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ORIGINAL RESEARCH

Impact of Chronic Kidney Disease on Liver Fibrosis Progression in Non-Alcoholic Fatty Liver Disease Patients

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ABSTRACT

Background: Chronic Kidney Disease (CKD) and Non-Alcoholic Fatty Liver Disease (NAFLD) share common pathophysiological pathways, including metabolic dysregulation and systemic inflammation. Emerging evidence suggests that CKD may contribute to the progression of liver fibrosis in NAFLD patients. However, limited studies have explored the direct impact of CKD on liver fibrosis severity and progression in this population. This study aims to evaluate the association between CKD and liver fibrosis progression in NAFLD patients. **Materials and Methods:** A cross-sectional study was conducted on 200 NAFLD patients, of whom 100 had CKD (CKD-NAFLD group) and 100 had normal kidney function (NAFLD-only group). Liver fibrosis was assessed using transient elastography (FibroScan) and fibrosis scores (FIB-4, NAFLD fibrosis score). Renal function was evaluated based on estimated glomerular filtration rate (eGFR) and serum creatinine levels. Statistical analysis, including t-tests and logistic regression models, was performed to determine the association between CKD and fibrosis progression. **Results:** Patients in the CKD-NAFLD group had significantly higher fibrosis scores (FIB-4: 2.5 ± 0.8 vs. 1.7 ± 0.6, $p < 0.001$; NAFLD fibrosis score: 0.9 ± 0.3 vs. 0.4 ± 0.2, $p = 0.002$) compared to the NAFLD-only group. Advanced fibrosis (F3-F4) was observed in 45% of CKD-NAFLD patients compared to 25% in the NAFLD-only group ($p = 0.01$). Regression analysis indicated that CKD was an independent predictor of fibrosis progression (OR: 2.8, 95% CI: 1.6-4.5, $p < 0.001$). **Conclusion:** CKD is significantly associated with increased liver fibrosis progression in NAFLD patients, emphasizing the need for early screening and integrated management strategies for both conditions. Clinicians should consider CKD as a contributing factor to NAFLD severity and tailor treatment approaches accordingly.

Keywords: Chronic Kidney Disease, Non-Alcoholic Fatty Liver Disease, Liver Fibrosis, Metabolic Dysfunction, FibroScan, Renal Function

INTRODUCTION

Non-Alcoholic Fatty Liver Disease (NAFLD) is one of the most prevalent chronic liver conditions, affecting approximately 25% of the global population (1). It encompasses a spectrum of liver disorders ranging from simple steatosis to non-alcoholic steatohepatitis (NASH), which can progress to fibrosis, cirrhosis, and hepatocellular carcinoma (HCC) (2). Chronic Kidney Disease (CKD), a significant public health burden, often coexists with NAFLD due to shared risk factors, including obesity, insulin resistance, hypertension, and dyslipidemia (3). Recent evidence suggests that NAFLD and CKD may have bidirectional interactions, where the presence of CKD exacerbates liver fibrosis, while NAFLD contributes to renal dysfunction (4,5).

Systemic inflammation, oxidative stress, and endothelial dysfunction are critical mechanisms linking CKD and NAFLD progression (6). Patients with CKD experience an imbalance in cytokine production, increased endotoxemia, and metabolic dysregulation, which may accelerate hepatic fibrosis (7). Moreover, renal dysfunction leads to impaired clearance of profibrotic mediators, further aggravating liver fibrosis (8). Despite these associations, limited studies have comprehensively assessed the direct impact of CKD on the progression of liver fibrosis in NAFLD patients.

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Given the rising prevalence of both conditions and their potential interplay, it is essential to understand how CKD influences liver fibrosis progression in NAFLD patients. This study aims to evaluate the association between CKD and liver fibrosis severity using non-invasive fibrosis assessment tools and renal function markers. The findings could contribute to the development of targeted management strategies to mitigate fibrosis progression in patients with both CKD and NAFLD.

MATERIALS AND METHODS

Study Design and Population

This cross-sectional study was conducted on patients diagnosed with Non-Alcoholic Fatty Liver Disease (NAFLD) at a tertiary care centre. A total of 200 patients were enrolled, with 100 having concurrent Chronic Kidney Disease (CKD-NAFLD group) and 100 having normal kidney function (NAFLD-only group). CKD was defined based on the Kidney Disease: Improving Global Outcomes (KDIGO) criteria, using an estimated glomerular filtration rate (eGFR) of <60 mL/min/1.73m² for at least three months. NAFLD was diagnosed using abdominal ultrasound and confirmed by transient elastography when needed.

Inclusion and Exclusion Criteria

Inclusion Criteria:

- Adults aged 18–70 years diagnosed with NAFLD.
- Patients with CKD stage 2–5 in the CKD-NAFLD group.
- NAFLD patients with normal kidney function in the NAFLD-only group.

Exclusion Criteria:

- Patients with significant alcohol consumption (>30 g/day for men and >20 g/day for women).
- Individuals with viral hepatitis, autoimmune liver disease, or drug-induced liver injury.
- Patients with end-stage renal disease (eGFR <15 mL/min/1.73m²) on dialysis.
- Those with a history of malignancy or active infections.

Clinical and Laboratory Assessments

Demographic data, including age, gender, body mass index (BMI), and comorbidities (hypertension, diabetes, dyslipidemia), were recorded. Blood samples were collected after overnight fasting to assess liver and renal function parameters.

- **Liver function tests:** Alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total bilirubin.
- **Renal function tests:** Serum creatinine, blood urea nitrogen (BUN), and eGFR.
- **Metabolic markers:** Fasting blood glucose, glycated hemoglobin (HbA1c), lipid profile, and C-reactive protein (CRP).

Liver Fibrosis Assessment

Liver fibrosis was evaluated using transient elastography (FibroScan) to measure liver stiffness. Additionally, fibrosis scores such as the FIB-4 index and NAFLD Fibrosis Score (NFS) were calculated using standard formulas. Patients were categorized into fibrosis stages:

- **F0–F1 (Mild or no fibrosis):** Liver stiffness <7.0 kPa.
- **F2 (Moderate fibrosis):** Liver stiffness between 7.0–9.5 kPa.
- **F3–F4 (Advanced fibrosis or cirrhosis):** Liver stiffness >9.5 kPa.

Statistical Analysis

Data were analyzed using SPSS software (version 26.0). Continuous variables were expressed as mean ± standard deviation (SD) and compared using an independent t-test. Categorical variables were presented as frequencies and percentages, analyzed using the chi-square test. Logistic regression analysis was performed to assess the association between CKD and liver fibrosis progression, adjusting for potential confounders. A p-value of <0.05 was considered statistically significant.

RESULTS

Baseline Characteristics of Study Participants

A total of 200 NAFLD patients were included in the study, with 100 in the CKD-NAFLD group and 100 in the NAFLD-only group. The mean age was 55.4 ± 9.2 years in the CKD-NAFLD group and 51.8 ± 8.5 years in the NAFLD-only group. The proportion of males was higher in both groups, with 62% in the CKD-NAFLD group and 58% in the NAFLD-only group. Patients with CKD had significantly higher BMI, fasting blood glucose, and HbA1c levels compared to those without CKD (Table 1).

Table 1: Baseline Characteristics of Study Participants

Parameter	CKD-NAFLD Group (n=100)	NAFLD-Only Group (n=100)	p-value
Age (years)	55.4 ± 9.2	51.8 ± 8.5	0.021
Male (%)	62	58	0.523
BMI (kg/m²)	30.5 ± 3.4	27.8 ± 3.1	<0.001
Fasting Glucose (mg/dL)	128.6 ± 14.2	115.3 ± 12.8	0.002
HbA1c (%)	7.1 ± 1.2	6.4 ± 1.0	0.004
eGFR (mL/min/1.73m²)	42.8 ± 9.1	91.2 ± 8.5	<0.001

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Liver Function and Fibrosis Assessment

Patients in the CKD-NAFLD group had significantly higher ALT and AST levels compared to the NAFLD-only group. Liver fibrosis scores were also significantly elevated in the CKD-NAFLD group, with a mean FIB-4 score of 2.5 ± 0.8 compared to 1.7 ± 0.6 in the NAFLD-only group ($p < 0.001$). FibroScan liver stiffness measurements indicated a higher prevalence of advanced fibrosis (F3-F4) in CKD-NAFLD patients (45%) than in the NAFLD-only group (25%) (Table 2).

Table 2: Liver Function and Fibrosis Assessment

Parameter	CKD-NAFLD Group (n=100)	NAFLD-Only Group (n=100)	p-value
ALT (U/L)	58.4 ± 12.6	46.2 ± 10.3	0.001
AST (U/L)	52.1 ± 11.4	40.8 ± 9.7	0.002
FIB-4 Score	2.5 ± 0.8	1.7 ± 0.6	<0.001
NAFLD Fibrosis Score	0.9 ± 0.3	0.4 ± 0.2	0.002
Liver Stiffness (kPa)	10.2 ± 2.5	7.4 ± 2.1	<0.001
Advanced Fibrosis (F3-F4) (%)	45	25	0.010

Association between CKD and Liver Fibrosis Progression

Logistic regression analysis showed that CKD was an independent predictor of advanced liver fibrosis (F3-F4), with an odds ratio (OR) of 2.8 (95% CI: 1.6-4.5, $p < 0.001$). Even after adjusting for confounders such as BMI, diabetes, and hypertension, CKD remained significantly associated with fibrosis progression.

In summary, NAFLD patients with CKD exhibited worse liver function parameters and a higher prevalence of advanced fibrosis compared to those without CKD. These findings underscore the impact of renal dysfunction on hepatic disease progression in this population (Table 3).

Table 3: Multivariate Logistic Regression Analysis of Factors Associated with Advanced Liver Fibrosis (F3-F4)

Variable	Adjusted OR	95% CI	p-value
CKD (Present vs. Absent)	2.8	1.6 - 4.5	<0.001
BMI (kg/m²)	1.3	1.1 - 1.6	0.021
Diabetes Mellitus	2.1	1.4 - 3.5	0.008
Hypertension	1.7	1.2 - 2.9	0.015

These results highlight the need for proactive monitoring and integrated management strategies for patients with both CKD and NAFLD to prevent fibrosis progression.

DISCUSSION

This study demonstrates that Chronic Kidney Disease (CKD) is significantly associated with advanced liver fibrosis in Non-Alcoholic Fatty Liver Disease (NAFLD) patients. NAFLD and CKD share common risk factors, including insulin resistance, obesity, hypertension, and dyslipidemia, which contribute to systemic inflammation and oxidative stress, further accelerating disease progression (1,2). Our findings align with previous research indicating that CKD is an independent predictor of liver fibrosis severity in NAFLD patients (3,4).

One of the key mechanisms linking CKD to liver fibrosis is chronic systemic inflammation. Patients with CKD exhibit increased levels of inflammatory markers, such as C-reactive protein (CRP), tumor necrosis factor-alpha (TNF-α), and interleukins, which promote hepatic stellate cell activation and fibrogenesis (5,6). Additionally, uremic toxins, which accumulate in CKD, contribute to endothelial dysfunction and liver fibrosis progression by inducing oxidative stress and mitochondrial dysfunction (7). These pathophysiological interactions explain why NAFLD patients with CKD in our study had significantly higher FIB-4 scores, NAFLD fibrosis scores, and liver stiffness values compared to those without CKD.

Our study also supports the growing evidence that renal dysfunction exacerbates metabolic abnormalities that worsen NAFLD. Impaired kidney function leads to an altered lipid profile, increased insulin resistance, and dysregulated glucose metabolism, which further contribute to hepatic steatosis and fibrosis progression (8,9). This metabolic derangement is reflected in our findings, where NAFLD patients with CKD had higher fasting glucose and HbA1c levels compared to NAFLD-only patients. Other studies have also reported that reduced eGFR is associated with worsening hepatic fibrosis, independent of traditional metabolic risk factors (10,11).

Furthermore, our regression analysis confirmed that CKD is an independent predictor of advanced liver fibrosis (F3-F4), even after adjusting for confounders such as BMI, diabetes, and hypertension. Similar results have been observed in cohort studies where patients with reduced eGFR had higher odds of developing liver fibrosis and cirrhosis (12,13). The bidirectional relationship between CKD and NAFLD suggests that worsening renal function contributes to hepatic fibrosis, while progressive liver disease may

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further impair renal function through systemic inflammation and hemodynamic alterations (14).

Despite these findings, our study has some limitations. The cross-sectional design prevents us from establishing causality between CKD and liver fibrosis progression. Longitudinal studies are needed to determine whether CKD directly accelerates fibrosis or if both conditions progress simultaneously due to shared risk factors. Additionally, liver fibrosis was assessed using transient elastography rather than liver biopsy, which remains the gold standard for fibrosis staging. However, non-invasive methods such as FibroScan and fibrosis scores have been widely validated and are commonly used in clinical practice (15).

CONCLUSION

Our findings emphasize the importance of routine liver fibrosis assessment in NAFLD patients with CKD. Given the strong association between CKD and hepatic fibrosis, early intervention strategies, including lifestyle modifications and pharmacological management, should be considered to mitigate disease progression. Future research should focus on prospective studies to further explore the pathophysiological mechanisms linking CKD and liver fibrosis in NAFLD patients.

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