

**URINARY MICROALBUMIN AND SERUM ADIPONECTIN
AS EARLY MARKERS OF SUBCLINICAL KIDNEY DYSFUNCTION
IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE
(NAFLD/MASLD): A PROSPECTIVE CROSS-SECTIONAL STUDY**

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Non-alcoholic fatty liver disease (NAFLD), recently reclassified as metabolic dysfunction-associated steatotic liver disease (MASLD) following the 2023 Delphi consensus, has emerged as the most prevalent chronic liver disease worldwide, affecting more than 30% of the adult population and showing a continuous upward trend. The clinical significance of NAFLD extends far beyond the liver — it is now recognized as a multisystem metabolic disorder associated with increased cardiovascular mortality, type 2 diabetes, and chronic kidney disease (CKD). Recent large-scale meta-analyses have demonstrated that NAFLD patients have a 1.79-fold higher risk of developing CKD compared with the general population, independently of traditional risk factors such as diabetes, hypertension, and obesity (Mantovani A et al., Gut 2022). The underlying pathophysiology involves a complex interplay between chronic low-grade systemic inflammation, adipokine dysregulation, insulin resistance, endothelial dysfunction, and oxidative stress — all of which contribute to progressive glomerular barrier damage and tubulointerstitial injury. Despite this well-documented association, clinical practice continues to rely primarily on serum creatinine for kidney function assessment, a marker that detects renal damage only after substantial nephron loss has occurred. Consequently, a considerable proportion of NAFLD patients with early, subclinical kidney involvement remain unrecognized and untreated, missing the critical window for nephroprotective intervention. The problem is particularly pressing in Central Asia, where epidemiological data on NAFLD-associated renal involvement are extremely limited, and standardized early-detection algorithms have not yet been established. There is therefore an urgent

clinical and public health need for sensitive, non-invasive, and cost-effective biomarkers that can identify subclinical kidney dysfunction in NAFLD patients at a stage when progression can still be prevented. Urinary microalbumin — a well-established marker of glomerular barrier integrity — and serum adiponectin — an adipokine with proven renoprotective properties — represent promising candidates, but their combined diagnostic value in NAFLD populations has not been systematically evaluated.

Objective. To evaluate the diagnostic value of urinary microalbumin and serum adiponectin as early markers of subclinical kidney dysfunction in patients with NAFLD/MASLD, to assess their discriminative performance for identifying chronic kidney disease stage G3 or higher through ROC analysis, and to determine the hidden prevalence of subclinical renal involvement in a Central Asian NAFLD population.

Methods. A prospective cross-sectional case-control study was conducted at the clinical bases of Bukhara State Medical Institute between 2025 and 2026. A total of 146 subjects were enrolled: 116 NAFLD patients (main group), diagnosed according to MASLD 2023 Delphi consensus criteria (hepatic steatosis confirmed by abdominal ultrasound plus at least one cardiometabolic risk factor, with exclusion of viral hepatitis, significant alcohol consumption, autoimmune, metabolic, and drug-induced liver diseases), and 30 age- and sex-matched healthy controls. Serum adiponectin, IL-6, IL-10, and TNF- α were measured by ELISA using Cusabio Biotech (China) reagents. Urinary microalbumin was determined by immunoturbidimetry. Estimated glomerular filtration rate (eGFR) was calculated using the race-free CKD-EPI 2021 formula, and CKD stages were classified according to KDIGO 2024 guidelines. Hepatic steatosis severity was graded (S0–S3) by ultrasound and the Hepatic Steatosis Index. The study was reported in accordance with STROBE guidelines, approved by the Ethics Committee of Bukhara State Medical Institute, and conducted in compliance with the Declaration of Helsinki (2013 revision). Written informed consent was obtained from all participants. Statistical analysis was performed in SPSS v.26 using the Mann-Whitney U test, Fisher's exact test, Spearman rank correlation, and ROC analysis with calculation of AUROC and 95% confidence intervals. A p-value < 0.05 was considered statistically significant.

Results. The study groups were comparable in age (49.4 ± 11.8 vs 48.2 ± 10.1 years; $p = 0.45$) and sex distribution ($p = 0.98$). NAFLD patients showed

markedly elevated urinary microalbumin (16.51 ± 14.10 vs 1.67 ± 3.80 mg/L; 10-fold difference; $p < 0.001$) and significantly reduced eGFR (78.0 ± 19.2 vs 88.9 ± 16.5 ml/min/1.73m²; $p = 0.003$) compared with controls. Serum adiponectin was significantly lower in the NAFLD group and showed a strong positive correlation with eGFR ($r = +0.404$; $p < 0.001$), while urinary microalbumin correlated inversely with eGFR ($r = -0.394$; $p < 0.001$). A striking finding was that CKD stage G3 or higher was identified exclusively in the NAFLD group (18 of 116; 15.5% vs 0 of 30; 0%; Fisher's exact test $p = 0.025$), representing previously undetected subclinical kidney disease in a substantial proportion of patients. ROC analysis for predicting CKD G3+ demonstrated excellent diagnostic performance of urinary microalbumin (AUROC = 0.813; 95% CI 0.730–0.896) and good performance of serum adiponectin (AUROC = 0.746; 95% CI 0.652–0.840). Both markers substantially outperformed conventional non-invasive indices such as the Hepatic Steatosis Index (AUROC = 0.532) and the AST/ALT ratio (AUROC = 0.618). Pro-inflammatory cytokines (IL-6, TNF- α) were also elevated in NAFLD patients, further supporting the inflammatory basis of NAFLD-associated renal involvement.

Conclusions. Urinary microalbumin and serum adiponectin are highly effective, non-invasive, and clinically accessible early markers for detecting subclinical kidney dysfunction in NAFLD/MASLD patients. The remarkable finding that 15.5% of NAFLD patients harbored previously undiagnosed CKD stage G3 or higher underscores the substantial hidden burden of renal involvement in this population — a burden that would remain invisible if clinicians rely solely on standard serum creatinine assessment. These findings strongly support the integration of routine urinary microalbumin and serum adiponectin screening into standard NAFLD management protocols in internal medicine practice, particularly within primary care and outpatient settings. Such an approach would enable earlier risk stratification, timely initiation of nephroprotective therapy, improved cardiovascular and renal outcomes, and reduced long-term healthcare costs associated with advanced CKD and dialysis. Larger multicenter longitudinal studies are warranted to validate these findings and establish standardized screening algorithms.

