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COMPARISON OF EGFR USING CREATININE AND CYSTATIN C BASED EQUATIONS IN PATIENTS WITH DECOMPENSATED CIRRHOSIS OF LIVER TO DETECT EARLY RENAL IMPAIRMENT

Gastroenterology

Srividya Manjunath — Resident, Department of Digestive Health and Diseases, Kilpauk Medical College, Chennai

Kani Shaik Mohammed* — Associate Professor, Department of Digestive Health and Diseases, Kilpauk Medical College, Chennai *Corresponding Author

A R Akilandeswari — Assistant Professor, Department of Digestive Health and Diseases, Kilpauk Medical College, Chennai

ABSTRACT

Renal injury impacts survival significantly in patients with decompensated cirrhosis of liver making early detection of the same imperative. Presently widely used markers like Serum creatinine and creatinine based equations overestimate the eGFR in these patients causing delayed diagnosis and treatment. The present study aims to detect early renal impairment/ reductions in eGFR in patients with Decompensated chronic liver disease with normal serum creatinine.

KEYWORDS

Decompensated cirrhosis, Serum creatinine, Serum Cystatin C , eGFR

INTRODUCTION

Renal impairment is an ominous complication of cirrhosis of liver, occurring in 20 to 40 % patients with advanced cirrhosis of liver. [1] Renal injury can be acute or chronic, acute injury can be functional (volume responsive – precipitated by infection, GI bleed, vomiting or volume unresponsive – AKI HRS) or structural. It is important to recognize early as this complication significantly reduces survival and is associated with high transplant wait list mortality.[1,2]

Serum creatinine is widely used to assess renal function but is fraught with limitations such as it is influenced by bodyweight, race, age, and gender, decreased formation of creatinine from creatinine in muscles, secondary to muscle wasting, increased tubular secretion of creatinine, the increased volume of distribution in cirrhosis that may dilute serum creatinine, interference with assays for serum creatinine by elevated Bilirubin [3]. Also, rise in serum creatinine lags behind renal impairment.

Hence, there is an interest in newer biomarkers to identify early renal injury in these group of patients. Cystatin C is a cysteine proteinase inhibitor produced at a constant rate - by nucleated cells also freely filtered through the glomeruli, reabsorbed and metabolized in renal tubules rather than being secreted and production is less dependent on hepatic function, age, gender or muscle mass.

In the present study, we aim to compare eGFR calculated using Creatinine (MDRD 4) and Cystatin C (CKD EPI) based equations for early detection of renal impairment.

MATERIALS AND METHODS:

A cross sectional study, conducted in the Department of Digestive Health and Diseases, attached to Government Kilpauk Medical College, Chennai, from June 2018 to November 2019.

INCLUSION CRITERIA:

Patients diagnosed with decompensated chronic liver disease, with normal serum creatinine.

EXCLUSION CRITERIA:

1. Serum creatinine > 1.2mg/dl
2. Spontaneous bacterial Peritonitis
3. Chronic kidney disease
4. Diabetes mellitus, Hypertension
5. Proteinuria
6. Hepatocellular carcinoma
7. Hypothyroidism

Baseline demographic data of all patients recorded, detailed clinical history, decompensations, Physical examination done. Complete blood count, blood urea, Serum creatinine, serum electrolytes, Liver function tests, prothrombin time , INR , Ultrasound abdomen was done for all patients . Serum Cystatin C (Nephelometry method) done at the time of inclusion into study.

eGFR calculation done using MDRD 4 and CKD EPI equations as shown below

Equation	Full expression (mL/min/1.73 m^2)
MDRD-4	$=175 \times (Pcr)^{-1.154} \times age(years)^{-0.203} \times 0.742$ (if female) $\times 1.21$ (if black)
MDRD-6	$=161.5 \times (Pcr)^{-0.999} \times$ age (years)$^{-0.176} \times$ (urea nitrogen)$^{-0.17} \times$ (albumin)$^{0.318} \times 0.762$ (if female) $\times 1.18$ (if black)
CKD-EPI-Pcr	$=141 \times \min(Pcr/\kappa, 1)^{\alpha} \times \max(Pcr/\kappa, 1)^{-1.209} \times 0.993^{age\,(years)} \times 1.018$ (if female) $\times 1.159$ (if black); κ is 0.7 for female and 0.9 for males; α is –0.329 for females and –0.411 for males; "min" is the minimum of Pcr/κ or 1 and "max" the maximum of Pcr/κ or 1
Hoek	$=-4.32 + 80.35 \times 1/$Cystatin C
CKD-EPI-Cys C	$=133 \times \min(\text{Cystatin C}/0.8, 1)^{-0.499} \times \max(\text{Cystatin C}/0.8, 1)^{-1.328} \times 0.996^{age\,(years)} \times 0.932$ (if female) $\times 1.159$ (if black); "min" is the minimum of Cystatin C/0.8 or 1 and "max" the maximum of Cystatin C/0.8 or 1
CKD-EPI-Pcr-Cys C	$=135 \times \min(Pcr/\kappa, 1)^{\alpha} \times \max(Pcr/\kappa, 1)^{-0.601} \times \min(\text{CystC}/0.8, 1)^{-0.375} \times \max(\text{CystC}/0.8, 1)^{-0.711} \times 0.995^{age\,(years)} \times 0.969$ (if female) $\times 1.08$ (if black); κ is 0.7 for female and 0.9 for males. α is –0.248 for females and –0.207 for males. "min" is the minimum of Pcr/κ or 1, or the minimum of Cystatin C/0.8 or 1. "max" is the maximum of Pcr/κ or 1, or the maximum of Cystatin C/0.8 or 1
MELD score	$=10 \times [0.957 \times \ln(Pcr) + 0.378 \times \ln(\text{Total Bilirubin}) + 1.12 \times \ln(INR^2) + 0.643]$

MDRD, modification of diet in renal disease; CKD-EPI, chronic kidney disease epidemiology collaboration; MELD, model for end-stage liver disease; Pcr, creatinine; Cys, serum cystatin C; INR, international normalized ratio.

Statistical Analysis:

The statistical analysis was performed by STATA 11.2 (College station TX USA). Students T test or Mann Whitney test were used for continuous variables and to find the significant difference between age, diagnosis in months, creatinine, MDRD and GFR with Cystatin C respectively. Receiver operator characteristic curve were used to determine best equation of eGFR. $P < 0.05$ considered statistically significant.

Table-1

Character	GROUP A	GROUP B	P value
Age (years)	49.17+/- 8.19	48.24+/- 10.13	0.748
Time since diagnosis	12.02+/- 11.41	9.38 +/- 8.32	0.425
Sex (male)	20 (87%)	16 (94%)	0.455
Sex (women)	3 (13%)	1 (6%)	0.455
Ascites present	16 (70%)	15 ?(88%)	0.455
Ascites absent	7 (30%)	2 (12%)	0.455
HBV	2 (12%)	5 (22%)	
HCV	0	1 (4%)	
NAFLD	2 (12%)	2 (8%)	0.648
Cardiac	0	1 (4%)	
Ethanol	13 (76%)	14 (60%)	
Creatinine	0.92 +/- 0.24	0.93 +/- 0.22	

RESULTS:

A total of 40 patients of decompensated chronic liver disease included in the study. 90% patients were male. Most common cause of cirrhosis was ethanol induced (62.16%) followed by hepatitis B (19.82%). 52% patients belonged to CTP class C, 40% CTP B and 8% CTP A. 23 patients has elevated serum Cystatin C (group A) and 17 patients had normal cystatin C levels (group B). Baseline data of two groups is presented in table 1.

Mean Serum creatinine was 0.92 +/- 0.23 (-.36 – 1.2), mean Serum Cystatin C was 0.953+/- 0.44 (0.27 – 2.08). Mean Cystatin C in CTP A B and C were (0.92 +/- 0.42), (0.88 +/- 0.49), (1.02 +/- 0.42) respectively with P = 0.656.

Mean eGFR using CKP EPI (creatinine) was 91.925 +/- 24.37, CKD EPI (Cystatin) was 96.93 +/- 47.02 and CKD EPI Cystatin and creatinine was (93.60+/- 30.83). AUROC for eGFR using MDRD equation was 0.55, CKD EPI (creatinine) was 0.59. However, AUROC for CKD EPI equations with Cystatin C and Creatinine and Cystatin C combined equation were 1 and 0.93 respectively. (Fig-1)

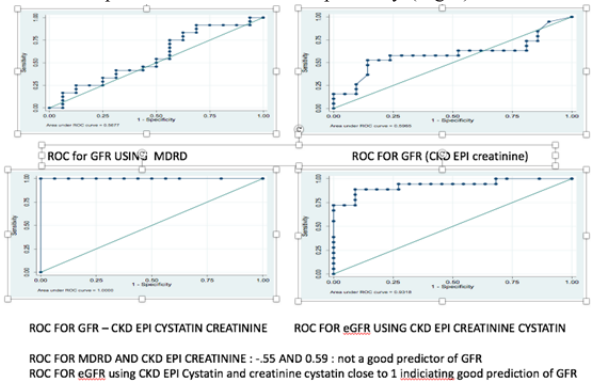

Figure – 1

DISCUSSION :

Measured GFR is a gold standard method to assess kidney function e.g. inulin, non-radiolabelled plasma or urinary iothalamate clearances).[4] However, they are labour and time-intensive and not applicable easily to all patients. Alternative methods of estimating GFR are measuring 24-hour creatinine clearance (CrCl), use of Cockcroft-Gault21 equation [4]. But serum creatinine based equations are known to overestimate GFR in patients with Decompensated cirrhosis. Overestimation of true GFR by the MDRD4 equation was observed in about 50% of patients, confirming that MDRD4 should be interpreted with caution in patients with cirrhosis. [5]

CKD EPI equations were proposed in 2009 (based on creatinine) and Cystatin C based equations were proposed in 2012. 202 patients awaiting liver transplant were evaluated with both MDRD and CKD EPI equations - showed that Cystatin C based equations performed better than creatinine based equations for accurate classification as CKD based on AUROC, similar to the present study. [6] They further showed that creatinine based equations performed worst in patients with large, refractory ascites and MELD > 15.

Another study in 95 patients of Decompensated cirrhosis also showed the superiority of Cystatin based equations in estimating GFR compared to creatinine when measured against a gold standard.[7]

Scores including Cystatin and MELD have been proposed for better prediction of acute kidney injury. Also, cystatin c in some studies has also shown to correlate with further

episodes of AKI, sarcopenia and mortality.[3,8]

The limitations of this study are a small sample size and lack of comparison with gold standard.

CONCLUSION:

In conclusion, a baseline estimation of Cystatin C may give a better estimate of renal status of patients with decompensated cirrhosis of liver. Equations based on Cystatin C (CKD EPI creatinine and CKD EPI Creatinine and Cystatin C provide more accurate measure if GFR, further studies are required to validate the same and to be included in regular clinical practice.

REFERENCES

1. Adebayo D, Wong F, Ascites and Hepatorenal Syndrome (2019) Clin Liver Dis 23, 659 - 682
2. Ginès, P., & Schrier, R. W. (2009). Renal Failure in Cirrhosis. New England Journal of Medicine, 361(13), 1279–1290
3. Maiwall, R., Kumar, A., Bhardwaj, A., Kumar, G., Bhadoria, A. S., & Sarin, S. K. (2017). Cystatin C predicts acute kidney injury and mortality in cirrhotics: A prospective cohort study. Liver International, 38(4), 654–664
4. Mindikoglu AL, Dowling TC, Magder LS, et al. Estimation of Glomerular Filtration Rate in Patients With Cirrhosis by Using New and Conventional Filtration Markers and Dimethylarginines. Clin Gastroenterol Hepatol. 2016;14(4):624.632.e2
5. Francoz C, Sola E. Assessment of renal function in cirrhosis: sarco. penia, gender and ethnicity matter. J Hepatol. 2019;70:828.830
6. De Souza, V., Hadj-Aissa, A., Dolomanova, O., Rabilloud, M., Rognant, N., Lemoine, S., … Dubourg, L. (2014). Creatinine- versus cystatine C-based equations in assessing the renal function of candidates for liver transplantation with cirrhosis. Hepatology, 59(4), 1522–1531
7. Torre A, Aguirre-Valadez JM, Arreola-Guerra JM, et al. Creatinine Versus Cystatin C for Estimating GFR in Patients With Liver Cirrhosis. Am J Kidney Dis. 2016;67(2):342.349
8. JianPing Wu,1 QianXia Wu Serum Cystatin C Predicts Mortality in HBV-Related Decompensated Cirrhosis, BioMed Research International / 2019diagnostic potential to