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A STUDY OF HEPATORENAL SYNDROME IN CASES OF DCLD AT TERTIARY CARE HOSPITAL

General Medicine

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ABSTRACT

Background: Hepatorenal syndrome indicates AKI in patients of Acute or chronic liver diaease. Sr. Cystatin c serves as an early marker in development of AKI and prevents ESRD **Aim:** A study of Hepatorenal Syndrome in DCLD patients to assess the role of Cystatin C as a biomarker in early detection of AKI in a tertiary care hospital. **Results:** Out of 50 DCLD patients, 38 showed Sr. Creatinine value and 50 showed Sr. Cystatin C levels above baseline on early testing **Discussion:** When the GFR decreases, Cystatin C levels rises proportionately. Serum Creatinine measurement and thereby GFR estimation is faulty in cirrhosis due to Defective synthesis of creatine and precursors of creatinine in liver ,Poor muscle mass and Malnutrition ,Higher volume of distribution, assay interference due to compounds like Bilirubin. b **Conclusion:** Sr Cys C has better clinical predictive value for HRS than Sr Creat and BUN. Cystatin C helps in early detection of HRS, Timely intervention to prevent the progression, Improvement of prognosis and reduction of mortality.

KEYWORDS

Serum Creatinine, DCLD, serum Cystatin C, HRS

INTRODUCTION:

Heptorenal Syndrome (HRS) is a condition which indicates the acute kidney injury in patients of acute or chronic liver disease Since AKI diagnosis is still based on an increase in serum creatinine levels or a decrease in urine output, both are insensitive, research has tried to find and confirm novel biomarkers for earlier AKI detection Use of serum creatinine have certain limitations in DCLD patients due to reduced synthesis and reduced production due to decreased muscle mass, drugs used in the treatment of DCLD and due to hyperbilirubinemia.

Serum Cystatin C does not get influenced by gender,age,protein intake, muscle mass and serum bilirubin. Thus serum Cystatin C serves as an early marker in the development of AKI in patients of DCLD and it helps in preventing the development of end stage renal disease.

This study focuses on the importance of serum Cystatin C level in the diagnosis of AKI in HRS patients and also the caluculation of eGFR based on the serum Cystatin C level. This helps in estimating the risk of developing HRS, which aids in early diagnosis by raising clinical awareness and decreasing the mortality and morbidity through early management with appropriate therapy .

AIM:

A study of Hepatorenal Syndrome in DCLD patients to assess the role of Cystatin C as a biomarker in early detection of AKI in a tertiary care hospital.

Objectives:

Primary Objective:

To assess the role of Cystatin C in Hepatorenl Syndrome

Secondary Objective:

1. To determine the causes of DCLD
2. To identify the complications of DCLD
3. To identify the advantages of Serum CystatinC over Serum Creatitine in the calculation of eGFR for the diagnosis of acute kidney injury at an early stage.

Study Design: This study is a cross sectional study

This study was conducted in: the Department of General Medicine at Government Medical College and General Hospital, Kadapa.

Study Duration: this study was conducted from March 2020 to April 2021 over a period of 1 year after the approval of hospital ethica; committee.

Study Population: This study was conducted in 50 patients of DCLD with HRS after omitting under exclusion criteria.

Inclusion Criteria:

- Patient age 18-65 yrs
- Decompensated liver diseases of all etiology with HRS

Exclusion Criteria:

- Known Renal Disease
- Known Renal Transplant
- Past History of Nephrotoxic Drugs.
- Immunocompromised state
- Past History of HRS

GFR Calculation:

For GFR calculation using serum creatinine,The CKD-EPI-CREATININE equation :eGFRcre= 141 × min(Scr/κ, 1)α× max(Scr/κ, 1)-1.209 × 0.993Age × 1.018 [if female] - 1.159 [if black] where Scr is serum creatinine, κ is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of Scr/κor 1, and max indicates the maximum of Scr/κ or 1. For GFR calculation using serum Cystatin C, The CKD-EPI Cystatin C equation: eGFRcys= 133 × min(Scys/0.8, 1)−0.499 × max (Scys/0.8, 1)−1.328 × 0.996Age [× 0.932 if female], where Scys is serum cystatin C, min indicates the minimum of Scr/κ or 1, and max indicates the maximum of Scys/κ or 1.

Statistical analysis:

The collected data were checked for completeness before entering it into the Microsoft excel spreadsheet. The validation of the data was checked at regular intervals. Data analysis was performed using Statistical Package for Social Sciences (SPSS IBM) 21. The data was presentated in the form of numbers and percentages for qualitative variables and mean or SD for quantitative variables. Suitable statistical test (according to the nature and the distribution of dataeg: paired t test) was applied to assess the significance of study findings.

Ethical consideration:

Institutional Ethical Committee approval was obtained before starting the study. The participants were explained that the data collected in this study would be used only for research purposes. The participants were explained about the freedom of withdrawal from the study at any time without penalty or loss of benefits.

RESULTS:

Serum creatinine and Serum Cystatin C distribution in the study population:

	Serum Cystatin	Serum Creatinine
Within the reference range: 0	12	
Above the reference range: 50	38	

Reference range:

Cystatin C = 0.62-1.12 mg/dl
Creatinine = 0.70-1.20 mg/dl

Paired sample t-test between serum cystatin and serum creatinine

		N	Mean ± S.D	S.E	t-value (p-value)	Statistical Sig.
Pair 1	Serum Cystatin	50	3.604 ± 1.529	0.216	14.748** (0.000)	P<0.001

	Serum Creatinine	50	2.120 ± 0.913	0.129		

**Highly significant;

This indicates that the Serum cystatin possess have high mean value and the serum creatinine showed less mean value (m=2.120) as compared to serum cystatin. The result of t test reveals that t-value = 14.748 and sig = 0.000 which is less than 0.01 (at 99% level of confidence) which indicates that there is significant difference.

Correlation between eGFR cys and Serum Cystatin

A correlation coefficient measured the strength of a linear between two variables. The correlation between eGFRCystatin and serum cystatin was -0.688 which indicates negative magnitude and significant at 0.01 level.

Correlation between eGFR cre and Serum Creatinine:

The correlation between eGFR ceatinine and serum creatinine was -0.774 which indicates negative magnitude and significant at 0.01 level. By the comparision of Pearson Correlation, eGFRcystatin C is better than eGFRcreatinine.

ROC Curve FOR Cystatin C and Creatinine

Optimal Cutoff values of

Index	AUC	Optimal Cutoff Value	Sensitivity	Specificity
Serum Cystatin	917	1.25	100	88.9
Serum Creatinine	908	1.65	95.5	42.9

DISCUSSION:

Renal insufficiency affects the prognosis of individuals with liver cirrhosis and increases mortality by sevenfold. [4]Clinicians face a hurdle when diagnosing HRS in the early stage. Patients must undergo appropriate volume resuscitation for 48 hours before the diagnosis of HRS can be confirmed, and diuretics and other causes of AKI must be ruled out. When HRS is suspected, this hurdle causes a delay in diagnosis and as a result postponement of suitable therapy with albumin infusions, terlipressin or other vasoconstrictors. Serum Cystatin C helps in early prediction of HRS and provides advantage in the intervention to prevent the impending kidney injury and in prioritising patients for the liver transplantation [7].

Serum Cystatin C is a non-glycosylated 13.3-kDa protein of Cystatinprotease inhibitors family[8]Cystatin C is produced not only by muscle but also by all the nucleated cells of our body. Concentration of serum Cystatin C does not get influenced by gender, age,race, protein intake and muscle mass. So, the production of Cystatin C varies less than the creatinine production between the individuals and serum concentration of Cystatin C is similar between the individuals of same GFR. Also, following the glomerular filtration, Cystatin C is entirely catabolized in the proximal tubule of the kidney. It is not returned to the bloodstream. It's an endogenous marker that's simple, accurate, and a rapid marker for GFR

When the GFR decreases, Cystatin C levels rises proportionately. Serum Creatinine measurement and thereby GFR estimation is faulty in cirrhosis due to the following reasons

1. Defective synthesis of creatine and precursors of creatinine in liver
2. Poor muscle mass and Malnutrition
3. Higher volume of distribution
4. Assay interference due to Jaffe positive compounds like Bilirubin.

Deceptively, normal creatinine values (<1mg/dl) wil mask the significant decline in Glomerular Filtration rate(GFR) This study reveals that in patients with kidney injury, serum Cystatin C rises before serum Creatinine rises, and it can be used as an early marker for the diagnosis of HRS in DCLD patients.In addition, Cystatin-based GFR estimation formulas have higher sensitivity and specificity than Creatinine-based formulations.

SUMMARY AND CONCLUSION:

This is a cross sectional study conducted among 50 DCLD patients with HRS dysfunction.

1. The Mean age of the Patricipants were 41.70 +/- 7.69 years with the majority of the participants were Male 80%.
2. Among the participants HRS type I (72%) is the most common type among the patients presenting with Hepatorenal dysfunction while the HRS Type II incidence is 14% only
3. 24% of the participants had normal serum creatinine levels with elevated serum Cystatin C levels.
4. Serum Cystatin C helps in predicting the renal failure earlier than Serum Creatinine and helps in avoiding the precipitating factors for the renal dysfunction and helps in early intervention for the kidney injury.
5. eGFRcaluculation using Cystatin C is better than eGFR calculation using Serum Creatinine in the diagnosis of Kidney injury
6. Also when GFR decreases, the level of serum Cystatin C rises significantly.
7. Among the etiologies of DCLD, Alcohol is the leading cause seen in 74% of the patients
8. The second most common etiology is Viral Hepatitis 28%
9. The most common presentation of the Portal hypertension which is a complication of DCLD is Upper Gastrointestinal Tract bleeding followed by Ascites.

This study concluded that

1. Serum Cystatin C and Serum Creatinine are independent risk factors for HRS.
2. Serum Cystatin C has better clinical predictive value for HRS than serum creatinine and BUN.
3. Serum Cystatin C helps in early detection of HRS, Timely intervention to prevent the progression, Improvement of prognosis and reduction of mortality.

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