered by portal hypertension.[5]

The pivotal prognostic role of renal function in cirrhosis is reflected by the inclusion of serum creatinine (sCr) in "the Model for End Stage Liver Disease (MELD) Score, which is currently used for assessment of severity of liver disease and prioritization of patients with advanced liver disease for liver transplantation.[10-12] As a consequence of systemic and splanchnic arterial vasodilatation and consecutive reduction in effective circulating blood volume, renal perfusion may be critically impaired in patients with advanced cirrhosis and portal hypertension".[13] As a result, patients with cirrhosis are prone to developing renal dysfunction.

Acute kidney injury (AKI), defined by a significant reduction in glomerular filtration rate (GFR) over a short time period, "is a common and severe complication in patients with cirrhosis and is often triggered by a precipitating event (i.e. overdose of diuretics, large-volume paracentesis without albumin replacement, gastrointestinal bleeding, bacterial infections, etc.).[14] AKI has an estimated prevalence of approximately 20–50% among hospitalized patients with cirrhosis and patients with cirrhosis are more likely to develop renal failure compared to individuals without liver disease.[15-19] AKI is associated with poor prognosis and represents an important predictor for short-term mortality in patients with cirrhosis.[15,16,20-22]

The spectrum of causes for AKI in cirrhosis includes (i) prerenal AKI (i.e. hypovolemia due to gastrointestinal bleeding, aggressive diuretic treatment, lactulose-induced diarrhea or infections), (ii) the hepatorenal syndrome-type AKI (HRS-AKI), which is defined as a potentially reversible deterioration of renal function unresponsive to volume resuscitation, caused by renal vasoconstriction in the absence of alternative identifiable causes",[23,24] (iii) intrinsic causes such as acute tubular necrosis and, although very rare, (iv) postrenal causes.[18]

With a yearly incidence of 8–12%, HRS-AKI is quite common in decompensated cirrhosis with ascites.[25-27] The correct "classification of AKI is essential since HRS-AKI, representing one of the most lethal complications of portal hypertension, requires a specific treatment approach. However, despite adequate treatment mortality is still about 60% and higher".[22,28,29] HRS-AKI is a diagnosis by exclusion and thus, often difficult to establish.[30,31]

Treatment includes general measures such as withdrawal of diuretics and intravascular volume expansion with albumin to rule out prerenal component and discontinuation of nephrotoxic medications. Other modalities of treatment include use of vasopressor drugs (eg.terlipressin), Renal Replacement Therapy & Orthoptic Liver Transplant. In general renal failure in chronic liver disease indicates a worse prognosis. Increased creatinine to be one of the factors (along with bilirubin and international normalized ratio) independently associated with higher mortality. Mortality is especially high with hepatorenal syndrome (HRS). The greatest chance to recover renal function and improve overall survival in patients with HRS is successful liver transplantation.

The accurate assessment of kidney function and injury is currently affected by the reliance on the measured concentration of serum creatinine, which is significantly affected by the degree of cirrhosis, hyperbilirubinemia and the nutritional state of the patient. Improved understanding of the pathophysiology of kidney injury and development of more accurate measures of kidney function and injury are necessary to evoke a positive shift in kidney injury diagnosis, treatment, and outcomes. Furthermore, the number of patients with chronic liver disease and chronic kidney disease continues to rise, due to the large numbers of individuals worldwide affected by viral hepatitis, obesity, hypertension, and diabetes. Consequently, preventative health care messages must be louder and further reaching in order to reverse this trend.

Hence the present study was done at our tertiary care centre to evaluate the assessment of renal function in chronic liver disease.

MATERIALS AND METHODS

A prospective cross sectional study was conducted among 65 patients to evaluate the assessment of renal function in chronic liver disease.

Source of Data

Patients admitted in the medicine ICU/WARDS OF BLDE (Deemed to be University) Shri. B. M. Patil Medical College and Research Centre, Vijayapur and who fulfilled the inclusion criteria.

Patients attending the medicine OPD/ executive health check-up schemes who fulfilled the inclusion criteria

Study Duration:

November 2016 to August 2018.

Types of study

A Prospective cross sectional study

Sample size

65 Patients

Sample size was calculated using the formula:

n= [z2p(1-p)]/d2

Where: Z = z statistic at 5% level of significance (0.95)

p = expected prevalence rate = 70%

d = margin of error = 5.5%

n= [0.95 x 0.95 x 0.7 (0.3)] / 0.055 x 0.55 = 62.6

A sample size of 65 subjects will allow the study to assess the renal function in CLD with a confidence interval of ±10% with finite population correction.

Inclusion Criteria

- Patients with Liver disease of more than 6 months duration of different etiology like Viral (Hepatitis B, Hepatitis C),
- Alcoholic chronic liver disease, Non alcoholic steatohepatitis, and Autoimmune (Wilson's disease, cryptogenic).
  - Age > 18 years
  - Of both sex

Exclusion Criteria

- Diabetes Mellitus
- Hypertension
- Chronic kidney disease
- Patients taking any nephrotoxic drugs

Methodology

The data was collected according to Performa in terms of details history, clinical examination and necessary investigations of the patients who fulfilled the inclusion criteria.Investigations or interventions required in this study were routine standard procedures. Investigations included:

1. CBC
2. LIVER FUNCTION TEST
3. USG/ELASTOGRAPHY
4. URINE ROUTINE AND MICROSCOPY
5. RENAL FUNCTION TEST
6. FBS PPBS
7. PT, INR
8. HbsAg
9. HCV

The study was conducted after obtaining necessary permission from institutional ethics committee. The schedule was designed after consultation with the experts of general medicine and pre testing was done in the general medicine outdoor among 10 patients of chronic liver disease, who came for follow up.

Informed written consent in vernacular was obtained from each patient before inclusion in the study. The consent form was also approved by the institutional ethics committee.

Patients were interviewed about duration of the disease, presence of alcoholism, presence of yellowish discoloration of urine, vomiting of blood and passage of black stool. General survey was done to assess presence of anemia, jaundice, clubbing and oedema. The patients were also examined for presence of ascitis, hepato-splenomegaly, distented veins, everted umbilicus, spider naevi, palmar erythema, gynaecomastia, testicular atrophy, and bleeding manifestation to assess the severity of liver dysfunction.

Biochemical examination like blood for hemoglobin, total count, differential count, ESR, and fasting and post prandial sugar was done. Laboratory investigations like total bilirubin with conjugated and un-conjugated fraction, Alanine amino transferase, Aspartate amino transferase, Alkaline Phosphatase, total protein, albumin ,globulin, prothrombin time, HbSAg, Anti nuclear antibody, Anti-Liver Kidney Microsomal antibodies 1, 2 & 3 were done. Ascitic fluid was examined to assess the aetiology and severity of chronic liver disease. For assessment of kidney function serum urea, creatinine, seum sodium and potassium were examined.

Radiographic examination like ultrasonography of upper abdomen and Kidney, Ureter, Bladder was done. Upper gastrointestinal endoscopy was done for detecting gastro-oesophagial varices, Routine and microscopic examination of urine, 24 h protein excretion and measurement of 24 h urine volume were also done.

Statistical Analysis

Quantitative data is presented with the help of Mean and Standard deviation. Qualitative data is presented with the help of frequency and percentage table. Association is assessed with the help of Fisher test, student 't' test and Chi-Square test. 'p' value less than 0.05 is taken as significant.

Pearson's chi-squared test

$$X^2 = \sum_{i=1}^{n} \frac{(O_i - E_i)^2}{E_i}$$

Where X2 = Pearson's cumulative test statistic.

Oi = an observed frequency;

Ei = an expected frequency, asserted by the null hypothesis;

n = the number of cells in the table.

Results were graphically represented where deemed necessary.

Appropriate statistical software, including but not restricted to MS Excel, SPSS ver. 20 will be used for statistical analysis. Graphical representation will be done in MS Excel 2010.

RESULTS

A prospective cross sectional study was conducted among 65 patients to evaluate the assessment of renal function in chronic liver disease.

Distribution of patients according to Age

Majority of the patients (32.4%) were in the age group of 31-40 years followed by 21.5% in the age group of 41-50 years, 16.9% in the age group of 61-70 years, 15.4% in the age group of 51-60 years, 9.2% patients in the age group of 21-30 years and 4.6% in the age group of >70 years. The mean age of the patients was 45.78 ± 13.19 years.

Table 1: Distribution of patients according to Age

Age	N	%
21-30	6	9.2%
31-40	21	32.4%
41-50	14	21.5%
51-60	10	15.4%
61-70	11	16.9%
>70	3	4.6%
Total	65	100%
Mean ± SD	45.78 ± 13.19	

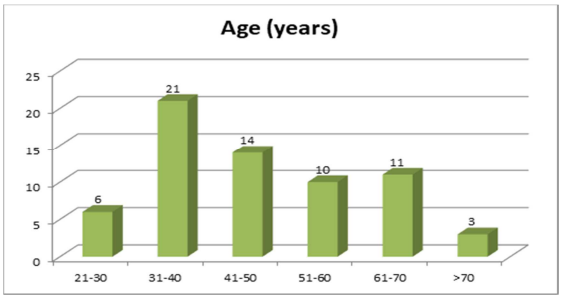

Figure 1: Distribution of patients according to Age

Distribution of patients according to Gender

There was male preponderance (90.8%) whereas female patients constituted 9.2% of the study group.

Table 2: Distribution of patients according to Gender

Gender	N	%
Male	59	90.8%
Female	6	9.2%
Total	65	100%

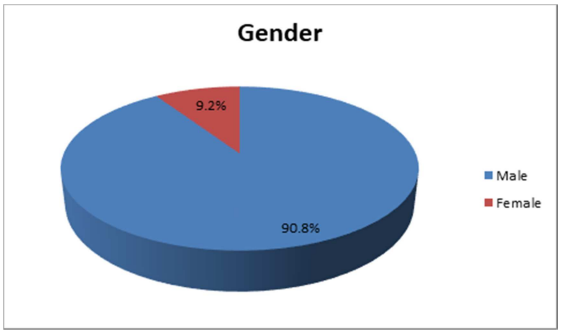

Figure 2: Distribution of patients according to Gender

Distribution of patients according to Etiology

47 (72.2%) patients suffered from Alcoholic liver disease while 9 (13.9%) and 7 (10.8%) patients had chronic Hepatitis-B and chronic Hepatitis-C respectively. 2 (3.1%) patients had Nonalcoholic steatohepatitis.

Table 3: Distribution of patients according to Etiology

Etiology	N	%
Alcoholic chronic liver disease	47	72.2%
Hepatitis B virus	9	13.9%
Hepatitis C virus	7	10.8%
Nonalcoholic steatohepatitis	2	3.1%
Total	65	100%

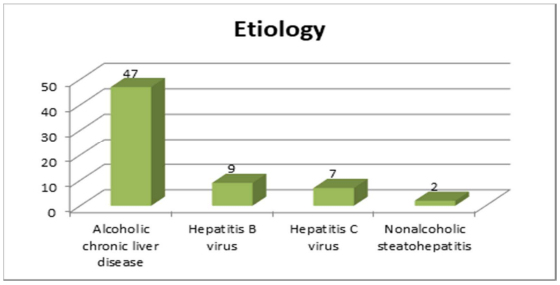

Figure 3: Distribution of patients according to Etiology

Distribution of patients according to Renal Dysfunction

It was observed that 24 (36.9%) patients had renal dysfunction.

Table 4: Distribution of patients according to Renal Dysfunction

Renal Dysfunction	N	%
Present	24	36.9%
Absent	41	63.1%
Total	65	100%

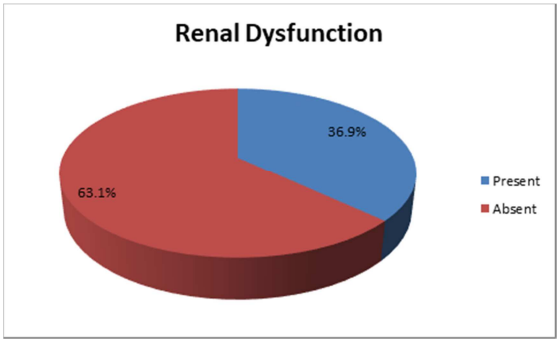

Figure 4: Distribution of patients according to Renal Dysfunction

Table 5: Distribution of patients according to Type of Renal Dysfunction (n=24)

Type of Renal Dysfunction	N	%
Acute Kidney Injury (AKI)	14	58.3%
Hepatorenal Syndrome (HRS)	10	41.7%
Total	24	100%

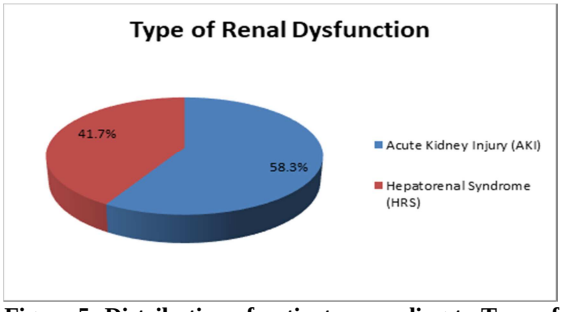

Figure 5: Distribution of patients according to Type of Renal Dysfunction (n=24)

Distribution of patients according to Type of Renal Dysfunction (n=24)

The most common type of renal dysfunction was Acute Kidney Injury (58.3%) followed by Hepatorenal Syndrome (41.7%).

Association of Etiology and Renal Dysfunction

Majority of the cases of renal dysfunction (19 out of 24; 79.2%) were associated with chronic alcoholic liver disease. However there was no significant association between the etiology and renal dysfunction as per Chi-Square test (p>0.05).

Table 6: Association of Etiology and Renal Dysfunction

Etiology	Normal Dysfunction		Renal Dysfunction		Chi-Square Value	p Value
	N	%	N	%		
Alcoholic chronic liver disease	28	43.1%	19	29.2%	1.426	>0.05
Hepatitis B virus	7	10.8%	2	3.1%		
Hepatitis C virus	5	7.7%	2	3.1%		
Nonalcoholic steatohepatitis	1	1.5%	1	1.5%		
Total	41	63.1%	24	36.9%		

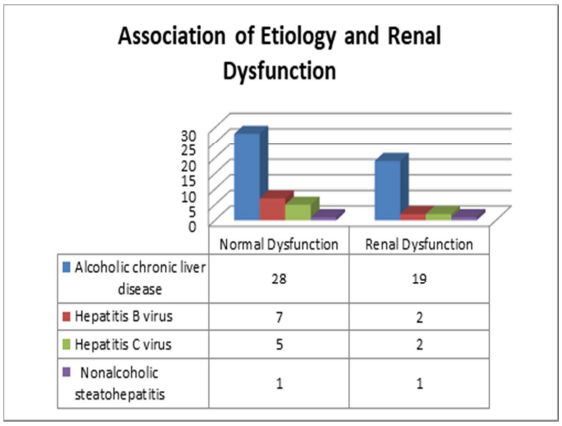

Figure 6: Association of Etiology and Renal Dysfunction

Renal Function Profile of patients

49 (75.4%) patients had serum urea in the range of 15-50 mg/dl while 31 (47.8%) patients had serum creatinine level of 1 mg/dl. 49 (75.4%) patients had serum sodium level in the range of 137-145mEq/L while 58 (89.3%) patients had serum potassium in the range of 3.5-5.1mEq/L. 56 (86.2%) patients had serum chloride level in the range of 97-110mEq/L while 59 (90.8%) patients had uric acid level in the range of 2.5-7.0 mg/dl.

Table 7: Renal Function Profile of patients

Parameters	N	%
Serum Urea (mg/dl)		
15-50	49	75.4%
>50	16	24.6%
Serum Creatinine (mg/dl)		
1	31	47.8%
2	16	24.6%
3	12	18.4%
4	6	9.2%
Serum Sodium (mEq/L)		
<137	10	15.4%
137-145	49	75.4%
>145	6	9.2%
Serum Potassium(mEq/L)		
<3.5	4	6.1%
3.5-5.1	58	89.3%
>5.1	3	4.6%
Serum Chloride(mEq/L)		
<97	5	7.7%
97-110	56	86.2%
>110	4	6.1%
Uric acid(mg/dl)		
2.5-7.0	59	90.8%
>7.0	6	9.2%

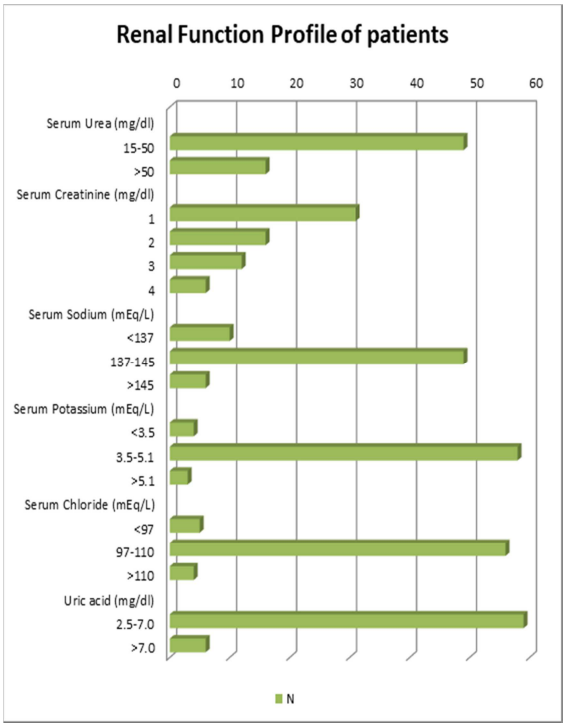

Figure 7: Renal Function Profile of patients

Liver Function Profile of patients

48 (73.7%) patients had total bilirubin level >3 mg/dl while 56 (86.2%) patientshad serum Alanine amino transferase (ALT) <100u/L.33 (50.8%) patients had serum Aspartate amino transferase (AST) <100 u/L and39 (60.1%) patientshad serum Alkaline phosphatase (ALP) within the range of 100-200 u/L. 61 (93.8%) had serum albumin level <3gmdl while 54 (83.1%) patients had serum globulin in the range of 2.5-4 gm/dl.

Association of Serum Urea and Child-Pugh classification

It was observed that there was significant increase in abnormal value of serum urea with increase in the

severity of liver disease as per Chi-Square test ($p<0.05$).

Table 8: Liver Function Profile of patients

Parameters	N	%
Total bilirubin (mg/dl)		
<2	12	18.5%
2-3	5	7.8%
>3	48	73.7%
Serum ALT(U/L)		
<100	56	86.2%
100-200	4	6.1%
>200	5	7.8%
Serum AST(U/L)		
<100	33	50.8%
100-200	22	33.8%
>200	10	15.4%
Serum ALP(U/L)		
<100	22	33.8%
100-200	39	60.1%
>200	4	6.1%
Serum albumin(gm/dl)		
<3	61	93.8%
3-3.5	3	4.6%
>3.5	1	1.5%
Serum globulin(gm/dl)		
<2.5	1	1.5%
2.5-4	54	83.1%
>4	10	15.4%

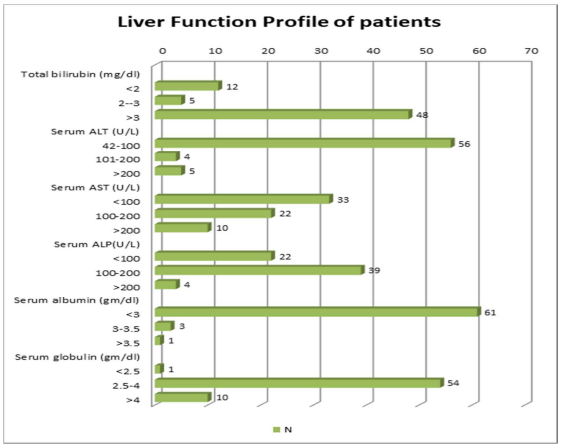

Figure 8: Liver Function Profile of patients

Table 9: Association of Serum Urea and Child-Pugh classification

Classification	Normal		Abnormal		Chi-Square Value	p Value
	N	%	N	%		
Child-Pugh A (n=2)	4	7.5%	0	-	29.60	<0.05
Child-Pugh B (n=54)	48	90.6%	4	33.3%		
Child-Pugh C (n=9)	1	1.9%	8	66.7%		
Total	53	100%	12	100%		

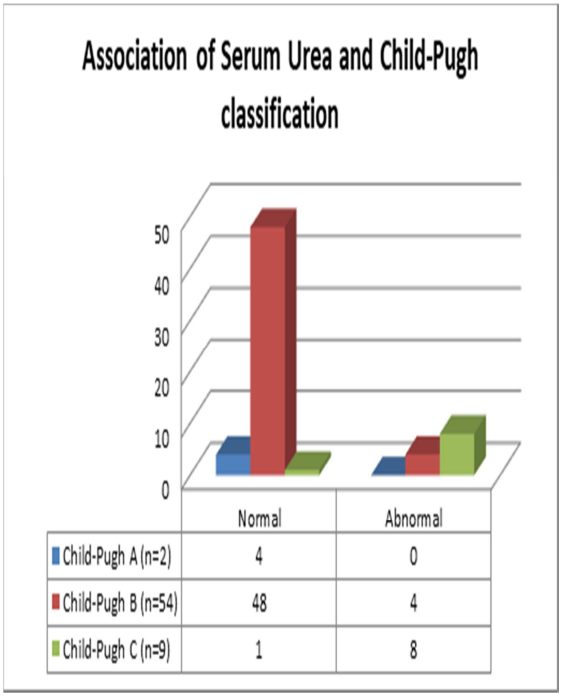

Figure 9: Association of Serum Urea and Child-Pugh classification

Association of Serum Creatinine and Child-Pugh classification

It was observed that there was significant increase in abnormal value of serum creatinine with increase in the severity of liver disease as per Chi-Square test ($p<0.05$).

Table 10: Association of Serum Creatinine and Child-Pugh classification

Classification	Normal		Abnormal		Chi-Square Value	p Value
	N	%	N	%		
Child-Pugh A (n=2)	2	3.6%	0	-	26.773	<0.05
Child-Pugh B (n=54)	48	94.6%	6	42.9%		
Child-Pugh C (n=9)	1	1.8%	8	57.1%		
Total	51	100%	14	100%		

Association of Renal Dysfunction and Child-Pugh classification

2 (4.9%) patients each corresponded to Child–Pugh A class and Child–Pugh C class while 37 (90.2%) patients corresponded to Child–Pugh B class.There was significant increase in renal dysfunction with increase in the severity of liver disease as per Chi-Square test ($p<0.05$).

DISCUSSION

A prospective cross sectional study was conducted among 65 patients in department of medicine Shri. B. M. Patil Medical College Hospital and Research Centre Vijayapur to evaluate the assessment of renal function in chronic liver disease.

The prevalence of CLD has been increasing since last few years which can both be attributed to early diagnosis and an increased incidence.[37] One of the

major concerns associated with CLD is its unrelenting course, as no therapies have been found to prevent its progression to advanced stages which are marked by fibrosis and cirrhosis as final outcome.

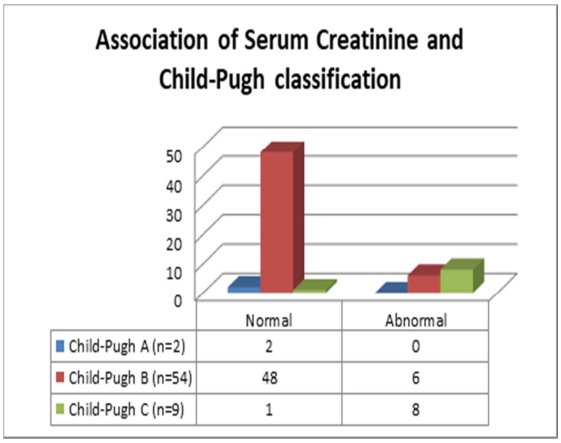

Figure 10: Association of Serum Creatinine and Child-Pugh classification

Table 11: Association of Renal Dysfunction and Child-Pugh classification

Classification	Normal Dysfunction		Renal Dysfunction		Chi-Square Value	p Value
	N	%	N	%		
Child-Pugh A (n=2)	2	4.9%	0	-	11.504	<0.05
Child-Pugh B (n=54)	37	90.2%	17	70.8%		
Child-Pugh C (n=9)	2	4.9%	7	29.2%		
Total	41	100%	24	100%		

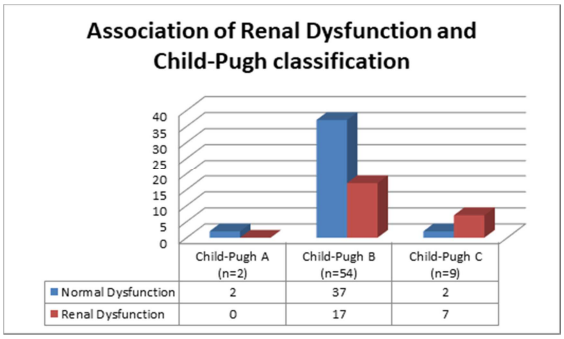

Figure 11: Association of Renal Dysfunction and Child-Pugh classification

Advancement of liver disease is generally associated with various consequences such as PHTN (Portal Hypertension), upper GI bleed, ascites and SBP (Spontaneous bacterial peritonitis). Deranged liver physiology has a profound effect on the homeostatic mechanisms of the body affecting various other organs, including lungs and kidneys.

Importance of renal involvement in CLD has long been recognized by many workers.[32,38] Renal dysfunction has been recently emphasized by Choi et al. in a retrospective study, where they concluded that renal derangement in CLD was not an uncommon phenomenon.[39] Renal failure in patients with CLD, particularly with advanced liver disease, seems to be common; however, the exact incidence is unknown and is probably underestimated. This may be explained by the fact that patients with cirrhosis tend to have falsely low SCr levels due to decreased hepatic creatinine synthesis and decreased skeletal muscle mass. ARF in patients with cirrhosis frequently accompanies complications such as bacterial peritonitis, sepsis or hypovolemia from gastrointestinal bleeding, excessive diuretic therapy or administration of nephrotoxic drugs/contrast agents.[40] The probability of the occurrence of HRS in patients with cirrhosis and ascites at 1and 5 years is 18% and 39%, respectively, with mortality approaching 100% in type 1 HRS without specific therapy. The median survival time in these patients without liver transplantation was only 12 days after diagnosis in one study.[26] However, this seems to have improved with terlipressin and albumin therapy. The development of ARF in patients with advanced liver disease has significant prognostic importance.[41] In patients with cirrhosis admitted to hospital with acute upper gastrointestinal hemorrhage, development of ARF forms an independent predictive factor for death.[19] There is considerable evidence that ARF in cirrhosis is primarily related to disturbances in circulatory function, mainly a reduction in systemic vascular resistance as a result of primary arterial vasodilatation in the splanchnic circulation, triggered by PHTN.[23] Furthermore, an intrinsic defect in cardiac performance termed cirrhotic cardiomyopathy lead to attenuated cardiac function, also contribute to renal dysfunction in cirrhotics particularly when exposed to stressful events like sepsis.[24]

The diagnosis of ARF in cirrhosis is traditionally made by a 50% increase in sCr with setting a fixed sCr threshold of ≥1.5mg/dl.[31] However, final consensus has not been reached yet on classification of cirrhosis-AKI. In the last decade, several attempts have been made. In 2002, the ADQI Working Group developed RIFLE criteria for AKI. Subsequent evidence that even small increase in sCr (as small as 0.3mg/dl) also has a negative impact on survival led to a modification of the RIFLE criteria called AKIN.[26]

More recently, the KDIGO criteria have been developed to reach a consensus drawing consolidating elements of both RIFLE and AKIN on staging AKI.[44] Whether these criteria improve the traditional criterion (a final threshold value for sCr of 1.5mg/dl) in terms of a better prediction of mortality is still a matter of debate.[45]

In the present study, majority of the patients (32.4%) were in the age group of 31-40 years followed by 21.5% in the age group of 41-50 years, 16.9% in the age group of 61-70 years, 15.4% in the age group of 51-60 years, 9.2% patients in the age group of 21-30 years and 4.6% in the age group of >70 years. The mean age of the patients was 45.78 ± 13.19 years. There was male preponderance (90.8%) whereas

female patients constituted 9.2% of the study group. This is similar to the studies of Aggarwal HK et al,[23] Mohan J et al,[24] Das N et al,[25] and Zhou F et al.[26]

Aggarwal HK et al,[46] study assessing the incidence and relationship of various factors for different types of renal failure in cirrhotic patients found mean age of patients was 46.12±11.33 years, with arange of 20–70 years. Ninety-six patients were males with only four females.

Mohan J et al,[47] retrospective study analyzing the profile of renal dysfunction in patients with cirrhosis found mean age of patients was 48.32 ± 10.19 years. Of these, majority were male (95% (95/100)) and females were 5% (5/100).

Das N et al,[32] cross-sectional, observational study assessing the renal function in chronic liver diseases found mean age of the patients were 43.58 years and majority of patients were male.

Zhou F et al,[36] retrospective analysis assessing the prognostic accuracy of absolute serum creatinine (sCr) changes ('Delta-sCr') on the long-term outcomes in cirrhotic patients found median age of the patients was 55.68±12.56 years, and 63.06% (n=210) of the patients were male.

In our study, 47 (72.2%) patients suffered from Alcoholic liver disease while 9 (13.9%) and 7 (10.8%) patients had chronic Hepatitis-B and chronic Hepatitis-C respectively. 2 (3.1%) patients had Nonalcoholic steatohepatitis. This is comparable to the studies of Das N et al,[32] Aggarwal HK et al,[46] Mohan J et al,[47] and Zhou F et al.[36]

Das N et al,[32] cross-sectional, observational study assessing the renal function in chronic liver diseases reported most common cause of chronic liver disease was alcohol followed by Hepatitis B and Hepatitis C.34 (68%) patients suffered from Alcoholic liver disease,7 (14%) patients had chronic Hepatitis-B, 3 (6%) patients had chronic Hepatitis-C, 3 (6%) patients had Non alcoholic fatty liver disease, 2 (4%) patients had Wilson's Disease and 1 (2%) patients had autoimmune hepatitis.

Aggarwal HK et al,[46] study assessing the incidence and relationship of various factors for different types of renal failure in cirrhotic patients reported major etiology to be alcohol (n=88) and all the patients in this group were males. Other etiologies included cryptogenic (n=5), hepatitis B (n=4), hepatitis C (n=2) and alcohol with hepatitis B (n=1). Icterus was present in 59 patients; 60 patients had clinically evident ascites with almost half of the patients having fluid thrill whereas, UGI bleed was present in 41 patients and 26 patients had features of hepatic encephalopathy (HE).

Mohan J et al,[47] retrospective study analyzing the profile of renal dysfunction in patients with cirrhosis reported most common etiology of cirrhosis was alcohol 85% (85/100), followed by Hepatitis B (11% (11/100)) and C virus (4% (4/100)). Renal dysfunction was observed in 33.3% (5/15) of cirrhotic cases with viral etiology. There is no significant association between the etiologies of cirrhosis and renal disorders ($p = 0.25$).

Zhou F et al,[36] retrospective analysis assessing the prognostic accuracy of absolute serum creatinine (sCr) changes ('Delta-sCr') on the long-term outcomes in cirrhotic patients reported most common etiology of cirrhosis was HBV infection (n=232, 69.7%), followed by miscellaneous (n=40,12%), Alcohol (n=30, 9%), Cholestasis (n=17, 5.1%), and Autoimmune (n=14, 4.2%).

It was observed in our study that 24 (36.9%) patients had renal dysfunction. The study of Mohan J et al,[17] analyzing the profile of renal dysfunction in patients with cirrhosis found renal diseases prevalance in 22% (22/100) of cirrhotic patients.

The most common type of renal dysfunction in our study was Acute Kidney Injury (58.3%) followed by Hepatorenal Syndrome (41.7%). This is concordant to the studies of Bucsics Tet al104, Mohan J et al,[26] and Zhou F et al.[36]

Bucsics T et al,[35] study summarized that Renal dysfunction is a common complication of liver cirrhosis and of utmost clinical and prognostic relevance. Patients with cirrhosis are more prone to developing acute kidney injury (AKI) than the non-cirrhotic population. Pre-renal AKI, the hepatorenal syndrome type of AKI (HRS-AKI, formerly known as 'type 1') and acute tubular necrosis represent the most common causes of AKI in cirrhosis.

Mohan J et al,[47] retrospective study analyzing the profile of renal dysfunction in patients with cirrhosis reported most common type of renal dysfunction in liver cirrhotic cases was AKI, present in 12% (12/100) of patients followed by HRS(7%, 7/100) and CKD (3%, 3/100).

Zhou F et al,[36] retrospective analysis assessing the prognostic accuracy of absolute serum creatinine (sCr) changes ('Delta-sCr') on the long-term outcomes in cirrhotic patients, and evaluating the performance of the 'Delta-sCr' approach to stage acute kidney injury (AKI), compared with the Kidney Disease Improving Global Outcomes (KDIGO) criteria reported prevalence of AKI in cirrhotic patients was 18.01% by the KDIGO criteria, and 25.22% by the 'Delta-sCr' system.

It was observed in the present study that majority of the cases of renal dysfunction (19 out of 24; 79.2%) were associated with alcoholic chronic liver disease. However there was no significant association between the etiology and renal dysfunction as per Chi-Square test ($p>0.05$).

Mohan J et al,[47] retrospective study analyzing the profile of renal dysfunction in patients with cirrhosis reported no statistically significant difference in renal parameters in different etiologies of liver cirrhosis.

In our study, 49 (75.4%) patients had serum urea in the range of 15-50 mg/dl while 31 (47.8%) patients had serum creatinine level of 1 mg/dl. 49 (75.4%)

patients had serum sodium level in the range of 137-145mEq/L while 58 (89.3%) patients had serum potassium in the range of 3.5-5.1mEq/L. 56 (86.2%) patients had serum chloride level in the range of 97-110mEq/L while 59 (90.8%) patients had uric acid level in the range of 2.5-7.0 mg/dl.

48 (73.7%) patients had total bilirubin level >3 mg/dl while 56 (86.2%) patients had serum Alanine amino transferase (ALT) <100u/L.33 (50.8%) patients had serum Aspartate amino transferase (AST) <100 u/L and39 (60.1%) patients had serum Alkaline phosphatase (ALP) within the range of 100-200 u/L. 61(93.8%) had serum albumin level <3gmdl while 54 (83.1%) patients had serum globulin in the range of 2.5-4 gm/dl. Similar observations were noted in the studies of Aggarwal HK et al,[46] and Das N et al.[32]

Aggarwal HK et al,[46] study assessing the incidence and relationship of various factors for different types of renal failure in cirrhotic patients reported at the time of presentation, 37 patients had renal dysfunction with RFIs indicating a pre-renal type of renal failure in 30 patients, whereas intrinsic renal disease in six patients and structural renal damage was found in only one patient. Five patients had features suggestive of HRS. Patients with PHTN as marked by PVD of ≥13mm and/or ascites had higher incidence of renal dysfunction. Patients with other forms of decompensation such as jaundice, upper gastro-intestinal bleed and HE were prone to develop renal derangements as compared to their counterparts. Infection in the form of SBP and/or sepsis predisposed patients to develop renal dysfunction.

Das N et al,[32] cross-sectional, observational study assessing the renal function in chronic liver diseases reported 39 patients (78%) had Serum total protein 6 gm/dl. Forty seven patients (94%) had Serum albumin level <3gmdl. Forty one patients (82%) had serum urea within the range of 15-40 mg/dl. Nine patients (18%) had serum urea > 41 mg/dl. Forty patients (80%) on day 1 had serum creatinine level 1 mg/dl, and 40 patients (80%) had serum creatinine level on day 3 as1 mgdl.66% patients had serum bilirubin level > 2mg/ 20 patients (40%) had Serum AST within the range of 42-100 u/L. Thirty five patients(70%) had Serum Alanine amino transferase (ALT) < 100 u/L 15 patients(30%) had Serum Alkaline phosphatase (ALP) < 100 u/L. Thirty three patients (66%) had Serum ALP within the range of 100-200 u/L. Two patients (4%) had Serum ALP > 200 u/L.

It was observed in the present study that there was significant increase in abnormal value of serum urea and serum creatinine with increase in the severity of liver disease as per Chi-Square test ($p<0.05$). 2 (4.9%) patients each corresponded to Child–Pugh A class and Child–Pugh C class while 37 (90.2%) patients corresponded to Child–Pugh B class.There was significant increase in renal dysfunction with increase in the severity of liver disease as per Chi-Square test ($p<0.05$). This is similar to the studies of Mohan J et al,[47] Das N et al,[32] Al-Mamun A et al,[48] and Fornari F et al.[49]

Mohan J et al,[47] retrospective study analyzing the profile of renal dysfunction in patients with cirrhosis reported out of the one hundred patients, sixteen patients (16%, 16/100) corresponded to Child–Pugh C class, 80% (80/100) to B class, and only 4% (4/100) were class A. There is an increase in the number of renal disorder with increase in the severity of cirrhosis. In the cirrhotic patients with higher severity of cirrhosis (Child Pugh class B and C), renal dysfunction was developed much more (OR=3.37; CI=1.08-10.5; P = 0.03).

Das N et al,[32] cross-sectional, observational study assessing the renal function in chronic liver diseases reported distribution of serum urea and creatinine, according to the severities of liver disease as per Child Pugh classification, was statistically significant, but serum creatinine level on day 1 and day 3 was not found to be significantly distributed among different aetiologies of chronic liver disease.

Al-Mamun A et al,[48] study reported no statistically significant relation between Child-Pugh score and serum creatinine. Fornari F et al,[49] study showed 30% of patients with cirrhosis had gall stones, risk of developing stones most strongly associated with Child's grade C & alcoholic cirrhosis with a yearly incidence of about 5%.

CONCLUSION

Physicians involved in the care of patients with cirrhosis have become even more interested in the assessment of renal function and creatinine was shown to be astrong prognostic marker. However, in cirrhosis, there is still a gap between serum creatinine and renal function. Serum creatinine and the widely used creatinine-based equations must be interpreted with caution.

This study emphasizes the fact that we should be more vigilant when treating Chronic Liver Disease (CLD) patients, regarding their renal function, as proper screening, prevention and treatment of renal dysfunction can decrease morbidity and mortality.

Patient need to be cautioned about the poor liver condition and further added complication of renal function for which they need to have regular follow-up and treatment.

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