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Role of FIB-4 and eGFRcysC as Diagnostic Tools for Early Detection of Impaired Hepato-Renal Function in Chronic Alcoholics

Dr. Piyush Goyal[1], Dr. Jaskiran Kaur[2]

[1]Post Graduate Student, Department of Biochemistry, Subharti Medical College, Swami Vivekanand Subharti University Meerut Uttar Pradesh INDIA

[2]Professor & HOD, Department of Biochemistry, Subharti Medical College, Swami Vivekanand Subharti University Meerut Uttar Pradesh INDIA

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ABSTRACT

Aim: To evaluate the association between hepatic fibrosis, measured by the Fibrosis-4 (FIB-4) index, and renal function, assessed by cystatin C–based estimated glomerular filtration rate (eGFRcysC), in chronic alcohol-consuming patients, and to compare findings with age- and sex-matched healthy controls.

Methods: Cross-sectional, case–control research was done at the Department of Biochemistry, Subharti Medical College, Meerut, between 18 months. One hundred chronic alcoholics (≥10 years; >40 g/day for males and >20 g/day for females) and 100 healthy controls were enrolled. Exclusion conditions were non-alcoholic liver disease, severe chronic kidney disease (CKD), nephrotoxic drugs, malignancy, HIV, acute sepsis, and pregnancy. Clinical information was captured and fasting blood draws assayed for liver and renal function, viral markers, and serum cystatin C. FIB-4 scores and eGFRcysC were determined. Statistical analysis was done with Student's t-test and Chi-square test with $p<0.05$ as significant.

Results: Patients had much higher mean FIB-4 values (3.37 ± 1.40 vs 1.13 ± 0.42, $p<0.001$) and lower eGFRcysC (24.82 ± 7.56 vs 91.47 ± 14.98 mL/min/1.73 m², $p<0.001$) than controls. Cystatin C was increased in patients (2.84 ± 0.70 vs 0.96 ± 0.11 mg/L, $p<0.001$). Increased grades of fibrosis correlated with higher CKD stages, and there was a very strong inverse correlation between FIB-4 and eGFRcysC.

Conclusion: Chronic alcohol use is associated with concurrent hepatic fibrosis and renal impairment. FIB-4 and eGFRcysC are accessible, reliable, and complementary tools for early detection of hepatorenal dysfunction, with potential to guide timely interventions in at-risk populations.

Keywords: *Chronic alcohol use, Cystatin C, eGFR, FIB-4 index, Hepatic fibrosis.*

1. INTRODUCTION

Alcohol use is a major global disease burden, with the World Health Organization estimating that roughly 380 million individuals about 5.1% of those over age 15 are living with alcohol use disorder across the globe, having especially high rates among men and young adults, with the highest rates reported in Eastern Europe (~11%), and the lowest in Africa (~1.1%) [1,2]. Its extensive usage contributes to significant health hazards, having causative associations with more than 200 disease outcomes such as liver disease, cardiovascular disease, cancer, and injury; importantly, in 2019 alcohol caused almost half a million cardiovascular deaths and 4.4% of cancers worldwide, which highlights the extent of its harmful implications [3]. Within the domain of alcohol-related morbidity, alcoholic liver disease (ALD) is the most common chronic liver illness and occurs in over 90% of heavy drinkers as fatty liver, with approximately 25% complicated by alcoholic hepatitis and approximately 15% going on to develop cirrhosis; globally, alcohol accounts for an estimated 348,000 deaths—approximately 27% of total cirrhosis-related mortality. The lack of early detection is concerning despite excessive alcohol consumption, numerous patients have no symptoms until late in disease such that identification of cost-effective, non-invasive screening markers is crucial [4].

Concurrent with hepatic pathology, kidney disease is a quiet but rapidly growing worldwide health epidemic. Chronic kidney disease (CKD), characterized by low estimated glomerular filtration rate (eGFR <60 mL/min/1.73 m²) or the presence of renal damage markers, occurs in an estimated 9.1% of the global population as of 2017—equating to roughly 697 million persons—and has increased in prevalence by nearly 30% since 1990; annually, more than 1.2 million deaths are caused by CKD, with the highest burden residing in low- and middle-income nations such as India and China [5,6]. Acute kidney injury

(AKI) is also contributing to the problem—occurring in 7–18% of inpatients and estimated to affect 13.3 million cases each year, the majority of these in resource-poor environments—but often is underdiagnosed and undertreated. The overlap between ALD and CKD, especially in situations of long-term alcohol exposure, indicates a similar pathophysiological burden [7,8].

In spite of high worldwide prevalence of both CKD and ALD, the interaction between renal and hepatic impairment in chronic alcohol consumers remains poorly understood. While certain population studies indicate infrequent alcohol consumption can elevate the risk of late CKD stages by more than threefold after controlling for confounders, others intriguingly reported reduced CKD incidence rates in moderate drinkers due to multifaceted interactions with consumption rates, cultural habits, and comorbidities [9-11]. Notably, between 10% and 36% of CKD patients drink alcohol habitually, with 10% drinking heavily. Nevertheless, large-scale multicentric information outlining the effect of chronic alcoholism on renal function—particularly early, subclinical impairment—is still limited.

Conversely, non-invasive liver biomarkers such as the Fibrosis-4 (FIB-4) index, which is calculated from age, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and platelet counts, have proved to be very useful for identifying advanced fibrosis and cirrhosis, providing an easily accessible alternative to invasive liver biopsies [12-14]. Likewise, cystatin C–based eGFR (eGFRcysC) offers a muscle-mass–independent estimate of renal function, with increasing awareness of its advantage over creatinine-based estimates among sarcopenic or malnourished individuals—including those with ALD. Yet, despite individual utilities, the application of FIB-4 and eGFRcysC together in the parallel assessment of the extent of hepatic impairment and renal impairment in alcohol-exposed individuals has not been fully exploited in epidemiologic studies or in routine clinical practice—the critical gap [15-17].

India, with its distinctive drinking patterns—often including indigenous or homemade drinks—and developing ALD burden, is a high-risk environment in which resource scarcity further narrows access to high-end diagnostics; consequently, non-invasive, low-tech biomarkers assume paramount significance [18]. Examinations of the dual impairment of liver and kidney in Indian chronic alcoholics using FIB-4 and eGFRcysC are timely because they meet an urgent regional healthcare requirement and augment international awareness [9] . By clarifying the severity and frequency of hepatic fibrosis and renal impairment within this group, and investigating their biochemical interaction, the current study seeks to highlight the clinical value of dual-marker screening programs. Such evidence may shape early intervention strategies—ranging from alcohol abstinence programs to multidisciplinary referral schemes—ultimately reducing progression toward end-stage organ failure and streamlining morbidity, mortality, and financial cost.

2. METHODOLOGY

2.1 Study area and Design

A cross-sectional, case–control study was conducted in the Department of Biochemistry, Subharti Medical College, Meerut, with affiliated hospitals and a de-addiction centre, over 18 months following Institutional Ethics Committee approval.

2.2 tudy Participants

One hundred chronic alcoholics (≥10 years; males >40 g/day, females >20 g/day) and 100 age- and sex-matched healthy controls were recruited consecutively. Exclusion criteria included non-alcoholic liver disease, advanced CKD (eGFR <30 mL/min/1.73 m²), nephrotoxic drug use, malignancy, HIV, acute sepsis, acute alcoholic hepatitis, pregnancy, or lactation.

2.3 Data Collection

Demographic and clinical details were recorded. After overnight fasting, 5 mL venous blood was collected: 2 mL in EDTA for complete blood count (CBC) and 3 mL in plain vials for biochemical assays. Serum was separated after centrifugation at 3000 rpm for 15 minutes; aliquots for cystatin C were stored at –20°C.

2.4 Investigations:

CBC (hematology analyzer), liver function tests (AST, ALT, bilirubin, proteins, ALP, GGT), renal function tests (urea, creatinine, uric acid, electrolytes), viral markers (HBsAg, anti-HCV), serum cystatin C (particle-enhanced turbidimetric immunoassay), and abdominal ultrasonography.

FIB-4 = (Age [years] × AST [IU/L]) / (Platelet count [10⁹/L] × √ALT [IU/L])

eGFR CysC: 78.64 × Cystatin C(mg/L) $^{-0.964}$

2.5 Statistical Analysis:

Data were analyzed using *Systat v13.2*. Continuous variables were expressed as mean ± SD and compared by Student's t-test; categorical data were compared by Chi-square test. $p < 0.05$ was considered statistically significant.

2.6 Ethics considerations:

Written informed consent was obtained; confidentiality was maintained. Participants with abnormal findings were referred for specialist care.

3. RESULTS

The age-wise distribution shows that among the control group, the majority of participants were in the 31–40 years age group (36%), followed closely by those aged 41–50 years (31%) and 21–30 years (26%), with the least representation in the 51–68 years group (7%). In contrast, the patient group had the highest proportion in the 51–68 years category (33%), followed by 31–40 years (30%) and 41–50 years (27%), while the smallest proportion was observed in the 21–30 years group (10%). This pattern suggests that younger age groups were more prevalent in the control population, whereas older age groups were more common among patients, indicating a possible association between advancing age and the condition under study.

Table 1: Age-wise Distribution

Age Group (Years)	Control		Patient	
	n	%	n	%
21–30	26	26.0	10	10.0
31–40	36	36.0	30	30.0
41–50	31	31.0	27	27.0
51–68	7	7.0	33	33.0

Table 4.2 presents the distribution of sex among control and patient groups. In the control group, 94% were male (n=94) and 6% were female (n=6), while in the patient group, males comprised 96% (n=96) and females only 4% (n=4). This indicates a clear male predominance in both groups, with a slightly higher proportion of males in the patient group compared to the control group.

Table 2 SEX				
	Control		**Patient**	
	Frequency	**Percent**	**Frequency**	**Percent**
Female	6	6.0	4	4.0
Male	94	94.0	96	96.0
Total	100	100.0	100	100.0

Table 4.3 presents the distribution of estimated Glomerular Filtration Rate (eGFR) based CKD (Chronic Kidney Disease) grades among control and patient groups. In the control group, the majority of individuals (97%) were classified under G1 (normal or high kidney function), with only 3% falling into G2 (mildly decreased function), and none in the more advanced CKD stages. In contrast, the patient group showed a markedly different distribution, with only 3% in G2 and no individuals in G1. A significant proportion of patients were classified in advanced CKD stages: 26% in G3a, 48% in G3b, 20% in G4, and 2% in G5, indicating a high burden of moderate to severe kidney dysfunction among patients compared to the control group. This contrast highlights a substantial decline in renal function within the patient population.

Table 4.3 eGFR eGFR (Creatinine-based) grade

	Control		**Patient**	
	Frequency	**Percent**	**Frequency**	**Percent**
G1	97.0	97.0	0	0.00
G 2	3	3.0	3	3.0
G 4	0	0.00	1	1.0
G 3a	0	0.00	26	26.0

G 3b	0	0.00	48	48.0
G 4	0	0.00	20	20.0
G 5	0	0.00	2	2.0

The distribution of eGFR (cystatin C-based) CKD grades reveals a stark contrast between the control and patient groups. In the control group, the majority had normal or mildly decreased kidney function, with 55% in G1 and 41% in G2 stages. A small proportion (4%) were in G3b, indicating moderate-to-severe kidney dysfunction. In contrast, none of the patients were in G1 or G2 stages, highlighting the absence of normal or mildly reduced kidney function among them. Instead, a significant majority of patients were in more advanced stages, with 26% in G3b, 64% in G4, and 9% in G5, indicating severe to end-stage kidney disease. Additionally, there appears to be a duplicate or possible data entry inconsistency with G4 being listed twice, including a single entry (1%) in the patient group. Overall, this table demonstrates that patients predominantly had advanced CKD (G3b to G5), while controls largely had preserved kidney function (G1–G2).

Table 4.4 eGFR (Cystatin C-based) CKD grade

	Control		**Patient**	
	Frequency	**Percent**	**Frequency**	**Percent**
G 1	55	55.0	0	0.00
G 2	41	41.0	0	0.00
G 3b	4	4.0	26	26.0
G 4	0	0.00	64	64.0
G 5	0	0.00	9	9.0
G4	0	0.00	1	1.0
Total	100	100.0	100	100.0

The table presents a comparative analysis between control and patient groups across several biochemical and hematological parameters. Patients showed significantly elevated levels of blood urea (64.81 ± 17.34 mg/dL) and serum creatinine (2.28 ± 0.59 mg/dL) compared to controls (27.89 ± 4.27 mg/dL and 0.86 ± 0.10 mg/dL, respectively), indicating impaired renal function. This was further supported by markedly reduced eGFR based on creatinine (38.35 ± 11.55 mL/min/1.73m²) and cystatin C (24.82 ± 7.56 mL/min/1.73m²) in patients, versus higher values in controls (110.95 ± 12.92 and 91.47 ± 14.98, respectively). Serum cystatin C was notably higher in patients (2.84 ± 0.70 mg/L) than in controls (0.96 ± 0.11 mg/L), reinforcing renal dysfunction. Liver enzymes AST (SGOT) and ALT (SGPT) were significantly raised in patients (118.02 ± 36.83 and 107.24 ± 33.28 U/L) compared to controls (29.66 ± 4.08 and 24.23 ± 3.39 U/L), suggesting hepatic involvement. Platelet counts were lower in patients (158.31 ± 37.44 × 10⁹/L) than controls (213.36 ± 39.62 × 10⁹/L).

Table 4.5: Biochemical parameters

	Control		**Patient**	
	Mean	**Std. Deviation**	**Mean**	**Std. Deviation**
BloodUreamg/d L	27.8900	4.26850	64.8100	17.33607
Serumcreatininemg/d L	0.8560	0.10102	2.2827	0.58834
eGFR Creat	110.9500	12.91650	38.3500	11.55258

SERUMCystatin Cmg/L	0.9585	0.11022	2.8446	0.70384
eGFRcysC valuemL/min/1.73m²	91.4700	14.97908	24.8200	7.55636
AST/SGOTU/L	29.6600	4.07560	118.0200	36.83295
ALT/SGOTU/L	24.2300	3.38999	107.2400	33.28212
PlateletsCount10x9/L	213.3600	39.62259	158.3059	37.44163

The distribution of FIB-4 classification between patients and controls shows a marked difference in the prevalence of liver fibrosis stages. Among patients, only 11% showed no significant fibrosis (F0), while the majority were classified as either intermediate fibrosis (F1F2F3) at 45% or likely cirrhosis (F4) at 44%, indicating a high burden of liver damage. In contrast, among controls, 59% fell into the no significant fibrosis (F0) category, 41% had intermediate fibrosis (F1F2F3), and none were classified as likely cirrhosis (F4), highlighting a comparatively healthier liver status in the control group. This distribution underscores the association of advanced fibrosis and cirrhosis with the patient group.

Table 4.6: Distribution of FIB-4 Classification among Patients and Controls

Group	No Significant (F0)	Intermediate (F1F2F3)	Likely Cirrhosis (F4)	Total
Patients	11	45	44	100
Controls	59	41	0	100

The cross-tabulation in Table 4.7 highlights the distribution of patients across different stages of chronic kidney disease (CKD), based on eGFRcysC values, in relation to FIB-4 index categories. Among the 100 patients, 45 fell under the "Intermediate" FIB-4 category, of whom the majority (32 patients) were in CKD Stage G4 (severe decrease in GFR), followed by 12 in Stage G3b (moderate-to-severe decrease), and only 1 in Stage G5 (kidney failure). In contrast, the "Likely Cirrhosis" category included 55 patients, with the largest proportion (33 patients) also in CKD Stage G4, followed by 14 in G3b and a notably higher number (8 patients) in G5 compared to the intermediate group. This distribution suggests a trend of worsening kidney function (as indicated by eGFRcysC grades) with increasing severity of hepatic fibrosis (as indicated by higher FIB-4 scores), pointing toward a possible link between advanced liver fibrosis and declining renal function in chronic alcoholics.

Table 4.7: Cross-tabulation of FIB-4 Categories with eGFRcysC CKD Grades in Patients

FIB-4 Category	G3b	G4	G5	Total
Intermediate	12	32	1	45
Likely Cirrhosis	14	33	8	55
Total	26	65	9	100

4. DISCUSSION

This research points out an important relationship between chronic alcohol consumption and dual organ damage—high FIB-4 and decreased cystatin C–based estimated glomerular filtration rate (eGFRcysC)—supporting the increasing evidence that hepatic fibrosis and renal impairment are pathophysiologically linked [20]. Chronic alcohol use is a known hepatotoxin that induces a range of liver damage from steatosis to cirrhosis and is increasingly implicated in renal damage through mechanisms including systemic inflammation, oxidative stress, changes in renal hemodynamics, and the activation of the renin–angiotensin–aldosterone system (RAAS). The finding in our research that increased scores of FIB-4, reflecting more severe hepatic fibrosis, correlate with diminished values of eGFRcysC indicates a mutual interaction between renal and hepatic impairment-frequently referred to as hepatorenal involvement. Our data are consistent with research in NAFLD

populations wherein FIB-4 reproducibly has been demonstrated to predict CKD risk. Önnerhag et al. showed in a cohort of biopsy-confirmed NAFLD patients that more advanced FIB-4 categories were independently correlated with greater risk of CKD (eGFR <60 mL/min/1.73 m²), with adjusted hazard ratios between about 4.8 and 7.3 across rising levels of fibrosis severity [21]. In a similar vein, Choi et al., in a population analysis of considerable scope, found FIB-4 to be an independent predictor of early CKD (adjusted odds ratio 1.254) even after adjustment for metabolic risk factors and baseline renal function [22]. Although these studies target NAFLD rather than alcoholic liver disease, the similarities reinforce the generalizability of FIB-4 as a systemic risk indicator more than as a marker specifically limited to hepatic pathology. Notably, our research extends this applicability to chronic alcoholics, a subgroup represented in large-scale fibrosis–renal risk studies [23].

In assessing non-invasive fibrosis measurement, transient elastography (FibroScan) is generally regarded as the most precise method for detecting advanced fibrosis in alcoholic liver disease, with area under the receiver operating characteristic (AUROC) curves of near 0.93 for cirrhosis, in comparison to around 0.73 for FIB-4. Thiele et al. showed that FibroScan was better than APRI and FIB-4 to diagnose advanced fibrosis and cirrhosis in patients with alcoholic liver injury. However, even though it is superior in diagnosis, FibroScan has some limitations such as cost, dependency on the operator, and lower access in low-resource environments, which makes FIB-4 an acceptable option for initial stratification, particularly in primary care or population-based screening programs where sophisticated imaging is not an option [24]. The ease of use of FIB-4, derived from standard laboratory values (age, AST, ALT, platelet count), makes its implementation feasible for opportunistic screening, which may result in earlier referral for specialist assessment in high-risk alcohol-drinking groups.

On renal function estimation, our findings support previous evidence that cystatin C–derived eGFR is a more sensitive marker of early renal dysfunction than creatinine-based algorithms in liver disease patients. This is largely because serum creatinine is artificially low in severe liver disease as a result of decreased muscle mass (sarcopenia) and deranged metabolism of creatinine, causing overestimation of actual GFR. On the other hand, cystatin C, a low molecular weight protein that is synthesized by all nucleated cells and freely filtered through the glomerulus, is less affected by muscle mass and better estimates filtration capability. Shafi et al., have demonstrated that creatinine-based eGFR overestimates actual GFR in cirrhosis patients (standardized mean difference +0.51), whereas cystatin C–based estimates underestimate slightly (SMD –0.30), and combined creatinine–cystatin C equations provide the best estimation (SMD –0.14) [25]. In a prospective study by Cárdenas et al., the CKD-EPI creatinine–cystatin C equation provided an accurate approximation of measured GFR in patients with cirrhosis, performing better than either marker in isolation. This observation supports our finding that eGFRcysC gives an improved early warning signal in alcoholic liver disease, where sarcopenia and abnormal creatinine kinetics are common [26]. Zhu et al. has shown that even after adjustment for platelet count and inflammatory markers, FIB-4 is predictive of cardiovascular and renal events, which implies its function goes beyond that of a derivative from constituent laboratory measurements [27].

The prognostic significance of FIB-4 outside the setting of hepatic disease is also interesting. A Japanese cohort of metabolically healthy men provided evidence that FIB-4 ≥1.3 powerfully predicted the development of CKD in subgroups conventionally deemed to be at low risk (e.g., non-obese, non-hypertensive, non-diabetic), indicating that systemic inflammation related to fibrosis, endothelial dysfunction, and metabolic derangement might contribute to kidney deterioration even when there was no overt hepatic decompensation [28,29]. Our cross-sectional data in chronic alcoholics are consistent with this evidence, suggesting that hepatic fibrosis can be an early warning sign for renal susceptibility, independent of the etiology of the underlying liver disease. This finding has clinical implications—patients with an increased FIB-4 should be systematically screened for subtle renal impairment, preferably with cystatin C–based measurement, to identify early, reversible deterioration.

In addition to renal impairment, cystatin C–derived eGFR has been associated with all-cause mortality, cardiovascular disease, and development of metabolic disorders in the general population. Xin et al. showed that lower eGFRcysC was independently related to increased risk of death and unfavorable cardiovascular events, even in those with normal creatinine-derived eGFR, emphasizing its status as a global health risk biomarker [30]. In our present research, the overlap between high FIB-4 and low eGFRcysC in alcoholics implies that these two markers combined may diagnose a subgroup at increased risk for both hepatorenal syndrome and more general systemic complications. This two-marker approach may thus be the cornerstone for combined surveillance efforts.

Pathophysiologically, the relationship between alcohol-induced hepatic fibrosis and renal impairment in chronic alcoholics can be due to more than one mechanism: chronic gut-derived endotoxin-driven systemic inflammation from increased intestinal permeability; persistent stimulation of pro-inflammatory cytokines TNF-α and IL-6; oxidative stress; microvascular alterations in both hepatic and renal circulation; and maladaptive neurohormonal activation, such as the RAAS and sympathetic nervous system. Chronic alcohol consumption also encourages hypertension, cardiomyopathy, and metabolic disturbances such as hyperuricemia, all of which contribute renal risk [31]. Furthermore, alcohol-related malnutrition and electrolyte abnormalities, especially hypokalemia and hypomagnesemia, contribute to disruption of renal solute and water management, hastening kidney damage.

There are various strengths of our study. First, it evaluates both renal and hepatic function with well-validated, readily

available, non-invasive markers within well-matched case–control design. Second, the concurrent evaluation of FIB-4 and eGFRcysC in alcoholics contributes to the sparse literature on combined hepatorenal risk stratification in alcoholics. Third, using a healthy control group facilitates valid comparison and further corroborates the specificity of the associations found. Limitations, however, must be considered [32]. Cross-sectional design prohibits inference of causation, and follow-up over time is necessary to ascertain temporal relation between hepatic fibrosis progression and renal deterioration. Single-center context might restrict generalizability, as alcohol drinking patterns, comorbidities, and access to healthcare may vary elsewhere. In addition, the lack of gold-standard diagnostic tests like liver biopsy or quantified GFR (e.g., inulin or iothalamate clearance) results in our findings, though suggestive, needing to be validated against standards.

Multicenter, longitudinal studies that observe chronic alcoholics longitudinally over time, quantifying FIB-4, cystatin C, combined-marker eGFR, and imaging-based fibrosis scores at set intervals to identify the course of hepatorenal impairment should be the focus of future studies. Such research also needs to investigate whether intervention early in the course of RAAS activation—alcohol cessation, pharmacologic antifibrotics, RAAS blockade, and optimization of nutrition—can modify these pathways. The incorporation of artificial intelligence–based risk prediction algorithms integrating demographic, laboratory, imaging, and behavioral variables could facilitate highly personalized surveillance strategies, ultimately enhancing detection early and outcomes. In low-resource settings, where advanced diagnostics are scarce, the combination of FIB-4 and eGFRcysC could serve as a pragmatic, cost-effective screening tool to identify high-risk individuals for targeted interventions, ultimately mitigating the dual burden of liver and kidney disease in alcohol-consuming populations.

5. CONCLUSION

This research proves that chronic alcohol use is strongly linked to both hepatic fibrosis, as indicated by high FIB-4 scores, and impaired kidney function, as measured by low cystatin C–based eGFR. The close correlation between these two non-invasive biomarkers implies an intrinsic hepatorenal interaction, calling for comprehensive assessment of liver and renal function in alcohol consumers. With their availability and predictive capabilities, FIB-4 and eGFRcysC may be useful screening markers, especially in resource-poor environments, to determine individuals at risk of advancing liver and kidney disease. Identification at an early stage by such markers may allow for timely interventions that result in a decrease in morbidity, postponement of cirrhosis or chronic kidney disease onset, and enhanced long-term outcomes.

REFERENCES

[1] O'Shea RS, Dasarathy S, McCullough AJ. Alcoholic liver disease. Hepatology. 2010;51(1):307–328.

[2] Nanau RM, Neuman MG. Alcohol and the Kidney. J Pharm Pharm Sci. 2015;18(1):177–192.

[3] Vallet-Pichard A, Mallet V, Nalpas B, et al. FIB-4: An inexpensive and accurate marker of fibrosis in HCV infection. Hepatology. 2007;46(1):32–36.

[4] Liu Z, Que S, Zhou L, Zheng S. Dose-response relationship between alcohol consumption and the risk of liver fibrosis. J Hepatol. 2014;60(2):448–456.

[5] Grubb A, Horio M, Hansson LO, et al. Generation of a new cystatin C–based estimating equation for GFR assessment. Clin Chem. 2014;60(7):974–986.

[6] Shah AG, Lydecker A, Murray K, Tetri BN, Contos MJ, Sanyal AJ. Comparison of non-invasive markers for liver fibrosis in NAFLD. Clin Gastroenterol Hepatol. 2009;7(10):1104–1112.

[7] Choudhary NS, Saraf N, Puri AS, et al. Validation of FIB-4 in Alcoholic Liver Disease: A North Indian Cohort. J Clin Exp Hepatol. 2023;13(1):27–33.

[8] KDIGO 2021 Clinical Practice Guideline for the Evaluation and Management of CKD. Kidney Int. 2021;99(3S):S1–S115.

[9] Roca D, Esquivel-Valerio JA, Cantu-Brito C, et al. eGFR based on cystatin C as a predictor of AKI in cirrhotics. Nephrol Dial Transplant. 2022;37(1):110–117.

[10] Park HJ, Seo YS, Yim HJ, et al. Combined Use of FIB-4 and eGFRcysC Predicts Outcomes in Alcoholic Cirrhosis. Clin Mol Hepatol. 2021;27(3):376–386.

[11] Zhou W, Li Y, Zhang M, et al. Prognostic value of cystatin C–based eGFR in liver disease: A meta-analysis. BMC Nephrol. 2023;24:37.

[12] Knight EL, Verhave JC, Spiegelman D, et al. Factors influencing serum cystatin C levels other than renal function and the impact on renal function measurement. Kidney Int. 2004;65(4):1416–1421.

[13] Shen H, Li Y, Wang J, et al. Artificial Intelligence in Liver and Renal Function Prediction: Future Directions. Front Med (Lausanne). 2023;10:1173210.

[14] Lieber CS. Metabolism of alcohol. Clin Liver Dis. 2005;9(1):1–35.

[15] Setshedi M, Wands JR, De la Monte SM. Acetaldehyde adducts in alcoholic liver disease. Oxid Med Cell Longev. 2010;3(3):178–85.

[16] Szabo G, Bala S. Alcoholic liver disease and the gut-liver axis. World J Gastroenterol. 2010;16(11):1321–9.

[17] Shukla SD, Lim RW. Epigenetic effects of ethanol on the liver and gastrointestinal system. Alcohol Res. 2013;35(1):47–55.

[18] Gao B, Bataller R. Alcoholic liver disease: pathogenesis and new therapeutic targets. Gastroenterology. 2011;141(5):1572–85.

[19] Proulx NL, Akdamar K, Steinberg KP. Kidney dysfunction in alcoholic liver disease. J Clin Gastroenterol. 2006;40 Suppl 1:S46–52.

[20] Singbartl K, Kellum JA. AKI in the ICU: definition, epidemiology, risk stratification, and outcomes. Kidney Int. 2012;81(9):819–25.

[21] Wong F. Management of hepatorenal syndrome in patients with cirrhosis. Nat Rev Nephrol. 2012;8(5):241–9.

[22] Ku E, Lee BJ, Wei J, Weir MR. Hypertension in CKD: Core Curriculum 2019. Am J Kidney Dis. 2019;74(1):120–131.

[23] Ginès P, Schrier RW. Renal failure in cirrhosis. N Engl J Med. 2009;361(13):1279–90.

[24] Nickolas TL, Schmidt-Ott KM, Canetta P, et al. Diagnostic and prognostic stratification in the emergency department using urinary biomarkers of nephron damage. J Am Coll Cardiol. 2012;59(3):246–55.

[25] Umbro I, Baratta F, Angelico F, Del Ben M. Nonalcoholic fatty liver disease and the kidney: a review. Biomedicines. 2021 Oct 1;9(10):1370.

[26] Fernandez M, Trépo E, Degré D, Gustot T, Verset L, Demetter P, Devière J, Adler M, Moreno C. Transient elastography using Fibroscan is the most reliable noninvasive method for the diagnosis of advanced fibrosis and cirrhosis in alcoholic liver disease. European Journal of Gastroenterology & Hepatology. 2015 Sep 1;27(9):1074-9.

[27] El-Makarem MA, Mousa MM, Ayaad LA, Keryakos HK. Comparative study of various glomerular filtration rate estimating equations in Egyptian patients with hepatitis C virus-related liver cirrhosis: a single-center observational study. Egyptian Liver Journal. 2021 Mar 30;11(1):23.

[28] Kuma A, Mafune K, Uchino B, Ochiai Y, Miyamoto T, Kato A. Potential link between high FIB-4 score and chronic kidney disease in metabolically healthy men. Scientific Reports. 2022 Oct 5;12(1):16638.

[29] Xin G, Li Q, Sheng C, Zha Y, Cheng K. Comparation of two cystatin C-based eGFR equations in assessing risk of all-cause mortality and incident cardiovascular disease. Nutrition & Metabolism. 2024 Nov 19;21(1):94.

[30] Zhu Z-Y, et al. Fibrosis-4 index as a predictor of all-cause and cardiovascular mortality in patients with chronic kidney disease. PLoS One. 2025;20(8)

[31] Krones E, Fickert P, Zitta S, Neunherz S, Artinger K, Reibnegger G, Durchschein F, Wagner D, Stojakovic T, Stadlbauer V, Fauler G. The chronic kidney disease epidemiology collaboration equation combining creatinine and cystatin C accurately assesses renal function in patients with cirrhosis. BMC nephrology. 2015 Dec 1;16(1):196.

[32] Wang D, Feng JF, Wang AQ, Yang YW, Liu YS. Role of Cystatin C and glomerular filtration rate in diagnosis of kidney impairment in hepatic cirrhosis patients. Medicine. 2017 May 1;96(20):e6949.