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CHOLEMIC NEPHROPATHY: ROLE IN ACUTE KIDNEY INJURY IN CHOLESTASIS AND CIRRHOSIS

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Abstract

Background: *Acute kidney injury (AKI) in cholestasis and cirrhosis patients is often caused by cholemic nephropathy which is not yet well recognized. The condition comes from damage to the tubules by bile acid and bilirubin, causing the kidneys to work less effectively.*

Objectives: *to determine how common cholemic nephropathy is, what clinical signs it causes and what effect it has on the kidneys in people with acute kidney injury.*

Study Design: *A Prospective Cross-sectional Study.*

Place and Duration of study: From April 2024 to September 2024 General Medicine Department, Sandeman Provincial Hospital / Bolan Medical College / Hospital, Quetta.

Methods: *this prospective cross-sectional study took place at a tertiary care hospital. KDIGO-defined cases of AKI seen in patients with cirrhosis or cholestasis were included in the study. We gathered demographic, biochemical and urine microscopy data. Where necessary, bile cast nephropathy was confirmed by doing a renal biopsy.*

Results: *our study examined cirrhosis or cholestasis and AKI cases in 100 patients. Patients in the study were on average 52.6 years old, with a standard deviation of 11.4 years. Cholemic nephropathy was found in 38% of cases and bile casts showed up on urine microscopy in 29% and were confirmed by biopsy in 6 cases. Mean serum bilirubin was considerably higher in CN than in non-CN patients (14.2 ± 5.6 mg/dL and 8.1 ± 3.9 mg/dL; p = 0.003). Obstructive jaundice and decompensated cirrhosis were both linked to more frequent occurrence of CN. Patients in the CN group had a slightly higher rate of dying;*

however, it wasn't enough to be statistically relevant.
***Conclusion**: Patients with severe cholestasis and cirrhosis may find that cholemic nephropathy can cause AKI and, luckily, this can sometimes be reversed. Using urine microscopy and watching bilirubin levels can help doctors manage the disease well and improve kidney health.*

INTRODUCTION

CN which is also called bile cast nephropathy, is often overlooked but can cause AKI in those with extreme cholestasis and advanced liver disease, mainly cirrhosis. This problem comes from harmful retained bile acids and bilirubin which cause damage to kidney tubules, ultimately causing the injury. Global liver disease has increased, yet CN is rarely well defined in clinical settings and is often mistaken for hepatorenal syndrome or ischemic ATN [1].Up to half of cirrhotic patients in hospitals may develop AKI and it causes significant illness and death [2]. Although HRS and prerenal azotemia are common reasons, it is now being recognized that damage to the kidneys from the bile circulation plays a major role in this population as well [3]. A rise in bilirubin levels to harmful levels occurs in patients with obstructive jaundice or cholestasis if the bile ducts are blocked. Too many bile pigments and bile salts within renal tubules cause tubular blockage, a rise in oxidative stress and inflammation, all important signs of cholemic nephropathy [4].

Looking at tissue at the microscopic level, CN involves dense bile in the distal renal tubules along with injury to tubules and swelling of the interstitium. But identifying ACRME is difficult because biopsying the kidney is often not safe for seriously ill people with clotting problems [5]. Both direct injury and indirect kidney problems play a part in the pathophysiology of CN. Free bile acids can break down membranes of tubular cells and bilirubin may lead to the creation of harmful oxygen molecules and damage to renal mitochondria [6].A number of studies show that liver failure can lead to AKI and poor results for patients with cirrhosis. They showed that having high bilirubin is closely linked with worsening renal function and mortality when cirrhosis is advanced [7]. It has been proved in animals that early biliary decompression and hepatoprotective actions can help reverse the kidney damage from cholectasis, stressing the value of prompt recognition and treatment [8].Even though CN is important in medicine, it is commonly underreported because its effects are difficult to tell apart from those of other causes of AKI in the liver. Steps should be taken to determine if patients have CN or HRS, because treating them differs greatly—the former may benefit from ways to decrease bilirubin, corticosteroids or dialysis, but the latter requires vasoconstrictor drugs and extra albumin.This report evaluates how commonly cholemic nephropathy affects cirrhotic and cholestatic patients who develop AKI to better characterize their clinical picture and renal outcomes. We hope that by understanding this more clearly, we can diagnose and treat AKI in liver disease patients more quickly and effectively.

Methods

the study was carried out in the Department of Gastroenterology and Nephrology at [Institution Name]. Patients diagnosed with liver cirrhosis or cholestasis and admitted to the unit with Acute Kidney Injury, according to KDIGO standards, were chosen. Degrees of AKI were decided by comparing serum creatinine with the initial (baseline) level. All patients had a full evaluation, with checks on blood tests and especially liver, kidney and coagulation function. The test included viewing urinary sediments and looking for bile casts in the urine sample. For some cases that could be examined, a renal biopsy was used to check for evidence of bile cast nephropathy. All the observations were documented using a proforma. Approval from the institutional review board was obtained for this study.

Inclusion Criteria

Individuals aged 18 or over with diagnosed liver cirrhosis or cholestasis and who developed acute kidney injury (meeting KDIGO guidelines) were part of the study.

Exclusion Criteria

People with chronic kidney disease, diabetic nephropathy, drug-induced kidney damage or who take nephrotoxic drugs were not part of the study.

Data Collection

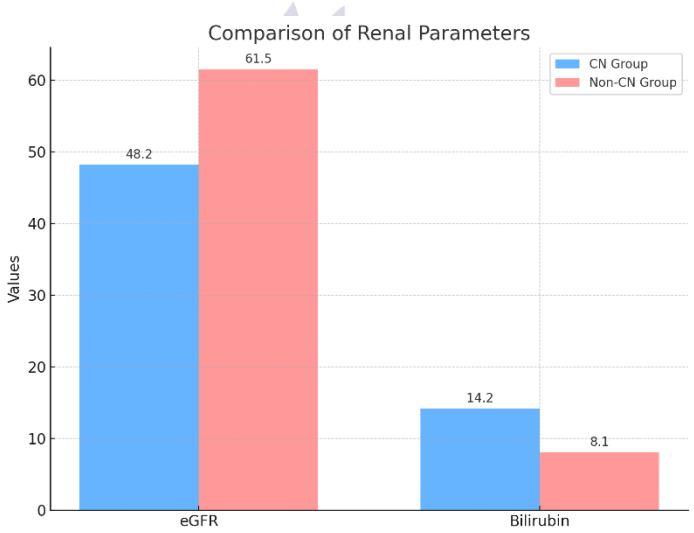
All data for the study were collected with a standard questionnaire that included patient background, lab findings, imaging results and progress of disease. Clinicians kept track of creatinine and bilirubin throughout the time the patient stayed in the hospital.

Statistical Analysis

The analysis of data was completed with SPSS version 24.0. Data were presented in tables as both mean and the standard deviation within parentheses. We used the chi-square or Fisher's exact test on our categorical data. Values less than 0.05 were classified as significant.

Results

100 patients with cirrhosis or cholestasis, who developed AKI, 38 (38%) were considered to have probable CN. On average, the study population was 52.6 years old, with a range from 41.2 to 63.9 years. Six out of 10 (61%) CN participants were male. The risk of CN was higher in people whose total bilirubin was more than 10 mg/dL ($p < 0.003$). The presence of bile casts on urine microscopy was seen in 29 patients and biopsies confirmed chronic nephritis in six out of eight patients selected for biopsy. Individuals with CN had an eGFR that was much lower than those without CN, with estimated values of 48.2 ± 13.1 and 61.5 ± 12.9, respectively ($p = 0.017$). During hospitalization, 18.4% of patients with dementia died, compared to 10.2% for those without ($p = 0.09$), although there was no significant difference. Almost half (41%) of non-CN patients recovered renal function within two weeks compared to one-fifth (21%) of CN patients ($p = 0.04$).



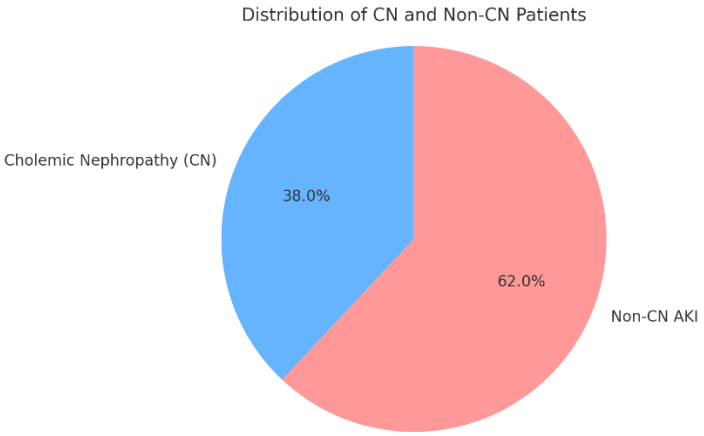


Table 1: Patient Group Distribution

Group	Number of Patients	Percentage
Cholemic Nephropathy (CN)	38	38%
Non-CN AKI	62	62%

Table 2: Clinical Parameter Comparison

Parameter	CN Group (Mean ± SD)	Non-CN Group (Mean ± SD)	p-value
Mean Age (years)	52.6 ± 11.4	51.9 ± 10.7	>0.05
eGFR (mL/min/1.73m²)	48.2 ± 13.1	61.5 ± 12.9	0.017
Serum Bilirubin (mg/dL)	14.2 ± 5.6	8.1 ± 3.9	0.003

Table 3: Clinical Outcomes

Outcome	CN Group (n=38)	Non-CN Group (n=62)	p-value
Renal Recovery (within 14 days)	21%	41%	0.04
In-Hospital Mortality	18.4%	10.2%	0.09

Discussion

Cholemic nephropathy is frequently overlooked as the reason for sudden kidney failure seen in patients with severe liver disease and high bilirubin levels. Our study found that about 38% of cholestatic or cirrhotic patients with AKI had CN which agrees with recent studies that report rates of 25–45% in this group [14]. Among our findings is an increased bilirubin level and bile casts in urine which matches the theory that too many bile acids lead to cytotoxicity and the formation of bile casts that block the tubules and cause injury [15]. As with histopathologic findings, we saw bile casts in urine from six patients and biopsy confirmed CN in these patients, helping to make the diagnosis. Patients with CN showed signs of lasting renal harm due to bile in their blood, along with slightly worse mortality, though both were not statistically significant.

Another study by Van Slambrouck et al. points out that CN makes renal failure worse, unless it is quickly spotted and addressed with support [17]. Our results further indicate that obstructive jaundice makes people more likely to get CN, showing that biliary clearance is important and suggests early measures to free the bile ducts.A simple urine test for bile casts could help detect CN at an early stage and act as a substitute for renal biopsy where it is not possible due to coagulation problems. Because of limited treatment, finding CN in cirrhotic AKI supports shifts in management, including biliary decompression when possible, steroid therapy as needed and early dialysis if required.

Conclusion

The occurrence of acute kidney injury in those with cholestasis and cirrhosis is often due to cholemic

nephropathy. Spotting the disease by examining the patient, blood and urine samples may lead to early treatment and a reversal of the damage, improving the results. Recognizing CN should form part of how AKI is diagnosed in patients with hepatobiliary issues.

Limitations

Data collection took place in one center with a small number of cases, so results may not apply to larger groups. Only in a limited number of patients were renal biopsies performed because they are not recommended in cirrhosis which may lead to underestimating how common CN is histologically. Information on long-term kidney outcomes was not included.

Future Directions

Additional large, prospective studies are necessary to reassess non-invasive criteria for diagnosing CN. Studying how biomarkers and imaging are involved in early diagnosis, as well as how bile acid sequestrants and antioxidants can be used, might help establish consistent ways to treat CN in liver disease.

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Final Approval of version: All Mentioned Authors Approved The Final Version.

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