Mental Wellness

Mental Wellness 2026; 4:74
doi: 10.4081/mw.2026.74

Clinical correlates of serum creatinine in alcohol dependence syndrome

Amit Amit, Geethanjali M Doddamani, Preity Yarlagadda, M. Pramod Kumar Reddy

Department of Psychiatry, Mamata Medical College, Khammam, Telangana, India

Abstract

Alcohol dependence syndrome (ADS) is associated with multisystem complications, including renal dysfunction. This hospital-based cross-sectional observational study evaluated serum creatinine levels and their clinical correlates in 129 patients diagnosed with ADS according to International Classification of Diseases, Tenth Revision criteria. Participants were recruited consecutively from a tertiary care teaching hospital. Sociodemographic and clinical data were collected using a semi-structured proforma. Alcohol use, dependence severity, nicotine dependence, and alcohol withdrawal were assessed using the Alcohol Use Disorders Identification Test (AUDIT), Severity of Alcohol Dependence Questionnaire (SADQ), Fagerström Test for Nicotine Dependence (FTND), and Clinical Institute Withdrawal Assessment for Alcohol–Revised (CIWA-Ar), respectively. Serum creatinine was estimated using an enzymatic dry-slide method. Data were analyzed using non-parametric tests, Spearman's correlation, and hierarchical multiple linear regression. The mean serum creatinine level was 0.88±0.33 mg/dL. Serum creatinine differed significantly across age groups, duration of alcohol use, duration of nicotine use, and place of residence ($p<0.05$), but showed no significant correlation with AUDIT, SADQ, FTND, or CIWA-Ar scores. In regression analysis, age was independently associated with serum creatinine in the present cohort ($\beta=0.417$, $p=0.014$). These findings suggest that routine assessment of renal function may be useful as part of the comprehensive clinical evaluation of patients with ADS.

Key words: alcohol-related disorders, creatinine, kidney function tests, substance withdrawal.

Correspondence to: Amit Amit, Department of Psychiatry, Mamata Medical College, Khammam, Telangana, India.
Tel.: 9873252279. E-mail: amitdoc7062@gmail.com

Introduction

Alcohol dependence syndrome (ADS) is a chronic relapsing disorder characterized by impaired control over alcohol consumption, tolerance, withdrawal symptoms, and continued alcohol use despite harmful consequences.[1] Chronic alcohol consumption affects multiple organ systems, including the kidneys, through mechanisms such as oxidative stress, inflammation, endothelial dysfunction, dehydration, and activation of the renin-angiotensin system, potentially resulting in impaired renal function.[2,3]

Renal function can be assessed using several biomarkers, including serum creatinine, estimated glomerular filtration rate, cystatin-C, urinary albumin-creatinine ratio, and novel markers of tubular injury. Among these, serum creatinine remains the most widely available and routinely used biochemical marker in clinical practice because it is inexpensive, standardized, and incorporated into routine laboratory evaluation. Although less sensitive than newer biomarkers for detecting early renal injury, serum creatinine continues to serve as the initial indicator of impaired renal function and forms the basis for estimating glomerular filtration rate.[3]

Previous studies evaluating alcohol-related renal dysfunction have produced inconsistent findings. While some studies have demonstrated preserved serum creatinine concentrations among chronic alcohol users, others have reported impaired renal function or an increased risk of chronic kidney disease associated with prolonged or heavy alcohol consumption.[2-5] More recent epidemiological studies have primarily focused on alcohol consumption and long-term chronic kidney disease outcomes rather than examining serum creatinine within clinically diagnosed ADS populations. Furthermore, little is known about whether renal function, as reflected by serum creatinine, varies according to the severity of alcohol dependence, nicotine dependence, or alcohol withdrawal assessed using validated psychiatric instruments.

Therefore, the present study aimed to evaluate serum creatinine levels and their clinical correlates among patients with ADS and to examine their relationship with standardized measures of alcohol use, alcohol dependence severity, nicotine dependence, and alcohol withdrawal severity.

Materials and Methods

Study design and setting

This study employed a cross-sectional observational design to examine the clinical correlates of serum creatinine with alcohol dependence. The study was conducted over 6 months from October 2025 to March 2026. The study design adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cross-sectional studies.[6]

Ethical considerations

The study protocol was reviewed and approved by the Institutional Ethics Committee prior to the initiation of data collection (Approval No.: MMC/IEC/2022/2945/144/2025). All procedures involving human participants were conducted in accordance with the ethical standards of the institutional ethics committee and the principles outlined in the World Medical Association Declaration of Helsinki (1975), as revised in 2013.[7]

Written informed consent was obtained from all participants before enrolment. Participation was voluntary, and participants were informed of their right to withdraw at any stage without consequences. Confidentiality and anonymity were maintained by assigning unique identification codes and avoiding collection of personally identifiable information. All data were securely stored and used solely for research purposes.

Sampling technique and participant recruitment

A consecutive sampling technique was employed. All consecutive patients attending the psychiatry inpatient and outpatient services who were diagnosed with ADS during the study period were screened for eligibility.

A total of 150 patients were screened during the study period. Of these, 12 patients did not satisfy the eligibility criteria and were excluded. The remaining 138 eligible patients were invited to participate. Seven patients declined participation, one participant withdrew after providing informed consent, and one participant did not permit the use of study data for publication purposes. Consequently, 129 participants completed the study and were included in the final analysis. The participant screening, recruitment, enrolment, and final inclusion process is presented in Figure 1 as a participant flow diagram.

Study participants

Participants comprised adult patients aged 18-65 years with a diagnosis of ADS according to the International Classification of Diseases, Tenth Revision,[1] confirmed by a qualified psychiatrist. Eligible participants were required to be clinically stable at the time of assessment, capable of understanding the study procedures, and able to provide written informed consent. Patients with acute alcohol intoxication, severe withdrawal requiring emergency stabilization, or impaired decision-making capacity at the time of recruitment were assessed only after achieving clinical stability. Consecutive sampling was employed to recruit all eligible patients presenting during the study period, thereby minimizing investigator-driven selection bias.

Patients were excluded if they had conditions that could independently alter serum creatinine concentrations or interfere with reliable assessment of ADS. These included a known history of chronic kidney disease, acute kidney injury, nephrotic syndrome, glomerulonephritis, or any other primary renal disorder; acute medical illnesses likely to influence renal function, including sepsis, rhabdomyolysis, shock, or severe dehydration; chronic liver disease complicated by hepatic encephalopathy or hepatorenal syndrome; uncontrolled diabetes mellitus or uncontrolled hypertension with documented nephropathy; current use of nephrotoxic medications (such as aminoglycosides, amphotericin B, cisplatin, or non-

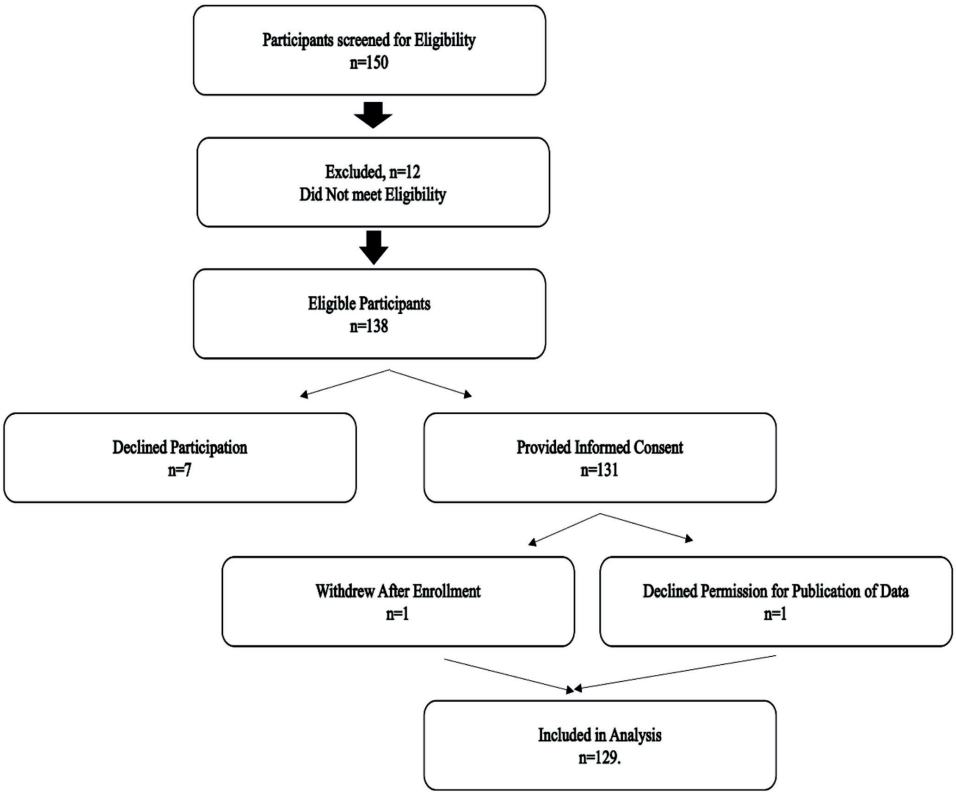

Figure 1. Participant flow diagram showing screening, eligibility assessment, recruitment, enrolment, and final inclusion of participants.

steroidal anti-inflammatory drugs in nephrotoxic doses) or creatine supplementation within the preceding 3 months; severe cognitive impairment, delirium, intellectual disability, or any psychiatric condition precluding reliable clinical evaluation; and inability or unwillingness to provide written informed consent.

These eligibility criteria were designed to minimize confounding from medical conditions or treatments known to influence renal function, thereby allowing a more valid assessment of the relationship between serum creatinine and the clinical characteristics of ADS. However, because of the observational nature of the study, residual confounding from factors such as nutritional status, muscle mass, hydration status, dietary protein intake, liver function, and other unmeasured comorbidities cannot be completely excluded.

Data collection

Following enrolment, participants underwent detailed clinical evaluation using a predesigned semi-structured proforma. Sociodemographic variables including age, sex, place of residence, marital status, educational status, occupation, family type, and per capita family income were recorded. Clinical information including duration of alcohol use, duration of nicotine use, and relevant medical history was obtained through patient interview and review of medical records.

All clinical assessments were conducted by the principal investigator, who received prior training in the administration and scoring of the study instruments. Since all participants were evaluated by the same assessor using standardized administration procedures, inter-rater variability was eliminated.

Tools used

Data were collected using a structured questionnaire consisting of sociodemographic variables and standardized psychometric instruments.

Alcohol Use Disorders Identification Test

The Alcohol Use Disorders Identification Test (AUDIT) was developed by the World Health Organization (WHO) as part of the WHO Collaborative Project on Early Detection of Persons with Harmful Alcohol Consumption.[8] It was developed by Saunders, Aasland, Babor, de la Fuente, and Grant in 1993 to provide a brief, reliable, and internationally applicable screening instrument for identifying hazardous and harmful alcohol consumption as well as possible alcohol dependence. It has been validated across diverse healthcare settings and populations and is widely recommended for use in primary care and psychiatric practice.

The AUDIT consists of 10 items divided into three domains: alcohol consumption (items 1-3), symptoms of alcohol dependence (items 4-6), and alcohol-related problems (items 7-10). Each item is scored on a 5-point Likert-type scale ranging from 0 to 4, resulting in a total score ranging from 0 to 40, with higher scores indicating greater severity of alcohol-related problems.

The recommended interpretation of scores is as follows:
- 0-7: low-risk alcohol use
- 8-15: hazardous alcohol use
- 16-19: harmful alcohol use
- 20-40: possible alcohol dependence requiring further assessment

The AUDIT has demonstrated excellent psychometric properties, with reported sensitivity and specificity generally exceeding 80% for detecting hazardous and harmful alcohol use. The instrument is available free of charge from the WHO for clinical practice and research, provided it is reproduced without modification and appropriate acknowledgment is given.

Severity of Alcohol Dependence Questionnaire

The Severity of Alcohol Dependence Questionnaire (SADQ) was developed by Stockwell, Hodgson, Edwards, Taylor, and Rankin in 1979 to quantify the severity of alcohol dependence.[9] It was designed to measure dependence as a continuous construct rather than simply classifying individuals as dependent or non-dependent. The questionnaire is particularly useful in specialist addiction settings for assessing dependence severity and planning detoxification.

The SADQ consists of 20 items grouped into five domains: physical withdrawal symptoms, affective withdrawal symptoms, relief drinking, frequency of alcohol consumption, and rapidity of reinstatement following abstinence.

Each item is rated on a 4-point Likert-type scale scored from 0 to 3, producing a total score ranging from 0 to 60, with higher scores indicating greater severity of dependence.

The commonly accepted interpretation is:
- 0-15: mild alcohol dependence
- 16-30: moderate alcohol dependence
- 31-45: severe alcohol dependence
- >45: very severe alcohol dependence

The SADQ has demonstrated good reliability and validity across different clinical populations and remains one of the most widely used instruments for measuring alcohol dependence severity in research. The scale is available and commonly reproduced for non-commercial academic research.

Fagerström Test for Nicotine Dependence

The Fagerström Test for Nicotine Dependence (FTND) was developed by Heatherton, Kozlowski, Frecker, and Fagerström in 1991 as a revision of the earlier Fagerström Tolerance Questionnaire.[10] It is one of the most widely used instruments for assessing the intensity of physical nicotine dependence among cigarette smokers and has demonstrated good validity in both clinical and research settings.

The FTND comprises six items evaluating smoking behavior, including time to first cigarette after waking, difficulty refraining from smoking, cigarettes smoked per day, and smoking patterns during illness. The instrument is not a Likert scale. Individual items have different scoring schemes ranging from 0-1, 0-2, or 0-3, yielding a total score between 0 and 10.

The standard interpretation is:
- 0-2: very low dependence
- 3-4: low dependence
- 5: moderate dependence
- 6-7: high dependence
- 8-10: very high dependence

Higher scores indicate greater nicotine dependence and predict increased difficulty with smoking cessation. The FTND is available free for non-commercial clinical and research use.

Clinical Institute Withdrawal Assessment for Alcohol-Revised

The Clinical Institute Withdrawal Assessment for Alcohol-Revised (CIWA-Ar) was developed by Sullivan, Sykora, Schneiderman, Naranjo, and Sellers in 1989 as a revision of the original CIWA-A scale.[11] The revision was intended to provide a brief,

reliable, and clinically practical instrument for quantifying the severity of alcohol withdrawal and guiding symptom-triggered benzodiazepine therapy. The CIWA-Ar consists of 10 clinician-rated items assessing nausea and vomiting, tremor, paroxysmal sweats, anxiety, agitation, tactile disturbances, auditory disturbances, visual disturbances, headache, and orientation/clouding of sensorium. The scale is not a conventional Likert questionnaire. Most items are scored from 0 to 7, whereas orientation is scored from 0 to 4, producing a maximum total score of 67.

The recommended interpretation is:

- <10: mild withdrawal
- 10-19: moderate withdrawal
- ≥20: severe withdrawal requiring close monitoring and aggressive pharmacological management

The CIWA-Ar has excellent inter-rater reliability and validity and is regarded as the gold standard for assessing alcohol withdrawal severity in both clinical practice and research. The instrument is freely available for clinical and academic use, with appropriate acknowledgment of the original publication.

Blood sample collection and laboratory analysis

Following clinical assessment, approximately 2-3 mL of venous blood was collected from each participant under aseptic precautions by trained laboratory personnel as part of the routine biochemical evaluation. Blood samples were collected in plain vacutainer tubes, allowed to clot, and centrifuged within 4 hours of collection to obtain serum. Serum samples were analyzed immediately or stored under recommended laboratory conditions until testing.

Serum creatinine estimation was performed in the Department of Biochemistry of the institute using the VITROS Chemistry System (Ortho Clinical Diagnostics, Rochester, NY, USA) with VITROS CREA Slides. The assay employs a dry-slide enzymatic method, wherein creatinine is sequentially hydrolyzed by creatinine amidohydrolase and creatine amidino hydrolase to generate sarcosine. Sarcosine is subsequently oxidized by sarcosine oxidase, producing hydrogen peroxide, which reacts in the presence of peroxidase to oxidize a leuco dye and generate a colored product. The rate of change in reflectance at 670 nm is measured using a two-point rate method at 37°C and is directly proportional to the serum creatinine concentration. Calibration and internal quality control procedures were performed according to the manufacturer's recommendations before analysis of patient samples. Serum creatinine concentrations were reported in mg/dL.

Statistical analysis

Data were entered into Microsoft Excel and analyzed using IBM Statistical Package for the Social Sciences (SPSS version 26.0) (IBM Corp., Armonk, NY, USA).[12] Continuous variables were expressed as mean ± standard deviation (SD), whereas categorical variables were summarized using frequencies and percentages. Normality of continuous variables was assessed using the Shapiro-Wilk test.[13] Since serum creatinine and several continuous variables were not normally distributed, non-parametric statistical tests were used. The Mann-Whitney U test was applied to compare serum creatinine between two independent groups,[14] whereas the Kruskal-Wallis H test was used for comparisons involving more than two groups.[15] Where the Kruskal-Wallis test demonstrated statistically significant differences, Bonferroni-adjusted pairwise post hoc comparisons were performed to identify specific between-group differences, and the detailed results are presented in *Supplementary Table 1*.[16] Associations between serum creatinine and AUDIT, SADQ, FTND, and CIWA-Ar scores were examined using Spearman's rank correlation coefficient.[17] Variables demonstrating significant or clinically relevant associations were entered into a hierarchical multiple linear regression model to identify independent predictors of serum creatinine.[18] Regression assumptions were assessed using residual plots, Cook's distance, tolerance, and variance inflation factor (VIF).[19,20] A two-tailed $p<0.05$ was considered statistically significant.

Results

A total of 129 patients diagnosed with ADS were included in the study. The baseline sociodemographic characteristics and clinical profile of the participants are presented in Tables 1 and 2.

The study population was predominantly male (96.9%), with the largest proportion of participants belonging to the 41-50-year age group (38.8%). Slightly more than half of the participants were from urban areas (51.9%), while 48.1% belonged to rural areas. Most participants were married (86.0%) and lived in nuclear families (81.4%). High school education was the most common educational status (36.4%), and more than half of the participants were semi-skilled workers (54.3%). Regarding socioeconomic status, 57.4% of participants belonged to the lowest income category included in the study. Duration of alcohol use ranged from 1 to 30 years, with the largest proportion reporting 16-20 years of alcohol consumption (31.0%). Similarly, the most common duration of nicotine use was 16-20 years (34.1%) (Table 1).

The mean AUDIT score was 18.29±4.83, mean FTND score was 3.91±1.79, mean SADQ score was 16.64±5.39, and mean CIWA-Ar score was 10.08±4.36. The mean serum creatinine level of the study population was 0.88±0.33 mg/dL. Nearly half of the participants (45.7%) were classified as having probable alcohol dependence according to the AUDIT, while 52.7% demonstrated moderate alcohol dependence on the SADQ. Moderate nicotine dependence was observed in 27.1% of participants, whereas most patients exhibited either mild or moderate alcohol withdrawal severity on the CIWA-Ar scale (Table 2).

The association between serum creatinine levels and selected sociodemographic and clinical variables is summarized in Table 3. Among the dichotomous variables analyzed using the Mann-Whitney U test, serum creatinine levels differed significantly according to place of residence, with rural participants demonstrating significantly higher serum creatinine levels than urban participants ($p=0.006$). No statistically significant differences were observed according to gender or family type.

Among variables analyzed using the Kruskal-Wallis test, significant differences in serum creatinine levels were observed across age groups ($p<0.001$), duration of alcohol use ($p<0.001$), and duration of nicotine use ($p<0.001$). However, marital status, educational status, occupation, and family income were not significantly associated with serum creatinine levels.

Bonferroni-adjusted post hoc analyses (*Supplementary Table 1*) showed that older participants (41-50 and 51-65 years) had significantly higher serum creatinine levels than younger participants (18-30 and 31-40 years). Similarly, significantly higher serum creatinine levels were observed among participants with longer durations of alcohol use (16-20 and 21-30 years) and nicotine use (16-20 and 21-30 years) compared with those with shorter durations of exposure.

Table 1. Sociodemographic and clinical characteristics of the study participants (n=129).

Variable	Category	n	%
Age (years)	18-30	22	17.1
	31-40	37	28.7
	41-50	50	38.8
	51-65	20	15.5
Gender	Male	125	96.9
	Female	4	3.1
Residence	Urban	67	51.9
	Rural	62	48.1
Marital status	Married	111	86.0
	Unmarried	13	10.1
	Divorced/separated	5	3.9
Type of family	Nuclear	105	81.4
	Joint	24	18.6
Education	Illiterate	3	2.3
	Primary school	11	8.5
	Middle school	27	20.9
	High school	47	36.4
	Intermediate	23	17.8
	Graduate	15	11.6
	Postgraduate	3	2.3
Occupation	Unemployed	24	18.6
	Semi-skilled worker	70	54.3
	Skilled worker	29	22.5
	Semi-professional	6	4.7
Per-capita family income	₹7,389-23,869	74	57.4
	₹23,870-39,829	43	33.3
	₹39,830-59,794	12	9.3
Duration of alcohol use	1-5 years	18	14.0
	6-10 years	19	14.7
	11-15 years	22	17.1
	16-20 years	40	31.0
	21-30 years	30	23.3
Duration of nicotine use	1-5 years	26	20.2
	6-10 years	17	13.2
	11-15 years	30	23.3
	16-20 years	44	34.1
	21-30 years	10	7.8
	31-40 years	2	1.6

Table 2. Clinical characteristics and scale scores of patients with alcohol dependence syndrome (n=129).

Continuous variables			
Variable	**Mean ± standard deviation**	**Minimum**	**Maximum**
AUDIT total score	18.29±4.83	6	32
FTND total score	3.91±1.79	0	7
SADQ total score	16.64±5.39	5	36
CIWA-Ar total score	10.08±4.36	2	24
Serum creatinine (mg/dL)	0.88±0.33	0.60	2.20
Severity categories			
Variable	**Category**	**n**	**%**
AUDIT	Low-risk drinking	4	3.1
	Hazardous drinking	26	20.2
	Harmful drinking	40	31.0
	Probable alcohol dependence	59	45.7
FTND	Very low dependence	32	24.8
	Low dependence	40	31.0
	Moderate dependence	35	27.1
	High dependence	22	17.1
SADQ	Low dependence	57	44.2
	Moderate dependence	68	52.7
	Severe dependence	4	3.1
CIWA-Ar	Mild withdrawal	57	44.2
	Moderate withdrawal	68	52.7
	Severe withdrawal	4	3.1

Percentages may not total exactly 100% because of rounding. AUDIT, Alcohol Use Disorders Identification Test; FTND, Fagerström Test for Nicotine Dependence; SADQ, Severity of Alcohol Dependence Questionnaire; CIWA-Ar, Clinical Institute Withdrawal Assessment for Alcohol-Revised.

Spearman's rank correlation analysis demonstrated no significant correlation between serum creatinine levels and the severity of alcohol use, nicotine dependence, alcohol dependence, or alcohol withdrawal severity. Although weak positive and negative correlation coefficients were observed, none reached statistical significance, indicating that serum creatinine levels were not linearly associated with AUDIT, FTND, SADQ, or CIWA-Ar scores in the present study (Table 4).

To identify independent predictors of serum creatinine levels, hierarchical multiple linear regression analysis was performed (Table 5). In the first model, demographic and substance-use variables (age, gender, residence, duration of alcohol use, and duration of nicotine use) accounted for 14.9% of the variance in serum creatinine levels (adjusted R^2=0.115, p=0.001). Addition of clinical severity measures (AUDIT, FTND, SADQ, and CIWA-Ar scores) in the second model (Table 6) resulted in only a marginal increase in the explained variance (R^2=0.167; ΔR^2=0.017), which was not statistically significant (p=0.650), indicating that these clinical scales did not substantially improve the predictive ability of the model beyond demographic and substance-use characteristics.

Within the final regression model (Table 6), age emerged as the only significant independent predictor of serum creatinine levels (β=0.417, p=0.014), suggesting that serum creatinine increased with advancing age after adjusting for all other variables included in the model. Gender, residence, duration of alcohol use, duration of nicotine use, AUDIT score, FTND score, SADQ score, and CIWA-Ar score were not independently associated with serum creatinine levels.

Regression diagnostics demonstrated that the assumptions underlying linear regression were adequately satisfied. Examination of the residual histogram and normal probability plot indicated approximate normality of residuals, while the scatterplot of standardized residuals against predicted values showed no evidence of heteroscedasticity. Multicollinearity was not considered problematic, with tolerance values ranging from 0.174 to 0.937 and VIF values ranging from 1.068 to 5.745. The maximum Cook's distance was 0.107, indicating that no single observation exerted an undue influ-

Table 3. Association between sociodemographic and clinical variables and serum creatinine levels (n=129).

Variable	Test statistic	p
Mann-Whitney U test		
Gender	U=162.000	0.224
Residence	U=1502.000	0.006*
Type of family	U=1091.000	0.298
Kruskal-Wallis H test		
Age group	H=22.819	<0.001
Marital status	H=0.827	0.661
Education	H=4.954	0.550
Occupation	H=2.316	0.509
Family income	H=1.685	0.431
Duration of alcohol use	H=21.259	<0.001*
Duration of nicotine use	H=26.327	<0.001*

Serum creatinine levels were compared using the Mann-Whitney U test for dichotomous variables and the Kruskal-Wallis H test for variables with three or more categories, as the data were not normally distributed. Bonferroni-adjusted pairwise Mann-Whitney tests were performed following significant Kruskal-Wallis tests. Only statistically significant pairwise comparisons are shown. *Statistically significant at p<0.05. U, Mann-Whitney U statistic; H, Kruskal-Wallis H statistic.

Table 4. Correlation between clinical scale scores and serum creatinine levels (n=129).

Variable	Spearman's rho (ρ)	p
AUDIT total score	−0.079	0.373
FTND total score	0.074	0.406
SADQ total score	−0.054	0.543
CIWA-Ar total score	0.046	0.604

Correlation between clinical scale scores and serum creatinine was assessed using Spearman's rank correlation coefficient (ρ) because the variables were not normally distributed. Statistical significance was set at p<0.05. AUDIT, Alcohol Use Disorders Identification Test; FTND, Fagerström Test for Nicotine Dependence; SADQ, Severity of Alcohol Dependence Questionnaire; CIWA-Ar, Clinical Institute Withdrawal Assessment for Alcohol-Revised; ρ (rho), Spearman's rank correlation coefficient.

Table 5. Hierarchical multiple linear regression models predicting serum creatinine levels (n=129).

Model	Predictors	R	R^2	Adjusted R^2	F	p
Model 1	Age, gender, residence, duration of alcohol use, duration of nicotine use	0.387	0.149	0.115	4.324	0.001*
Model 2	Model 1 + AUDIT + FTND + SADQ + CIWA-Ar	0.408	0.167	0.104	2.647	0.008*

Hierarchical multiple linear regression was performed to identify independent predictors of serum creatinine. Sociodemographic and clinical variables significantly associated with serum creatinine in univariate analyses were entered in Model 1. Clinical scale scores were subsequently added in Model 2. *Statistically significant at p<0.05. AUDIT, Alcohol Use Disorders Identification Test; FTND, Fagerström Test for Nicotine Dependence; SADQ, Severity of Alcohol Dependence Questionnaire; CIWA-Ar, Clinical Institute Withdrawal Assessment for Alcohol-Revised.

ence on the regression model. Although one standardized residual marginally exceeded ±3 SD, overall diagnostic assessment suggested that the regression model was robust and appropriate for interpretation (Table 6).

Discussion

Summary of key findings

This study evaluated the clinical correlates of serum creatinine among 129 patients with ADS. The mean serum creatinine level was 0.88±0.33 mg/dL, which largely remained within the normal physiological range. Serum creatinine showed significant associations with age, place of residence, duration of alcohol use, and duration of nicotine use on univariate analysis. However, no significant correlations were observed between serum creatinine and AUDIT, SADQ, FTND, or CIWA-Ar scores. In multivariable analysis, age was independently associated with serum creatinine in the present cohort, while measures of alcohol dependence severity, nicotine dependence, and withdrawal severity were not independently associated.

Interpretation in the context of existing evidence

The mean serum creatinine observed in the present study is consistent with the study by Majumdar *et al*., who reported that plasma creatinine levels remained within the normal range among chronic alcoholics despite prolonged alcohol consumption, suggesting that alcohol dependence alone may not invariably result in clinically significant renal dysfunction.[4] Similarly, Keso and Salaspuro observed relatively stable serum creatinine values in alcohol-dependent patients and demonstrated that short-term abstinence had minimal influence on creatinine concentrations in men.[21] These findings support our observation that serum creatinine remained largely normal despite varying degrees of alcohol dependence.

Unlike earlier Indian studies by Singaravelu and Kumari, which reported significantly elevated serum creatinine among chronic alcoholic men compared with healthy controls, the present study did not identify alcohol dependence severity as an independent determinant of serum creatinine.[22] This discrepancy may be explained by differences in study design. While the previous study compared alcohol-dependent individuals with healthy controls and evaluated renal dysfunction as the primary outcome, the present study investigated correlations within an exclusively ADS population after excluding patients with known renal disease, thereby reducing the influence of overt renal impairment.

Our finding that serum creatinine was not significantly correlated with AUDIT, SADQ, FTND, or CIWA-Ar scores highlights that conventional severity measures of alcohol use and withdrawal may not adequately reflect renal functional status. This observation is novel, as no previous studies have directly examined the relationship between serum creatinine and validated psychiatric measures of alcohol dependence. Joo *et al*. reported that heavy alcohol consumption was associated with faster progression of chronic kidney disease in patients with established CKD. In contrast, the present study found no association between serum creatinine and the severity of alcohol dependence, suggesting that in patients with ADS without known CKD, renal function is influenced more by age and duration of substance use than by dependence severity.[22]

Lai *et al.* reported that moderate alcohol consumption was associated with a lower risk of incident chronic kidney disease in the general population. In contrast, the present study among patients with ADS found no association between serum creatinine and the severity of alcohol dependence, indicating that renal function was more closely related to age and duration of substance use than to dependence severity.[23] Similarly, Lin *et al.* (2025) observed lower serum creatinine and higher estimated glomerular filtration rate among alcohol consumers in the Taiwan Biobank.[24] These studies, however, evaluated alcohol consumption in community populations rather than clinically diagnosed ADS patients and focused on chronic kidney disease outcomes rather than dependence severity. Therefore, direct comparison with the present study should be interpreted cautiously.

Although age emerged as the only independent correlate of serum creatinine, these findings should be interpreted cautiously. Serum creatinine is influenced by multiple physiological and clinical factors beyond renal function, including muscle mass, nutritional status, hydration, dietary protein intake, liver function, and other concurrent medical conditions. While several major confounders were minimized through the eligibility criteria, these variables were not systematically measured and may have contributed to the observed associations.

An important consideration is that the mean serum creatinine concentration in the present study (0.88±0.33 mg/dL) was within the normal laboratory reference range for most adults. Consequently, the statistically significant associations observed should not be interpreted as evidence of clinically overt renal dysfunction. Rather, these

Table 6. Final hierarchical multiple linear regression model for factors associated with serum creatinine (Model 2).

Predictor	B	Standardized β	p	VIF
Age	0.146	0.417	0.014	3.983
Gender	−0.039	−0.020	0.818	1.111
Residence	0.083	0.126	0.152	1.088
Duration of alcohol use	−0.033	−0.136	0.497	5.745
Duration of nicotine use	0.030	0.118	0.370	2.444
AUDIT total score	−0.007	−0.108	0.314	1.645
FTND total score	−0.012	−0.064	0.460	1.068
SADQ total score	−0.002	−0.027	0.810	1.848
CIWA-Ar total score	0.002	0.032	0.760	1.526

Model 2 represents the final hierarchical multiple linear regression model. Statistically significant at $p<0.05$. B, unstandardized regression coefficient; β, standardized regression coefficient; VIF, variance inflation factor. Regression diagnostics: maximum standardized residual = 3.969; maximum Cook's distance = 0.107; tolerance = 0.174-0.937; VIF = 1.068-5.74; no influential observations were identified based on Cook's distance (<1.0).

findings indicate variability in serum creatinine within the normal physiological range, suggesting that demographic and clinical factors, particularly age, may influence renal function markers even in the absence of clinically apparent kidney disease. The clinical implications of these relatively small differences remain uncertain and require confirmation through longitudinal studies incorporating more sensitive measures of renal function.

Strengths and limitations

A major strength of this study is that it is among the first to evaluate serum creatinine in relation to multiple validated clinical instruments, including AUDIT, SADQ, FTND, and CIWA-Ar, within a well-characterized ADS population. The comprehensive assessment of demographic, substance-use, and clinical variables, together with multivariable regression analysis, enabled identification of independent predictors while controlling for potential confounders.

The study cohort primarily comprised clinically stable adults with ADS without known renal disease or major medical conditions expected to substantially alter renal function, allowing evaluation of serum creatinine while minimizing the influence of overt renal pathology. Nevertheless, several limitations should be acknowledged. The cross-sectional design precludes causal inference, and the absence of longitudinal follow-up limits the ability to evaluate temporal changes in renal function or determine whether the observed associations predict subsequent renal impairment. The single-center hospital-based setting may also limit the generalizability of the findings to the broader ADS population. Furthermore, the absence of a comparison group comprising healthy individuals or non-dependent alcohol users limits the ability to determine whether the observed serum creatinine profile is specific to ADS. Although consecutive sampling and stringent eligibility criteria were employed to reduce selection bias and minimize confounding from conditions known to affect renal function, residual confounding from factors such as nutritional status, body composition, liver function, hydration status, dietary protein intake, and other unmeasured comorbidities cannot be excluded. Serum creatinine alone may not detect early renal injury and can be influenced by several physiological factors; therefore, more sensitive renal biomarkers, including cystatin-C, estimated glomerular filtration rate, urinary albumin-creatinine ratio, neutrophil gelatinase-associated lipocalin, and other markers of tubular injury, were not evaluated. In addition, alcohol and nicotine consumption were assessed using validated clinical instruments; however, these measures rely partly on participant self-report and are therefore subject to recall bias and under-reporting. Finally, the predominantly male study population limits the generalizability of the findings to female patients.

Implications and mechanisms

The findings suggest that serum creatinine may have limited utility as a standalone biomarker of alcohol dependence severity or withdrawal severity in ADS. The absence of significant associations with AUDIT, SADQ, and CIWA-Ar indicates that renal function, as reflected by serum creatinine, may remain preserved despite substantial clinical variability in dependence severity. Physiologically, serum creatinine reflects both glomerular filtration and muscle metabolism and is influenced by several non-alcohol-related factors. Chronic alcohol use may produce renal injury through oxidative stress, inflammation, endothelial dysfunction, and dehydration; however, these changes may precede measurable elevations in serum creatinine or require more sensitive biomarkers for detection.

Controversies and novel insights

The relationship between alcohol use and renal function remains controversial. While experimental studies suggest alcohol-induced nephrotoxicity, several large epidemiological studies have paradoxically reported lower risks of chronic kidney disease among light-to-moderate drinkers.[2,3,23] Such discrepancies likely reflect differences in alcohol exposure, study populations, outcome measures, and residual confounding. The present study contributes a novel perspective by demonstrating that within patients already diagnosed with ADS, serum creatinine is unrelated to validated measures of alcohol dependence or withdrawal severity after adjustment for demographic variables, with age emerging as the principal determinant.

Future research directions

Prospective multicenter studies with larger and more gender-balanced samples are needed to clarify temporal relationships between chronic alcohol exposure and renal function. Future research should incorporate sensitive renal biomarkers, including cystatin-C, urinary albumin-creatinine ratio, estimated glomerular filtration rate, and novel markers of tubular injury. Longitudinal studies evaluating changes during abstinence and relapse may further elucidate the effects of sustained alcohol exposure on renal physiology.

Conclusions

In conclusion, serum creatinine demonstrated significant associations with selected demographic and clinical variables among patients with ADS, with age emerging as the only independent correlate after adjustment for potential confounders. However, because serum creatinine values largely remained within the normal reference range and the study employed a cross-sectional design without a comparison group, the clinical significance of these associations should be interpreted with caution. Larger multicenter longitudinal studies incorporating comprehensive renal biomarkers are warranted to determine whether these findings translate into meaningful clinical outcomes.

References

1. World Health Organization. The ICD-10 classification of mental and behavioural disorders: diagnostic criteria for research. 1993. Available from: https://iris.who.int/handle/10665/37108
2. Cheungpasitporn W, Thongprayoon C, Kittanamongkolchai W, et al. High alcohol consumption and the risk of renal damage: a systematic review and meta-analysis. QJM 2015;108:539-48.
3. Yuan HC, Yu QT, Bai H, et al. Alcohol intake and the risk of chronic kidney disease: results from a systematic review and dose-response meta-analysis. Eur J Clin Nutr 2021;75:1550-7.
4. Majumdar SK, Shaw GK, O'Gorman P, Thomson AD. Plasma urea and creatinine status in chronic alcoholics. Drug Alcohol Depend 1982;9:97-100.
5. Singaravelu S, Kumari S. A study of renal dysfunction in chronic alcoholic men in a tertiary care hospital. Int J Clin Biochem Res 2015;2:246-9.
6. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol 2008;61:344-9.
7. World Medical Association. World Medical Association

Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA 2013;310:2191-4.
8. Saunders JB, Aasland OG, Babor TF, et al. Development of the alcohol use disorders identification test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption--II. Addiction 1993;88:791-804.
9. Stockwell T, Murphy D, Hodgson R. The severity of alcohol dependence questionnaire: its use, reliability and validity. Br J Addict 1983;78:145-55.
10. Heatherton TF, Kozlowski LT, Frecker RC, Fagerström KO. The Fagerström Test for Nicotine Dependence: a revision of the Fagerström Tolerance Questionnaire. Br J Addict 1991;86:1119-27.
11. Sullivan JT, Sykora K, Schneiderman J, et al. Assessment of alcohol withdrawal: the revised clinical institute withdrawal assessment for alcohol scale (CIWA-Ar). Br J Addict 1989;84:1353-7.
12. IBM Corp. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY, USA: IBM Corp.; 2019.
13. Shapiro SS, Wilk MB. An analysis of variance test for normality (complete samples). Biometrika 1965;52:591-611.
14. Mann HB, Douglas RW. On a test of whether one of two random variables is stochastically larger than the other. Ann Math Stat 1947;18:50-60.
15. Kruskal WH, Allen Wallis W. Use of ranks in one-criterion variance analysis. J Am Stat Assoc 1952;47:583-621.
16. Dunn OJ. Multiple comparisons among means. J Am Stat Assoc 1961;56:52-64.
17. Spearman C. The proof and measurement of association between two things. Am J Psychol 1987;100:441-71.
18. Kutner MH, Nachtsheim CJ, Neter J, Li W. Applied linear statistical models. 5th ed. New York, NY, USA: McGraw-Hill; 2005.
19. O'brien RM. A caution regarding rules of thumb for variance inflation factors. Qual Quant 2007;41:673-90.
20. Cook RD. Detection of influential observation in linear regression. Technometrics 1977;19:15-8.
21. Keso L, Salaspuro M. Serum creatinine values and changes in alcohol consumption among alcohol dependent patients. Alcohol Alcohol Suppl 1987;1:611-3.
22. Joo YS, Koh H, Nam KH, et al. Alcohol consumption and progression of chronic kidney disease: results from the Korean cohort study for outcome in patients with chronic kidney disease. Mayo Clin Proc 2020;95:293-305.
23. Lai YJ, Chen YY, Lin YK, et al. Alcohol consumption and risk of chronic kidney disease: a nationwide observational cohort study. Nutrients 2019;11:2121.
24. Lin FC, Luo SK, Tu HP, et al. Association between alcohol consumption and renal function in patients with diabetes mellitus and hypertension: insights from the Taiwan Biobank. BMC Nephrol 2025;26:256.

Online supplementary material:

Supplementary Table 1. Bonferroni-adjusted post hoc pairwise comparisons following significant Kruskal-Wallis tests (n=129).

Received: 22 July 2026; Accepted: 31 July 2026.

Contributions: Amit Amit: conceptualization, study design, definition of intellectual content, literature search, data acquisition, data analysis, statistical analysis, manuscript preparation, manuscript editing, manuscript review, and supervision. Geethanjali M Doddamani: conceptualization, study design, definition of intellectual content, literature search, data acquisition, data analysis, statistical analysis, manuscript preparation, manuscript editing, and manuscript review. Preity Yarlagadda: conceptualization, study design, literature search, data acquisition, data analysis, manuscript preparation, and manuscript editing. M. Pramod Kumar Reddy: conceptualization, study design, definition of intellectual content, data acquisition, manuscript editing, manuscript review, and supervision. All authors have read and approved the final manuscript.

Conflict of interest: the authors declare no conflicts of interest for this study.

Ethics approval and consent to participate: the study protocol was reviewed and approved by the Institutional Ethics Committee prior to the initiation of data collection (Approval No.: MMC/IEC/2022/2945/144/2025); approved on 30 September 2025).

Informed consent: written informed consent was obtained from all participants prior to their inclusion in the study.

Participant consent for publication: participants provided consent for the use of anonymized study data for publication purposes in the informed consent form.

Availability of data and materials: the data set for the current study is available from the corresponding author upon reasonable request.

Declaration of generative artificial intelligence and artificial intelligence-assisted technologies in the writing process: AI-assisted tool (ChatGPT) was used for grammar checking and language refinement during the preparation of this manuscript. The authors reviewed and edited all content and take full responsibility for the accuracy, integrity, and originality of the work.