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Role Of Cystitien-C Based Estimated Glomerular Filtration Rate In Early Detection Of Hepatorenal Syndrome In Chronic Alcoholic Liver Disease Patients

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1. INTRODUCTION

Cirrhosis can be defined as the histological development of regenerative nodules surrounded by fibrous bands in response to chronic liver injury.[1] Hepatorenal syndrome is development of renal failure in patients with severe liver disease.[2] Patients with advanced cirrhosis will mostly develop hepatorenal syndrome and will usually have jaundice and other stigmata of chronic liver disease.[2] Hepatorenal syndrome can be classified as hepatorenal syndrome type-1 and type-2 based on mild or high serum creatinine elevations.[3]

Glomerular filtration rate (GFR) is widely used as an indicator of kidney function and serum creatinine is commonly used marker for calculating GFR. Cystatin C, a protein freely filtered by the glomerulus has emerged as an alternative marker for estimating GFR.[4] Serum cystatin C is currently being investigated for the prediction of Acute kidney injury in patients with cardiac surgery, advanced liver diseases, and patients undergoing liver transplantation.[5] Cystatine-C based GFR can help identify early renal parameters derangement in acute on chronic liver failure patients even during the period of mild-to-moderate renal dysfunction.[5]

Cystatin C is known to be a superior marker of renal function than creatinine because it is produced not just in muscle cells but in all nucleated cells.[6] Renal impairment is a common finding in patients with chronic liver disease and it impacts on the patients survival.[7]

The incidence of chronic alcoholic liver disease is increasing every day and hepatorenal syndrome is most common complication seen is chronic alcoholic liver disease patients. Development of hepatorenal syndrome is associated with high risk of mortality in these patients.

Creatinine based estimated glomerular filtration rate is most commonly used but creatinine value can be effected by factors like muscle and diet. Cystitine-C based estimated glomerular filtration rate is considered superior as cystitine-c is not affected by diet or muscle mass.

Early detection of renal impairment in chronic alcoholic liver disease patients and if indicated therapeutic intervention can help in reducing mortality in these patients. This study assesses if cystitine-C based estimated glomerular filtration is better than creatitine based estimated glomerular filtration rate in early detection of hepatorenal syndrome.

2. MATERIAL AND METHODS

A prospective study was undertaken in Department of General Medicine of R L Jalappa Hospital, Sri Devaraj Urs Medical College, Tamaka, Kolar. Clearance from institutional ethics committee was obtained before the study was started. Sample size was estimated by using correlation coefficient (r) of GFR with Serum cystatin C as 0.817 (i.e. r = - 0.817) from the study by Bhuyan et al. Using these values at 95% confidence level and 90% power and substituting in the below formula, sample

size of 13 was obtained. Considering 10% Non-response rate a sample size of 13 + 1.3 = 15 subjects were included in the study. Patients of age 18 – 80 years who were diagnosed with cirrhosis of liver either clinically or by laboratory findings or by ultrasonography were included in to the study. The patients with end stage renal disease. Hepatocellular carcinoma, congestive heart failure, sepsis, dehydration, a history of gastrointestinal bleeding, spontaneous bacterial peritonitis, hyperthyroidism or hypothyroidism was excluded from the study.

The data regarding age, gender, history of hypertension, renal and cardiac diseases was collected from all the patients included in to the study. The serum creatinine was estimated and reference range for serum creainine levels was defined as 0.66 to 1.25 mg/dL of males and 0.52 – 1.04 mg/dL for females. Serum Cystatin C estimation was carried out using semi auto analyser. The test was based on the immune turbidimetric method. The reference range was delineated as 0.61 to 1.01 mg/L. KDIGO classification for chronic kidney disease was used for categorization of GFR values.

GFR was also calculated using the simple formula GFR=100/serum cystatin C (mg/L), which is based on serum cystatin C levels. In the context of the current study, this method provides a straightforward yet efficient way to estimate GFR.

The data thus obtained was compiled using excel sheet and analysed using Statistical Package for social services.

3. RESULTS

Table 1. Distribution of study group according to age

Age group	Frequency	Percent
41 – 50 years	1	6.7
51 – 60 years	5	33.3
More than 60 years	9	60.0
Total	15	100

This study had shown that about 60.0% of the cases were aged more than 60 years.

Table 2. Distribution of study group according to gender

Gender	Frequency	Percent
Male	12	80.0
Female	3	20.0
Total	15	100

About 80.0% of the cases were males in this study.

Table 3. Distribution of study group according to CKD grade

CKD grade	Frequency	Percent
Grade 1	1	6.7
Grade 2	6	40.0
Grade 3a	3	20.0
Grade 3b	3	20.0
Grade 4	2	13.3
Total	15	100

About 40.0% of the cases in this study had Grade 2 CKD.

Table 4. Distribution of study group according to Comorbidity

Co morbidity	Frequency	Percent
Autoimmune disease	2	13.3
Diabetes Mellitus	7	46.7
Hypertension	6	40.0
Total	15	100

About 46.7% of the cases in this study had diabetes mellitus, 40.0% had hypertension and 13.3% had autoimmune disease.

Table 5. Distribution of study group according to Habits

Habits	Frequency	Percent
H/O smoking	6	40.0
H/O alcohol	4	26.7

About 40.0% of the cases in this study had history of smoking and 26.7% had history of alcohol consumption.

Table 6. Distribution of study group according to correlation of Biomarkers

Biomarkers	Mean ± SD	Correlation Coefficient	P value, Sig
Creatinine	2.01 ± 0.42	0.055	0.847, NS
GFR based on creatinine	55.8 ± 24.3		
Cystatin C	2.54 ± 0.53	0.094	0.739, NS
GFR based on Cystatin C	43.8 ± 16.6		

Mean creatinine level was 2.01 mg/dl and GFR based on creatinine level was 55.8 mg/dl. The correlation coefficient was 0.055 and it was not statistically significant. Mean cystatin C was 2.54 and GFR bases Cystatin C was 43.8 and correlation coefficient was 0.094 which was not statistically significant.

Table 7. Distribution of study group according to correlation of Biomarkers

Biomarkers	Mean ± SD	Correlation Coefficient	P value, Sig
GFR based on creatinine	55.8 ± 24.3	0.876	0.000, Sig
GFR based on Cystatin C	43.8 ± 16.6		

Mean GFR based on creatinine was 55.8 and GFR based on Cystatin C was 43.8 and corresponding correlation coefficient was 0.876 and it was statistically significant.

4. DISCUSSION

This study was mainly undertaken in order to assess the use of cystatin C based estimated glomerular filtration rate in early detection of development of hepatorenal syndrome in chronic liver disease patients.

According to this study, around 60.0% of the cases included people over the age of 60. In this study, men made up about 80.0% of the cases. In this study, Grade 2 CKD was present in about 40.0% of the cases. About 40.0% of the cases in this study had hypertension, 13.3% had autoimmune illness, and 46.7% had diabetes mellitus. About 40.0% of the study's cases

had a history of smoking, and 26.7% had a history of drinking alcohol.

GFR was 55.8 mg/dl based on creatinine levels, with a mean creatinine level of 2.01 mg/dl. There was no statistical significance in the correlation coefficient, which was 0.055. The correlation value was 0.094, which was not statistically significant, and the mean cystatin C was 2.54 and the GFR bases cystatin C was 43.8. There was a statistically significant link between the mean GFR based on creatinine (55.8) and GFR based on Cystatin C (43.8), with a corresponding correlation coefficient of 0.876.

A number of studies reported that, cystatin C is useful and has more significant correlation with GFR in comparison with serum creatinine in detection of moderate to severe renal impairment in patients with liver cirrhosis.[8, 9] According to the current study's findings, cystatin C and cystatin C-based formulas or equations consistently shown a substantial association to GFR in patients with liver cirrhosis and were the measurements that best distinguished early renal impairment. Finding indicators that can diagnose renal impairment early on is crucial since patients with liver cirrhosis are highly sensitive to even slight changes in GFR, which can significantly affect their survival.[10]

Cystatin C-based GFR-estimating equations are helpful in all age groups, including the elderly, and perform better than creatinine-based equations in predicting end-stage renal disease, according to Grubb A's investigation into the utility of cystatin C in the assessment of renal failure.[11] Herget-Rosenthal S et al. found that blood cystatin C identified acute renal injury 1-2 days before serum creatinine measurement in a brief follow-up investigation on patients with severe illness.[12] According to a longer follow-up research by Seo YS et al., individuals with severe cirrhosis and normal creatinine who subsequently developed HRS within a year had significantly higher levels of cystatin C, suggesting that cystatin C is a reliable indicator of HRS.[13]

5. CONCLUSION

This study had shown that the Cystatin C levels are significantly higher in patients with liver cirrhosis developing renal dysfunction. Even before the serum creatinine level rises, an increased level of cystatin C may be a sign of a decline in GFR. As a result, in individuals with liver cirrhosis, serum cystatin C level measurement may be a helpful technique for the early identification and tracking of renal failure.

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