NON-INVASIVE DIAGNOSTIC ALGORITHM FOR TUBULOINTERSTITIAL FIBROSIS IN CHRONIC GLOMERULONEPHRITIS BASED ON CLINICAL AND LABORATORY MARKERS

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https://doi.org/10.5281/zenodo.20589870

ARTICLE INFO

Received: 04th June 2026
Accepted: 06th June 2026
Online: 08th June 2026

KEYWORDS

chronic glomerulonephritis, tubulointerstitial fibrosis, KIM-1, TGF-β1, NGAL, non-invasive biomarkers, diagnostic algorithm, eGFR

ABSTRACT

Chronic glomerulonephritis (CGN) is one of the leading causes of end-stage renal disease worldwide, accounting for approximately 20–25% of all cases requiring renal replacement therapy (1). A critical determinant of renal prognosis in CGN is the degree of tubulointerstitial fibrosis (TIF), which reflects irreversible structural damage and correlates more strongly with long-term renal function decline than glomerular lesions alone (2). Traditionally, TIF assessment has relied on renal biopsy — an invasive procedure associated with significant risks and patient discomfort (3). Emerging non-invasive biomarkers, including TGF-β1, KIM-1 (kidney injury molecule-1), NGAL, and urinary α1-microglobulin, offer promising alternatives for monitoring fibrotic progression (4). However, no validated clinical-laboratory algorithm integrating these markers has been established for routine use (5). Development of such an algorithm would substantially improve early detection and management of TIF in CGN patients.

Introduction

Chronic glomerulonephritis (CGN) is one of the leading causes of end-stage renal disease worldwide, accounting for approximately 20–25% of all cases requiring renal replacement therapy [1]. A critical determinant of renal prognosis in CGN is the degree of tubulointerstitial fibrosis (TIF), which reflects irreversible structural damage and correlates more strongly with long-term renal function decline than glomerular lesions alone [2]. Traditionally, TIF assessment has relied on renal biopsy — an invasive procedure associated with significant risks and patient discomfort [3]. Emerging non-invasive biomarkers, including TGF-β1, KIM-1 (kidney injury molecule-1), NGAL, and urinary α1-microglobulin, offer promising alternatives for monitoring fibrotic progression [4]. However, no validated clinical-laboratory algorithm integrating these markers has been established for routine use [5]. Development of such an algorithm would substantially improve early detection and management of TIF in CGN patients.

Objective

To develop a non-invasive clinical-laboratory diagnostic algorithm for early detection of tubulointerstitial fibrosis in patients with chronic glomerulonephritis based on serum and urinary biomarkers.

Materials and methods

A prospective observational study will be conducted at [muassasa nomi]. The study population will include:

• **Main group:** 60–80 patients with confirmed CGN diagnosis

• **Control group:** 20–25 healthy age- and sex-matched individuals

Inclusion criteria: biopsy-confirmed CGN diagnosis, age 18–65 years, written informed consent.

Exclusion criteria: diabetes mellitus, secondary glomerulonephritis, active infections, malignancy, immunosuppressive therapy within 3 months.

The following diagnostic parameters will be assessed:

Parameter	Method
Serum creatinine & eGFR	CKD-EPI formula
TGF-β1 (serum & urine)	ELISA
KIM-1 (urinary)	Immunoturbidimetry
NGAL (urinary)	ELISA
Urinary α1-microglobulin	Nephelometry
Proteinuria (24-hour)	Quantitative method
Renal biopsy (Banff score)	Light microscopy + immunofluorescence

Statistical analysis will be performed using SPSS v.26.0, including ROC curve analysis, multivariate logistic regression, and Spearman correlation to determine optimal diagnostic cutoff values [6].

Expected results

Based on current literature and pathophysiological rationale [7, 8], the following outcomes are anticipated:

1. Significant elevation of urinary KIM-1 and TGF-β1 levels correlating with histological TIF grade (Banff score)

2. NGAL and α1-microglobulin serving as early tubular damage markers preceding eGFR decline[9]

3. Strong positive correlation between urinary biomarker levels and degree of interstitial fibrosis on biopsy

4. Development of a two-step non-invasive diagnostic algorithm with sensitivity ≥80% and specificity ≥75%

5. Identification of optimal biomarker cutoff values for TIF staging in clinical practice[10]

Conclusion

A validated non-invasive diagnostic algorithm integrating urinary KIM-1, TGF-β1, NGAL, and α1-microglobulin may enable early and reliable detection of tubulointerstitial fibrosis in chronic glomerulonephritis patients without the need for repeated renal biopsy. This approach has the potential to significantly improve monitoring of fibrotic progression, guide therapeutic decisions, and ultimately preserve renal function in this high-risk population.

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