

Sonographic evaluation of liver disease severity and renal stone presence in different chronic liver diseases

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ABSTRACT

Objectives: To evaluate the prevalence of CLD causes and investigate the relationship between different CLD etiologies as well as severity of liver disease with renal stone presence.

Material and Methods: A cross-sectional study was conducted on 385 patients at District Headquarter Hospital Nankana Sahib, Punjab. Data was collected after approval for research ethical committee and hospital administration. Participants underwent trans-abdominal ultrasound using a GE Logic P7 machine. Data were scrutinized for liver disease causes, renal stone prevalence, and demographic factors using chi-square tests and logistic regression models.

Results: Among others, most common etiology of CLD was NAFLD (55.6%), followed by hepatitis C (25.7%) and hepatitis B (14.3%). Renal stones were observed in 32.7% of NAFLD patients, 42.4% of hepatitis C patients, and 48.1% of hepatitis B patients. Ultrasound imaging revealed that increased liver echogenicity and nodularity with ascites and increase in portal vein diameter were key markers of disease progression and renal complications. Advanced liver disease stages correlated with increased renal stone prevalence in patients without history of urinary tract stone ($p < 0.05$).

Conclusion:

The findings also underscore the metabolic syndrome as a central driver of hepatic and renal dysfunction and emphasize the necessity for multidisciplinary approaches in managing CLD patients. NAFLD and viral hepatitis are major contributors to CLD, with significant renal complications. Ultrasound proved to be a valuable diagnostic tool, emphasizing the need for integrated hepatic and renal health assessments. Preventive strategies targeting metabolic syndrome could mitigate these systemic complications.

Introduction

Chronic liver disease (CLD) is a leading health issue around the globe, subsidizing economic burden with significant morbidity and cause of over 1.5 million deaths worldwide. Annually major portion of these fatalities are with complicated forms like cirrhosis and liver cancer. In Pakistan also, CLD posing a crucial public health suffering, it is among the 8th leading cause of hospital admissions and have high mortality rate (1). The condition is primarily caused by wide array of etiologies but are different from developed countries, including viral infections (Hepatitis B and C), alcohol consumption common in developed countries, while non-alcoholic cause of fatty liver disease (NAFLD) and fibrotic fatty liver as Non-Alcoholic Steatohepatitis (NASH) are more prevalent etiologies in Pakistan and other developing countries (2, 3). Along with other causes, the norm like traditional use of herbal medicine, also contributes to liver parenchymal changes leading to CLD (4).

Advance destruction and then restoration of liver parenchyma causes fibrosis which then leads to cirrhosis of liver in chronic disease (3). Also liver malfunction owing to disease process takes more than six months, detoxification of harmful by products in metabolism is affected causing increase in blood toxicity irreversible damage to liver called cirrhosis. In recent years, Pakistan had a very high load of CLD, and labeled as cirrhotic state (1). Multiple contemporary studies have reported non-viral related liver disease as the major etiology of cirrhosis and has ominously increased over the last decade (5).

With chronic liver disease not only impairment in hepatic function deteriorates the health, causing myriad of clinical complications, but it also has systemic effects, including renal dysfunction or renal stones (6). Synchronicity of chronic liver disease with an increased risk of nephrolithiasis, or kidney stones due to distinctive, metabolic and physiological changes (7). Multiple epidemiological studies suggest factors like age, race, obesity and numerous diseases like hypertension, insulin resistant diabetes and metabolic disturbances affects the formation of kidney stone. The metabolic syndrome causes altered urine components results from changes in the process of urine concentration and dilution, decreased urine pH and citrate excretion while uric acid and calcium excretion are increased causing an augmented risk of both uric acid and calcium oxalate stone formations (4). Familial history of hypertension increases the tend to having hypercalciuria and hyperuricosuria, which results in renal stones (8). Liver malfunction and renal stone assessment require all three physical or clinical, laboratory and imaging examinations. Liver biopsy is gold standard for liver disease staging while CT is for renal stone evaluation. However use of ultrasound, in initial procedure gives ample information without any invasive attempt and radiation exposure to the patient (9, 10)

To avoid another painful malady, renal stones in the CLD patients, understanding of the interaction between CLD and renal complications, especially renal stones is crucial and improves clinical management and patient outcomes.

This study is intended to explore the relationship between chronic liver disease and the prevalence of renal stones, with a focus on the etiological factors contributing to liver disease. By scrutinizing the severity of liver disease, the study also investigates how liver dysfunction influences renal health, with a specific emphasis on the ultrasonic markers and key findings.

Methodology

An observational, cross-sectional study was conducted at the District Headquarter Hospital Nankana Sahib. Study sample consisted of 385 patients, attending the radiology department for liver disease assessment through abdominal ultrasound, specifically those presenting signs of liver dysfunction lasting more than six months. These patients were diagnosed based on clinical examination, laboratory findings (such as altered liver function test, deranged renal function test, positive viral markers). Ultrasound imaging was done with LOGIC P 7 machine, utilizing convex and linear probes for comprehensive evaluation of liver and renal health.

The inclusion criteria for the study were following:

1. Patients of both gender and aged 18 years and older.
2. Patients known case of CLD based on clinical and laboratory criteria.
3. Patients presenting with signs and symptoms suggestive right upper quadrant pain.

The exclusion criteria included individuals with acute liver disease, malignancies, or any other conditions that might interfere with the evaluation of chronic liver disease and renal stones. Data was collected after approval for research ethical committee (IRB/FASH/Allied-HS/10/24/MS/RS-3591) and hospital administration. Informed consent including study objectives and procedure, was taken from participants. Data collection include numerous factors like demographic, clinical symptoms, comorbid conditions (e.g., diabetes, increased BMI, hypertension), lifestyle stimuli (e.g., alcohol consumption, smoking) and family history of liver and renal disease, recorded on a detailed questionnaire.

The prevalence of renal stones among CLD patients were calculated and how liver disease etiology and severity influenced renal stone formation were analyzed. Binary logistic regression analysis was castoff to categorize potential predictors for renal calculi, while statistical tests such as chi-square and ANOVA were applied to evaluate associations between liver disease severity and renal stone prevalence with focusing on different etiologies of CLD.

Results

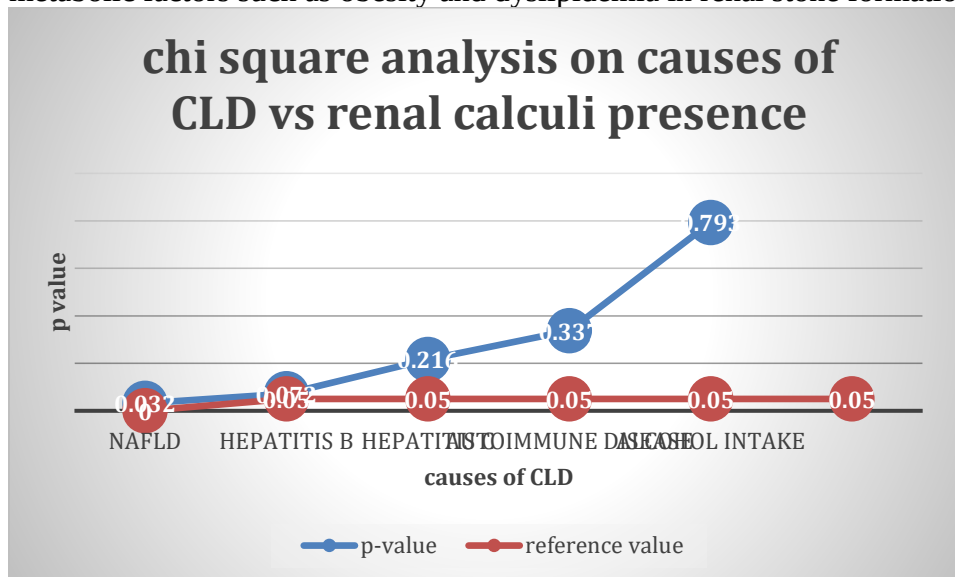
The results from the study population (60% females and 40% males), mostly with high BMI range 25-30 were aged 30-50 in 61.3%, majorly urban residents 62.9%, revealed NAFLD as the most prevalent cause of CLD, accounting for 55.6% of cases, followed by Hepatitis C (25.7%) and Hepatitis B (14.3%). The underlying cause of liver dysfunction greatly varies the occurrence of renal stones in chronic liver disease patients. The study also recorded family history of liver and renal disease with co-morbidities like smoking (28.6%), diabetes in 28.8% and hypertension in 29.6%.

Cause of CLD	Male (%)	Female (%)
Autoimmune Disease	50.0	50.0
Alcohol Intake	100.0	0.0
Hepatitis B (HBV)	38.2	61.8
Hepatitis C (HCV)	30.3	69.7
Non-alcoholic Fatty Liver Disease (NAFLD)	43.0	57.0

The distribution of renal stones among different causes of CLD is summarized in the tables:

Cause of CLD	Frequency (n)	Total Patients without the history of renal stone	Patients with Renal Stones	Prevalence (%)
Alcohol Intake	12	9	3	33.3
Autoimmune Disease	10	9	2	22.2
Hepatitis B (HBV)	55	52	25	48.1
Hepatitis C (HCV)	99	92	39	42.4
Non-Alcoholic Fatty Liver Disease (NAFLD)	214	171	56	32.7

Hepatitis B (48.1%) had the highest prevalence of renal stones, followed closely by Hepatitis C (42.4%) and NAFLD (32.7%) among the patients without history of urinary tract stone. The smaller sample sizes in groups of patients with autoimmune liver disease (22.2%) and alcohol-related liver disease (33.3%) also showed low prevalence of renal stones in them. The association between renal stone prevalence across CLD etiologies was judged through chi square, showed statistically significant association between NAFLD and renal stones (chi square value: 4.578; p value: 0.032), underscoring the role of metabolic factors such as obesity and dyslipidemia in renal stone formation.

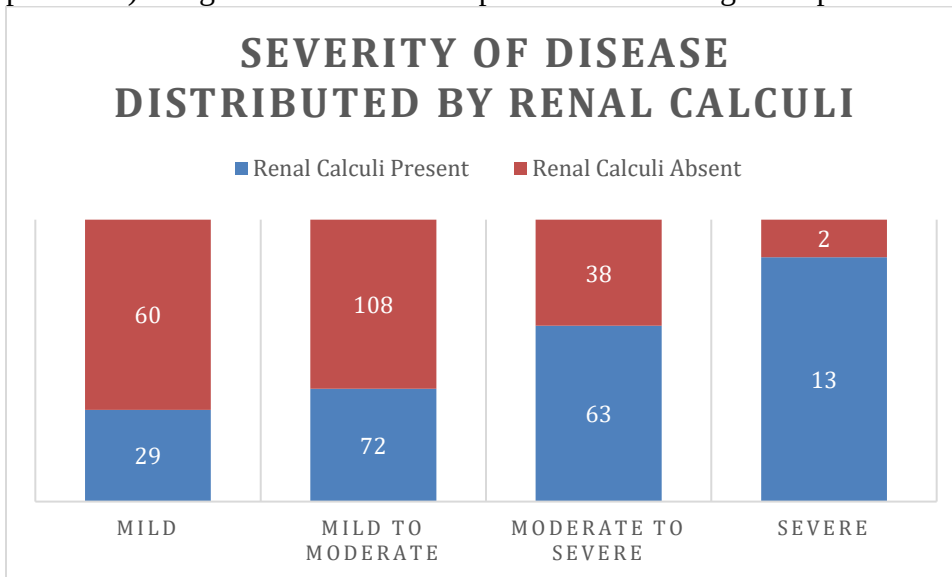


Predictors of renal calculi such as liver size, liver echogenicity, and serum creatinine were found to be significant (p values < 0.001), through logistic regression analysis model fits the data well (Hosmer-Lemeshow p = 0.633), with a high explanatory power (Nagelkerke $R^2=0.775$ $R^2=0.775$ $R^2=0.775$) while Viral Serology (Hepatitis B) (Exp (B) = 8.941; p < 0.05) showed strong positive association after adjustment for confounder.

Variable	Model Adjustment	p-value	Exp(B)	Interpretation
History of Alcohol Intake	Without Confounders	0.793(not significant)	0.762	No association observed before adjusting for confounders.
	With Confounders	0.028	0.000	Significant protective effect; reduced odds of renal calculi, likely mediated by disease severity.
Viral Serology (Hep B)	Without Confounders	0.086	>1	Weak positive association.
	With Confounders	<0.05	8.941	Strong positive association; Hepatitis B increases odds of renal calculi, mediated by liver dysfunction.
NAFLD	Without Confounders	0.857	1.380	No significant association; potential confounding by severity of liver disease.
	With Confounders	0.802	0.778	Remains not significant; no independent contribution to renal calculi risk.
Hepatitis C	Without Confounders	0.931	1.154	No significant association.
	With Confounders	0.876	1.166	Remains not significant; minimal contribution to renal calculi risk.
Autoimmune Disease	Without Confounders	0.527	0.467	No significant association.

	With Confounders	0.527	0.467	Remains not significant; weak protective effect
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Moreover, the Disease severity evaluated by the clinical signs and laboratory tests, was also a strong predictor of renal stone formation $p < 0.001$. The study also validate a clear correlation between the sonographically assessed severity of liver disease and the increased risk of renal stones, as patients in the severe disease category presenting a prevalence rate of 86.7% compared to those with milder forms of CLD and **ANOVA** ($F(1, 384) = 29.073$, $p < 0.001$). Progressive liver disease patients had much greater prevalence of renal stones.



Discussion

Systemic repercussions specifically the formation of kidney stones from chronic liver disease is considerably shown in this study and it supports the growing body of literature that links liver dysfunction to renal complications. The utmost common causes of CLD, including Hepatitis B, Hepatitis C and NAFLD, were predominant in the cohort mirrors to the findings from S. Cheemerla and M. Balakrishnan, showed prevalence of various etiologies of CLD as non-alcoholic fatty liver disease (59%), hepatitis B (29%), and hepatitis C (9%) (11). Moreover, Ali et al. and Khan et al. exposed high prevalence of HCV associated CLD and also demonstrate symptoms of HCV related decompensation of liver disease patients, similar to this study finding HCV as 2nd common cause (25.7%), first was NAFLD (55.6%) (2, 12).

The key factors contributing in high prevalence of NAFLD is metabolic dysfunction, often seen in patients, which includes conditions such as obesity, diabetes, and dyslipidemia causing metabolic syndrome also revealed by Badillo et al. study which had higher prevalence of renal stone in NAFLD patients (13). Metabolic disturbances demonstrated in Bargagli et al., contributed to alterations in urine composition, including reduced urinary citrate and increased calcium and oxalate excretion, which are known risk factors for kidney stone formation (14). Hou et al. in their study highlights the higher prevalence of upper urinary tract calculi in HBsAg positive patients (OR2.175; 95% CI 1.267–3.734;

$P=0.004$), consistent to the strong positive association between hepatitis B and renal stone presence (Hepatitis B) ($\text{Exp (B)} = 8.941$; $p < 0.05$) (15). Correspondingly, Qin et al. showed significant risk of urolithiasis in NAFLD patients (OR 1.73), accrediting this to mutual metabolic factors disturbing hepatic and renal health (16). The study also aligns with the finding from Sametzadeh et al. and Nupur Das et al that illustrated progressive stages of liver disease with aggravating renal complications and higher prevalence of urolithiasis (3, 17).

The severity of liver ailment also plays a crucial part in the development of renal stones. As liver function deteriorates, metabolic changes such as altered calcium and oxalate metabolism, increased urinary calcium excretion, and decreased urinary pH contribute to a higher risk of kidney stones. This study found a clear correlation between the severity of liver disease and the presence of renal stones, with patients in the severe disease category showing an 86.7% prevalence of nephrolithiasis ($p < 0.001$). Qudsieh et al. and Memon et al. underscores the utility of ultrasound as first line modality for examine hepatic and renal health, demonstrated the ultrasonographic markers associated with CLD severity like liver echogenicity and nodularity in predicting complications. These literatures supports the findings and methodology of this study (18, 19). Shen et al. highlights the role of liver echogenicity in predicting fibrosis in HBV patients ($P < 0.009$), also synchronize with this study as increased liver echogenicity ($p = 0.007$) indicated by ultrasound in advance liver disease patients had renal stone prevalence (20).

Conclusion

Valuable insights into the association between chronic liver disease and renal stone formation is provided in this study. The findings underscore the prerequisite formation by clinicians to monitor renal function in Hepatitis B, Hepatitis C, and NAFLD patients. To prevent renal complications and improving patient outcomes early detection and interventions are necessary.

Metabolic factors that contribute to both liver and kidney dysfunction are also highlighted in the study. Conditions causes metabolic disturbances such as obesity, diabetes, and hyperlipidemia leading to hypertension, could be early managed by healthcare providers, would reduce the risk of both liver and kidney diseases. The study findings have numerous clinical implications, signifying that advanced liver disease patients require careful assessment for renal complications.

Limitations

This study delivers important comprehensions but it has several constraints. With cross-sectional strategy it limits the formation of contributing inferences between CLD and renal stone formation. Moreover, the single centered sample collection, confines the generalizability of the findings to other populations. The statistical power is low due to small number of cases for certain liver disease etiologies, such as autoimmune liver disease and alcohol-related liver disease.

Further Suggestions

Longitudinal studies should be conducted to clarify the causal relationship between renal stone absences even in severe live disease patients. Furthermore, studies with larger sample sizes and conducted on multiple centers would provide more robust data and help establish clearer configurations across different populations. The pathophysiology linking liver dysfunction to renal stone formation is also necessary and could be focused in future researches. Expanding the Studies to investigate the role of metabolic pathways, such as

the disruption of calcium and oxalate metabolism, could also provide deeper insights into the shared mechanisms of liver and kidney dysfunction.

In clinical trials, the preventive strategies, such as dietary modifications, weight management, and improved glycemic control, should be tested to determine their effectiveness in reducing the risk of both liver and kidney diseases.

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