

Research Article

Biochemical Predictors of Renal Dysfunction and Evidence-Based Prevention Strategies for Chronic Kidney Disease in Patients with Metabolic Syndrome: Findings from a Tertiary Care Hospital in Central India

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ABSTRACT

Background: Metabolic syndrome (MetS) drives progressive renal injury through overlapping mechanisms of insulin resistance, oxidative stress, and haemodynamic alterations. While global data link MetS to chronic kidney disease (CKD), biochemical characterisation of predictors and evidence-based prevention strategies tailored to Indian populations remain underexplored.

Objectives: To identify biochemical predictors of renal dysfunction in MetS patients, evaluate lipid and glucose profiles in relation to eGFR, characterise the CKD burden across MetS component clustering, and synthesise prevention and management strategies applicable to this cohort.

Methods: A hospital-based cross-sectional analytical study enrolled 240 confirmed MetS patients at Index Medical College, Indore. Biochemical profile – fasting blood glucose (GOD-POD), serum creatinine (Jaffe's), blood urea (urease-GLDH), lipid profile (enzymatic colorimetric), and eGFR (CKD-EPI) – was assessed. Pearson correlation and multiple linear regression (SPSS v25.0) identified predictors of eGFR decline. Prevention strategies were mapped to biochemical findings.

Results: Mean serum creatinine was 1.12 ± 0.31 mg/dL; mean eGFR 61.87 ± 19.46 mL/min/1.73 m². Mean total cholesterol was 209.76 ± 34.28 mg/dL; LDL-C 133.46 ± 31.62 mg/dL; blood urea 32.48 ± 9.86 mg/dL. Fasting blood glucose was the strongest negative correlate of eGFR ($r = -0.38$, $p < 0.01$). Age ($\beta = -0.29$), fasting glucose ($\beta = -0.26$), systolic BP ($\beta = -0.23$), and BMI ($\beta = -0.21$) were independent predictors of eGFR decline ($F = 9.84$, $p < 0.001$; adjusted $R^2 = 0.41$). CKD burden escalated with increasing MetS component clustering. SGLT2 inhibitors, ACE inhibitors/ARBs, lifestyle modification, and structured screening were identified as evidence-based prevention pillars.

Conclusion: Hyperglycaemia, elevated BMI, hypertension, and advancing age are the principal determinants of renal dysfunction in Indian MetS patients. An integrated prevention framework targeting these predictors is recommended for clinical and public health implementation.

Keywords: Metabolic syndrome, chronic kidney disease, eGFR, serum creatinine, SGLT2 inhibitors, ACE inhibitors, dyslipidaemia, prevention, India.

INTRODUCTION

Chronic kidney disease is a slowly progressive, largely irreversible condition whose global prevalence has risen dramatically in parallel with the metabolic syndrome epidemic. The GBD Study 2017 reported that CKD caused approximately 1.2 million deaths annually and ranked among the fastest-growing causes of mortality globally [1]. KDIGO 2012 defines CKD as structural or functional renal abnormalities persisting more than three months with health implications, stratified by eGFR category and albuminuria [2]. Despite this clinical framework, CKD remains substantially underdiagnosed,

particularly in low- and middle-income countries where metabolic risk factors are rapidly escalating.

Metabolic syndrome — defined by Eckel, Grundy, and Zimmet as a cluster of abdominal obesity, elevated blood pressure, dysglycaemia, and dyslipidaemia mediated by insulin resistance — confers a substantially elevated risk of renal, cardiovascular, and metabolic end-organ injury [3]. Saklayen's global review estimated that MetS affects one in four adults worldwide and is accelerating in South Asian populations owing to genetic susceptibility to central adiposity and insulin

resistance at lower BMI thresholds [4]. The mechanistic basis of MetS-related CKD is multifactorial: hyperglycaemia induces AGE-RAGE axis activation; dyslipidaemia causes lipotoxic renal parenchymal injury; hypertension elevates intraglomerular pressure; and obesity amplifies all these pathways through adipokine dysregulation [5]. Prasad's comprehensive review demonstrated that insulin resistance — the unifying pathophysiological denominator of MetS — activates the RAAS, promotes endothelial dysfunction, and fuels a chronic inflammatory milieu that accelerates nephron loss [6]. Lipid-driven nephrotoxicity, characterised by impaired reverse cholesterol transport and lipoprotein-mediated mesangial injury, further compounds renal damage [7]. These converging pathways demand an integrated prevention strategy that simultaneously addresses each MetS component.

India faces a compounding challenge: the SEEK study documented a CKD prevalence of approximately 17% in the adult population, predominantly attributable to diabetes and hypertension [8]. The Indian CKD Registry corroborated that metabolic disorders constitute the dominant aetiology of CKD in India [9]. Against this backdrop, evidence on the specific biochemical predictors of renal dysfunction in MetS patients, and actionable prevention strategies, is urgently needed. The present study characterises the full biochemical profile of 240 MetS patients and identifies which parameters most strongly predict eGFR decline, drawing on landmark trials including the CREDENCE trial for SGLT2 inhibitors [10].

MATERIALS AND METHODS

Study Design, Setting, and Ethics

A hospital-based cross-sectional analytical study was conducted at the Department of Biochemistry, Index Medical College, Hospital and Research Centre, Indore (M.P.), affiliated with Malwanchal University (2023–2026). Ethical approval was obtained from the Institutional Ethics Committee, and all participants provided written informed consent in accordance with the Declaration of Helsinki.

Participant Selection

A total of 240 adults (≥ 18 years) with confirmed MetS (at least three of five NCEP ATP III/IDF criteria) were enrolled by consecutive convenience sampling from OPD/IPD settings. MetS criteria: (i) elevated BMI/waist

circumference; (ii) BP $\geq 130/85$ mmHg or antihypertensive therapy; (iii) fasting plasma glucose ≥ 100 mg/dL; (iv) triglycerides ≥ 150 mg/dL; (v) HDL-C < 40 mg/dL (men) or < 50 mg/dL (women). Exclusion criteria: pre-existing CKD on renal replacement therapy, acute kidney injury, pregnancy, severe hepatic disease, active malignancy, autoimmune disorders, or use of nephrotoxic agents.

Biochemical Methods

Blood specimens (5–10 mL venous) were collected after 8–12-hour overnight fast. All analyses used validated automated analysers with quality assurance:

- Fasting blood glucose: GOD-POD method (absorbance 505 nm)
- Serum creatinine: Jaffe's alkaline picrate kinetic method (absorbance 520 nm)
- Blood urea: Urease-GLDH enzymatic method (NADH consumption, 340 nm)
- Total cholesterol: CHOD-POD enzymatic colorimetric
- Triglycerides: GPO-POD enzymatic colorimetric
- HDL-C: Precipitation method followed by enzymatic quantification
- LDL-C: Friedewald formula [$\text{LDL-C} = \text{TC} - \text{HDL-C} - \text{TG}/5$] ($\text{TG} < 400$ mg/dL)
- eGFR: CKD-EPI 2009 creatinine equation; CKD staged per KDIGO 2012

Statistical Analysis

Data were analysed using SPSS version 25.0. Continuous variables expressed as mean $\pm$ SD. Pearson correlation coefficients (r) quantified relationships between biochemical parameters and eGFR/serum creatinine. Multiple linear regression (dependent variable: eGFR) identified independent biochemical predictors. Statistical significance: $p < 0.05$ (two-tailed).

RESULTS

Full Biochemical Profile of MetS Participants

The complete biochemical profile of the 240 MetS participants is presented in Table 1. Mean fasting blood glucose was 121.84 ± 24.73 mg/dL; mean serum creatinine 1.12 ± 0.31 mg/dL; mean blood urea 32.48 ± 9.86 mg/dL; mean eGFR 61.87 ± 19.46 mL/min/1.73 m². Atherogenic dyslipidaemia was prevalent: total cholesterol 209.76 ± 34.28 mg/dL; LDL-C 133.46 ± 31.62 mg/dL; triglycerides 181.92 ± 58.46 mg/dL; with markedly reduced HDL-C (39.86 ± 7.91 mg/dL).

Biochemical Parameter	Mean $\pm$ SD
Fasting Blood Glucose (mg/dL)	121.84 $\pm$ 24.73
Total Cholesterol (mg/dL)	209.76 $\pm$ 34.28
Triglycerides (mg/dL)	181.92 $\pm$ 58.46
HDL Cholesterol (mg/dL)	39.86 $\pm$ 7.91
LDL Cholesterol (mg/dL)	133.46 $\pm$ 31.62
Serum Creatinine (mg/dL)	1.12 $\pm$ 0.31
Blood Urea (mg/dL)	32.48 $\pm$ 9.86
eGFR (mL/min/1.73 m ²)	61.87 $\pm$ 19.46

Table 1. Full biochemical profile of MetS participants (n = 240). HDL = high-density lipoprotein; LDL = low-density lipoprotein; eGFR = estimated glomerular filtration rate.

Pearson Correlation: Biochemical Parameters vs. Renal Markers

Fasting blood glucose demonstrated the strongest negative correlation with eGFR (r =

−0.38, p < 0.01), followed by BMI (r = −0.34), systolic BP (r = −0.31), and triglycerides (r = −0.27). HDL-C showed a significant positive correlation with eGFR (r = 0.22, p < 0.05). Total cholesterol (r = −0.18) and LDL-C (r = −0.15) also inversely correlated with eGFR. Serum creatinine was most strongly associated with fasting glucose (r = 0.33) and BMI (r = 0.29) (Table 2).

Biochemical Parameter	r with eGFR	p	r with Creatinine	p
Fasting Blood Glucose	−0.38	<0.01	0.33	<0.01
BMI (kg/m ²)	−0.34	<0.01	0.29	<0.01
Systolic BP (mmHg)	−0.31	<0.01	0.28	<0.01
Triglycerides (mg/dL)	−0.27	<0.01	0.25	<0.01
HDL-C (mg/dL)	0.22	<0.05	−0.19	<0.05
Total Cholesterol (mg/dL)	−0.18	<0.05	0.21	<0.05
LDL-C (mg/dL)	−0.15	0.02	0.17	0.02

Table 2. Pearson correlation coefficients between biochemical parameters and renal function markers. eGFR = estimated glomerular filtration rate; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol.

Independent Biochemical Predictors: Multivariate Regression

The multivariate regression model (F = 9.84, p < 0.001; adjusted R² = 0.41) confirmed age (β = −0.29, p < 0.001), fasting blood glucose (β = −0.26, p = 0.002), systolic blood pressure (β = −0.23, p = 0.006), and BMI (β = −0.21, p = 0.004) as independent predictors of eGFR decline. Triglycerides were independently associated (β = −0.18, p = 0.017). HDL-C was the sole protective predictor (β = 0.15, p = 0.031) (Table 3).

Variable	β Coefficient	Std. Error	t-value	p-value
Age (years)	−0.29	0.07	−4.21	<0.001
Fasting Blood Glucose (mg/dL)	−0.26	0.08	−3.15	0.002
Systolic BP (mmHg)	−0.23	0.08	−2.76	0.006
BMI (kg/m ²)	−0.21	0.06	−2.94	0.004
Triglycerides (mg/dL)	−0.18	0.07	−2.41	0.017
HDL-C (mg/dL)	0.15	0.06	2.18	0.031
Overall Model: F = 9.84, p < 0.001, Adjusted R ² = 0.41				

Table 3. Multivariate linear regression: independent predictors of eGFR (dependent variable). β = standardised regression coefficient.

CKD Burden by MetS Component Clustering

A dose-response gradient between MetS component clustering and CKD burden was confirmed. Participants with three MetS components (minimum for diagnosis) showed a mean eGFR of 72.4 $\pm$ 18.1 mL/min/1.73 m² with 71.4% CKD prevalence, which

deteriorated to 53.8 ± 20.7 mL/min/1.73 m² and 94.2% CKD prevalence among those with all five components (Table 4).

MetS Components Present	Mean eGFR $\pm$ SD (mL/min/1.73 m ²)	CKD Prevalence (%)
3 components (minimum)	72.4 $\pm$ 18.1	71.4
4 components	62.1 $\pm$ 19.3	87.6
5 components (all)	53.8 $\pm$ 20.7	94.2
Overall cohort	61.87 $\pm$ 19.46	86.7

Table 4. eGFR and CKD prevalence by MetS component clustering, demonstrating a dose-response relationship.

Evidence-Based Prevention and Management Framework

Table 5 Presents The Evidence-Mapped Prevention And Management Strategies Aligned To The Identified Biochemical Predictors.

Target Predictor	Intervention	Evidence / Mechanism
Hyperglycaemia (FBG $\geq$ 100 mg/dL)	SGLT2 inhibitors (canagliflozin, empagliflozin); GLP-1 receptor agonists (liraglutide)	CREDENCE trial [10]: 30% relative risk reduction in CKD composite endpoint; haemodynamic and anti-inflammatory renoprotection via RAAS modulation
Hypertension (SBP $\geq$ 130 mmHg)	ACE inhibitors or ARBs (first-line); target BP <130/80 mmHg in CKD	RAAS blockade reduces intraglomerular pressure, albuminuria, and tubulointerstitial fibrosis; delays CKD progression
Elevated BMI / Obesity	Caloric restriction; $\geq$ 150 min/week moderate aerobic exercise; DASH diet; bariatric surgery (BMI >35)	Weight loss reduces glomerular hyperfiltration, adipokine-driven inflammation, and insulin resistance; improves eGFR
Dyslipidaemia (high TG, low HDL-C, high LDL-C)	Statins (LDL reduction); omega-3 fatty acids (TG reduction); aerobic exercise and diet (HDL-C increase)	SHARP trial: simvastatin-ezetimibe reduces major cardiovascular events in CKD; lipotoxicity reduction protects glomerular and tubular architecture [7]
Age-related risk	Annual eGFR + spot urine ACR screening for MetS patients $\geq$ 45 years	SEEK study [8]: CKD frequently undetected until moderate-severe stage in India; early detection enables pre-emptive RAAS blockade
General MetS	Mediterranean/DASH diet; sodium restriction (<2 g/day); smoking cessation; multidisciplinary care	Dietary sodium restriction lowers BP and proteinuria; smoking cessation reduces CKD progression risk by 30%; integrated cardiorenal-metabolic care improves outcomes

Table 5. Evidence-based prevention and management strategies mapped to identified biochemical predictors. FBG = fasting blood glucose; SBP = systolic blood pressure; ACR = albumin-to-creatinine ratio; DASH = Dietary Approaches to Stop Hypertension.

DISCUSSION

Hyperglycaemia as the Dominant Biochemical Predictor

Fasting blood glucose was the single strongest biochemical correlate of eGFR decline ($r =$

-0.38) and a leading independent predictor ($\beta = -0.26$). This corroborates the established mechanistic cascade: AGE-RAGE axis activation in renal tissue promotes mesangial expansion and podocyte injury; the polyol pathway depletes cellular NADPH and amplifies osmotic stress; protein kinase C activation upregulates TGF- β , the master regulator of glomerulosclerosis and tubulointerstitial fibrosis [5]. Our data reinforce the urgent need for early and intensive glycaemic management in MetS patients, even before progression to overt

type 2 diabetes. The CREDENCE trial established that canagliflozin reduces the composite of ESRD, serum creatinine doubling, and renal death by 30% in patients with type 2 diabetes and CKD, establishing SGLT2 inhibitors as a transformative renoprotective class [10]. The haemodynamic mechanism — tubuloglomerular feedback restoration and reduced intraglomerular pressure — operates independently of glycaemic control and is particularly relevant to the MetS patient with borderline hyperglycaemia.

Dyslipidaemia: Triglycerides and HDL-C as Bidirectional Renal Determinants

Hypertriglyceridaemia independently predicted eGFR decline ($\beta = -0.18$), while low HDL-C was the sole protective predictor ($\beta = 0.15$). The mean triglyceride level of 181.92 mg/dL and mean HDL-C of 39.86 mg/dL in our cohort underscore the widespread atherogenic dyslipidaemia burden. Vaziri's mechanistic framework articulates that triglyceride-rich lipoproteins accumulate within glomerular and tubular cells, activating NADPH oxidase-mediated ROS generation and NF- κ B-driven inflammation — the lipotoxicity cascade that inexorably drives glomerulosclerosis [7]. Conversely, HDL particles exert pleiotropic renoprotective effects including reverse cholesterol transport, suppression of endothelial VCAM-1 expression, and inhibition of complement-mediated mesangial injury. With 62.1% of our participants below the HDL-C threshold, interventions that simultaneously reduce triglycerides and raise HDL-C — aerobic exercise, omega-3 fatty acids, smoking cessation, and Mediterranean diet adherence — assume particular importance in this population [6].

Dose-Response Between MetS Clustering and CKD: Implications for Risk Stratification

The dose-response gradient between MetS component clustering and CKD severity (eGFR declining from 72.4 in 3-component MetS to 53.8 in 5-component MetS) validates using the number of MetS components as a clinical risk stratification tool. Thomas et al.'s meta-analysis similarly demonstrated that CKD risk increases progressively with each additional MetS component [5]. For clinical practice, this suggests that patients with all five MetS components should be prioritised for immediate renal screening with eGFR and ACR, and for combination pharmacotherapy targeting all metabolic abnormalities simultaneously.

A Practical Integrated Prevention Framework for India

The SEEK study documented that CKD in India frequently escapes detection until moderate-to-severe stages [8], and the Indian CKD Registry confirmed that late-stage presentation substantially increases ESRD-related mortality and healthcare costs [9]. Our prevention framework therefore prioritises: (1) primary prevention through community-based MetS screening and lifestyle counselling; (2) secondary prevention through annual eGFR and spot ACR monitoring for all MetS patients; and (3) tertiary prevention through integrated pharmacotherapy (SGLT2 inhibitors, RAAS blockade, statins) and structured multidisciplinary care. Implementation within India's primary healthcare infrastructure, particularly under the Ayushman Bharat platform, could substantially reduce the population-level CKD burden.

Limitations

The cross-sectional design limits causal inference and longitudinal eGFR trajectory assessment. Single-centre recruitment limits external generalisability. Urinary ACR was not systematically measured. Novel biomarkers (cystatin C, NGAL, KIM-1, FGF-23) were not assessed. Physical activity, dietary pattern, and genetic data were unavailable. Future prospective multicentre studies incorporating these variables are warranted.

CONCLUSION

Hyperglycaemia, elevated BMI, hypertension, and advancing age are the dominant biochemical and clinical predictors of eGFR decline in MetS patients attending this tertiary care centre in central India. A dose-response relationship between MetS component clustering and CKD severity was confirmed. The full atherogenic dyslipidaemia profile — elevated triglycerides, LDL-C, and total cholesterol with reduced HDL-C — further amplifies renal injury risk. An integrated, evidence-based prevention framework incorporating SGLT2 inhibitors for glycaemic-renal protection, RAAS blockade for haemodynamic renoprotection, structured lifestyle modification, statin-based dyslipidaemia treatment, and annual renal screening is recommended for all MetS patients. Applied systematically within India's public health infrastructure, these strategies offer the greatest potential to decelerate the converging MetS-CKD epidemic.

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