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Transaminits In Compensated CLD Patients Correlate with Renal Dysfunction: A Prospective Observational Study

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Abstract

Background: Renal dysfunction commonly occurs in patients of liver disease. It has been estimated that acute kidney injury (AKI) occurs in up to 19% of cirrhotic patients admitted to hospital for whatever reason. Assessment of renal function by using GFR based on MDRD equation, which is based on serum creatinine, is problematic in cirrhotic patients. Objectives: This study was aimed to early assessment renal function by using TmP/GFR. **Materials and Methods:** we conducted a prospective observational case control study between July 2023 to August 2024 to assess the strength of association of TmP/GFR as an early marker of proximal renal tubular dysfunction in compensated CLD patients. **Results:** we selected 130 CLD patients visited in gastroenterology OPD and we found that TmP/GFR was higher in CLD patients ($p < 0.001$) than in healthy controls. **Conclusions:** our study showed significantly higher TmP/GFR in CLD patients than in healthy controls even if there is normal serum creatinine value so TmP/GFR could be a better earlier marker of renal dysfunction in compensated CLD patients.

Keywords: Renal dysfunction, liver disease, compensated CLD.

Introduction

Amniotic fluid plays a vital role in pregnancy, facilitating fetal growth, protecting against trauma, preventing cord compression, and aiding in Renal dysfunction commonly occurs in patients of liver disease. It has been estimated that AKI occurs in up to 19% of cirrhotic patients admitted to hospital for whatever reason. Kidney function is defined on the basis of GFR by using the biomarker creatinine, with which it is inversely correlated. All methods for GFR calculation rely on serum creatinine and are problematic in patients with cirrhosis. These patients often have low serum creatinine levels due to reduced production of creatinine from creatine in the liver, a greater volume of distribution due to increases in extracellular fluid and ascites, and significant muscle wasting. Newly found tubular injury markers like CysC, NGAL and KIM 1 are more sensitivity but have limited application in routine use. Tubular injury significantly affects serum phosphorus level because phosphorus handling mainly occurs at the level of proximal renal tubule. The concentration of phosphate ion (Pi) in the fluid in Bowman's space is nearly equivalent to the concentration of free phosphate in the plasma.¹ The kidney is essential for maintaining phosphate balance in the body. The filtration of inorganic phosphate occurs in the form of HPO_4^{2-} and H_2PO_4^- , often in a 4:1 ratio. Studies using micropuncture techniques in the superficial nephrons have shown that over 80% of the phosphate that is filtered is typically reabsorbed in the proximal tubule. The usual urine excretion accounts for roughly 10% of the filtered load. The process of phosphate reabsorption in the proximal tubule occurs via transcellular transport. Transport across the apical membrane occurs by either NPT2a (SLC34A1) or NPT2c (SLC34A3), both of which are Na^+ phosphate cotransporters. NPT2a is the primary contributor, with its expression being influenced by physiological control. An increased intake of phosphate decreases the number of NPT2a cotransporters in the apical membrane, whereas a decreased intake of phosphate increases their number. PTH and glucocorticoids decrease the quantity of NPT2a cotransporters in the apical membrane, resulting in an increase in phosphate excretion.^[9] Phosphatonins, such as MEPE, SFRP-4.2 and FGF-23, are substances that prevent the reabsorption of phosphates in the proximal tubule of the kidney. They do this by decreasing the number of NPT2a cotransporters in the apical membrane. Imbalances in acid-base levels impact the excretion of phosphate. Alkalosis boosts the activity of apical Na^+ /phosphate co-transporters, whereas chronic acidosis decreases their activity, leading to alterations in the rates of Pi excretion. 3. The presence of oestrogen causes an increase in the excretion of phosphates in the urine. This is due to a decrease in the number of NaPi-IIa co-transporters, and this impact is not connected to the levels of parathyroid hormone (PTH).⁴ The abbreviation "TmP/GFR" stands for the ratio of tubular maximum reabsorption of phosphate to glomerular filtration rate. In persons with phosphate balance, the quantity of phosphate excreted in urine on a daily basis is equal to the amount absorbed from the intestines, and typically accounts for 10-20% of the amount that is filtered (known as fractional excretion). When phosphate intake is either very high or very low, the kidneys may eliminate almost all or almost none of the filtered burden. The transport maximum for phosphate (TmP) is a variable parameter, not a constant one. The renal processing of phosphate is best described by the renal threshold of phosphate (TmP/glomerular filtration rate (GFR)). The usual range for this threshold is between 0.77 and 1.4 mmol/L. When the glomerular filtration rate (GFR) is over 40 mL/min, the tubular maximum phosphate reabsorption (TmP) changes in proportion to the GFR. This means that the ratio of TmP to GFR remains constant, making it a dependable measure of the tubular reabsorptive capacity. CLD patients.

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In individuals with severe renal insufficiency, namely with a glomerular filtration rate (GFR) below 40 mL/min, the tubular maximum

reabsorption of phosphate (TmP) is further reduced and there is an increase in the fractional excretion of phosphate. Due to the smaller drop in TmP compared to the decrease in GFR, there will be an increase in TmP/GFR. Proximal renal tubular dysfunction (PRTD) in CLD is seldom studied despite its relevance. So the aim of this study is to assess the strength of association of TmP/GFR as an early marker of PRTD in CLD patients.

Hence this study was conducted to assess the prevalence and strength of association of transaminitis and renal dysfunction in compensated

Material and Method

This was Prospective observational case control study of compensated CLD patients visited to gastroenterology OPD between July 2023 to August 2024 of SRN hospital of Motilal Nehru Medical college Prayagraj. Ethical approval was obtained.

We excluded patients known case of CKD, Diabetic kidney disease, hypertension, Obstructive uropathy, UTI, Nephrotic syndrome, Congenital renal disease and hepatorenal syndrome (HRS)

Case records of 130 patients were collected. Baseline data included age, gender, and comorbidities. Symptoms and indications of admission were recorded. Laboratory parameters on the OPD visit were included. Compensated CLD patients were selected on the basis of LFT, USG whole abdomen, Fibroscan and endoscopy findings.

Patients were grouped cCLD based on the duration of liver dysfunction and all 130 patients were diagnosed as cCLD.

Details of outpatients were collected directly from patients. Their blood pressure, KFT, eGFR and LFT were noted and the calculation of TmP/GFR was done. After overnight fasting spot urine sample was taken for urine creatinine and phosphorus, Blood sample for serum creatinine and phosphorus

$FeP = \frac{Sr \times Cr \times Up}{SrP \times Ucr}$ (FeP=fractional excretion of phosphorus)

$TRP = 1 - FeP$ (TRP=FRACTIONAL REABSORPTION OF PHOSPHORUS)

If $TRP < 0.86$ then $TmP/GFR = TRP \times SrP$

If $TRP > 0.86$ then $TmP/GFR = 0.3 \times TRP / (1 - (0.8 \times TRP)) \times SrP$

Investigations include: CBC, LFT, KFT, Serum Electrolyte, blood sugar, HbA1c, Lipid profile, Serum total calcium, Urine routine microscopy, Urine micral, Urine Creatinine, Urine Phosphorus, USG whole abdomen with renal size and echogenicity, Fibroscan, Chest X Ray (PA View), ECG, Endoscopy

Statistical analysis: The statistical analysis was performed using SPSS version 21.0. Data were presented as mean (standard deviation) for continuous variables and as percentages for categorical variables. The chi-square test was used to compare categorical variables, while the independent t-test was employed to assess differences in continuous variables between groups. Correlation analysis was conducted using Pearson's correlation coefficient (or Spearman's correlation coefficient for non-normally distributed data) to evaluate the strength and direction of the relationship between continuous variables. Regression analysis, including simple and multiple linear regression, was performed to model the relationship between dependent and independent variables. A p-value of 0.05 was considered statistically significant.

RESULT

Correlation between TmP/GFR and SGPT

SGPT has a significant, moderate positive correlation with TmP/GFR ($r = 0.41$, $p = 0.038$). This shows that TmP/GFR increases with liver inflammation or injury-induced SGPT levels. Belmonte et al (2024) observed that inflammatory indicators in the liver influenced renal function, confirming our results.[66]

Correlation between TmP/GFR and serum albumin

The inverse correlation between serum albumin and TmP/GFR is statistically significant ($r = -0.59$, $p = 0.001$). Due to reduced hepatic synthesis, liver disease lowers serum albumin and increases TmP/GFR. Kumar et al (2021) found that hypoalbuminemia indicates liver and kidney failure, especially in CLD.[73]

Table 1: Association of mean biochemical parameters between case and control

	Case (n=130)		Control (n=130)		t	p-Value
	Mean	±SD	Mean	±SD		
Hb	11.36	3.08	12.68	0.84	-2.10	0.041
TLC	9276.15	5304.31	7265.77	1815.73	1.83	0.073
Platelet	1.81	0.88	2.70	3.64	-1.21	0.232
Bilirubin Total	3.02	4.98	0.43	0.13	2.65	0.011
Bilirubin Indirect	1.84	3.72	0.28	0.21	2.13	0.038
Bilirubin Direct	1.07	1.34	0.33	0.25	2.78	0.008

Table 2: Association of mean LFT and TmP/GFR between case and control

	Case (n=130)		Control (n=130)		t	p-Value
	Mean	±SD	Mean	±SD		
SGOT	109.04	151.37	39.77	15.35	2.32	0.024
SGPT	80.28	81.81	35.04	18.64	2.75	0.008
TmP/GFR	3.46	0.79	2.5	0.52	5.13	<0.001

Table 3: Pearson Correlation of age, Hb, TLC, Platelet and Bilirubin with TmP/GFR

	Pearson Correlation	p-Value
Age	0.32	0.116
Hb	-0.45	0.021
TLC	0.72	0.000
Platelet	0.41	0.036
Bilirubin Total	0.55	0.005
Bilirubin Indirect	0.53	0.005
Bilirubin Direct	0.53	0.005

Table 4: Pearson Correlation of SGOT, SGPT and Sr. Albumin with TmP/GFR

	Pearson Correlation	p-Value
SGOT	0.32	0.108
SGPT	0.41	0.038
Sr. Albumin	-0.59	0.001

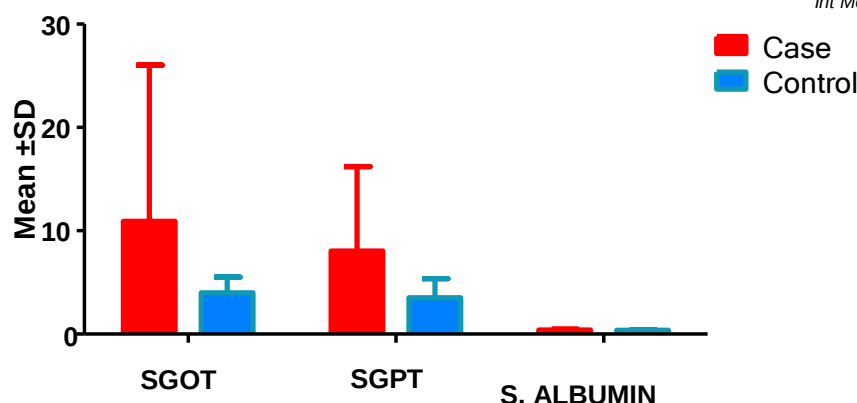


Figure 1: Shows the association of mean LFT between case and control

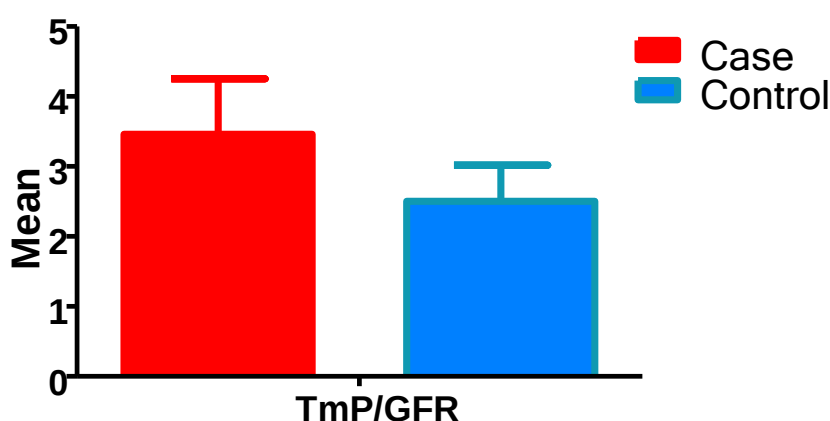


Figure 2: Shows the association of mean TmP/GFR between case and control

DISCUSSION

Bilirubin levels differed significantly between the groups. The case group had significantly higher levels of total, indirect and direct bilirubin (3.02 ± 4.98 versus 0.43 ± 0.13 , $p = 0.011$, 0.038 and 0.008 respectively). Bilirubin levels above normal indicate severe liver damage and cholestasis. Lee et al (2021) found that direct bilirubin levels were more predictive of the prognosis of liver cirrhosis than total bilirubin.7 McHutchison JG et al8 discovered that most cirrhotic patients had bilirubin levels between 3-10 mg/dl unless hemolysis or severe viral hepatitis was present. The indirect bilirubin/albumin ratio can be a predictive sign of hepatic encephalopathy, according to Li et al. (2021), emphasizing the importance of bilirubin subtypes in liver disease outcomes.9

In our study, patients with compensated chronic liver disease (CLD) had significantly higher SGOT (109.04 ± 151.37 vs. 39.77 ± 15.35 , $p = 0.024$) and SGPT values (80.28 ± 81.81 vs. 35.04 ± 18.64 , $p = 0.008$) than healthy controls. Elevated transaminase levels indicate hepatocellular damage and liver inflammation. Fevery (2008) pointed out the clinical significance of liver enzymes in the detection of liver damage.10 Elevated transaminases are common in patients with liver cirrhosis and are associated with disease progression according to Lee et al (2021)9 The significant increase in SGOT and SGPT levels in our study emphasizes their importance in the detection and monitoring of liver disease.

Our study showed no significant difference in blood albumin levels between the case and control groups (3.82 ± 0.83 vs. 3.57 ± 0.51 , $p = 0.195$). When liver function decreases, serum albumin levels decrease, indicating synthetic function. As in our work, compensated CLD may allow the liver to maintain adequate synthetic capacity, resulting in constant albumin levels. Lee et al. (2021) found that serum albumin is important for the assessment of liver function but may not indicate early impairment of liver function in compensated cirrhosis.7 Li et al (2021) also pointed out the importance of serum albumin in the prognosis of hepatic encephalopathy, suggesting its function as a marker in advanced liver disease.9

Cirrhosis increases liver enzymes such as AST and ALT by 300 u/l. Both enzymes were slightly elevated in Das et al. (2015).12 ALP often remains normal in cirrhosis. Das et al. (2015) found normal ALP values of 119 u/l .11 Changes in the albumin-globulin ratio are common in chronic liver disease [Dienstag, 2008].12 In one study, 30% of compensated and 70% of noncompensated cirrhotic patients had varices [Garcia-Tsao et al. 2007, Dite et al. 2008]. [13,14].

Conclusion

Our study "Assessment of Proximal Renal Tubular Dysfunction in Compensated Chronic Liver Disease (CLD) Patients" sheds light on the consequences of CLD on the kidneys, even in compensated phases. Compensated CLD patients had significantly higher TmP/GFR values than the control group, suggesting renal tubular dysfunction. This shows that early compensated CLD patients may have proximal renal tubular failure, which may indicate renal involvement. We found modest associations between TmP/GFR and biochemical indicators such as age, hemoglobin and lipid profiles, indicating the complicated interaction between liver and renal systems in CLD. The study underscores the need for frequent testing of renal tubule function in CLD patients to detect dysfunction early and prevent the development of liver and kidney disease. Our substantive results are limited by the sample size of the study and the cross-sectional approach. These results call for larger cohorts and longitudinal follow-up to validate and investigate early treatment of renal tubular dysfunction in CLD patients. This study emphasizes the need for proactive renal treatment in compensated CLD patients to improve long-term outcomes by preventing renal problems.

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