GMR
The Original

ASSESSMENT OF URINARY ALBUMIN-TO-CREATININE RATIO WITH ENDOTHELIAL, INFLAMMATORY AND CARDIOMETABOLIC BIOMARKERS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AND CORONARY ARTERY DISEASE

Shinde Yogita Mahendra[1], Badade ZG[2]*, Rai Sandeep[3], Kadam Shilpa[4], Kshitij Badade[5]

[1]Shinde Yogita Mahendra, Assistant Professor, Department of Biochemisty, MGM Medical College, Kamothe, Navi Mumbai,
Mail ID: yogis8stars@rediffmail.com ORCID: 0009-0006-1172-8939
[2]Badade ZG* Professor, Department of Biochemistry, MGM Medical College, Kamothe, Navi Mumbai, Mail ID: badadezg@gmail.com ORCID: 0000-0001-6752-1896
[3]Sandeep Rai, Professor, Department of General Medicine, MGM medical College, Kamothe, Navi Mumbai, Mail ID: doctorsandeeprai@gmail.com ORCID: 0000-0001-8235-2525
[4]Kadam Shilpa, Professor, Department of Cardiology, MGM Medical College, Kamothe, Navi Mumbai,
Mail ID: drshilpapvk@rediffmail.com ORCID: 0000-0002-2740-1766
[5]Badade Kshitij Z, Assistant Professor, Department of Orthopaedics, MGM Medical College & Hospital, Kamothe, Navi Mumbai,
Mail ID: kshitij03badade@gmail.com ORCID:0000-0002-5030-9626
*Corresponding Author: Badade ZG, Mail ID: badadezg@gmail.com

ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) and coronary artery disease (CAD) are closely interconnected disorders associated with chronic hyperglycaemia, systemic inflammation, endothelial dysfunction and progressive renal injury. Although urinary albumin-to-creatinine ratio (UACR) is an established marker of diabetic kidney disease, its relationship with endothelial, inflammatory and cardiometabolic biomarkers in patients with concomitant T2DM and CAD remains inadequately characterized.

Objective: To evaluate UACR in relation to endothelial, inflammatory and cardiometabolic biomarkers in patients with T2DM, CAD and concomitant T2DM with CAD, and to determine their integrated role in assessing cardiorenal risk.

Materials and Methods: This hospital-based cross-sectional observational study included 300 participants (30–75 years), divided into four groups (n=75 each): healthy controls, T2DM, CAD and T2DM with CAD. Fasting plasma glucose, HbA1c, serum nitrite, high-sensitivity C-reactive protein (hs-CRP), lipid profile, urinary albumin, urinary creatinine and UACR were measured using standard laboratory methods. The Atherogenic Index of Plasma (AIP) and non-HDL cholesterol were calculated. Group comparisons were performed using one-way ANOVA, and Pearson's correlation analysis was used to evaluate associations between UACR and selected biomarkers.

Results: Patients with concomitant T2DM and CAD demonstrated the highest fasting plasma glucose (269.4±25.8 mg/dL), hs-CRP (11.01±1.30 mg/L), UACR (31.21±6.4 mg/g), total cholesterol (238.2±15.4 mg/dL), LDL-C (160.28±13.5 mg/dL), non-HDL-C (200.60±31.6 mg/dL) and AIP (0.72±0.02), together with the lowest serum nitrite concentration (12.46±2.13 µmol/L) ($p<0.01$ for all). UACR showed significant positive correlations with HbA1c ($r=0.61$), AIP ($r=0.64$) and hs-CRP ($r=0.76$), and a significant negative correlation with serum nitrite ($r=-0.71$) ($p<0.01$ for all), indicating a close association between renal injury, metabolic dysregulation, inflammation and endothelial dysfunction.

Conclusion: The coexistence of T2DM and CAD is associated with marked deterioration in metabolic, inflammatory, endothelial and renal biomarkers, reflecting progressive cardiorenal injury. The novelty of the present study lies in the integrated evaluation of UACR together with serum nitrite, hs-CRP, AIP and conventional cardiometabolic biomarkers within a single cohort, demonstrating that these complementary biomarkers collectively provide a more comprehensive assessment of cardiorenal risk than any individual marker alone. This multimarker approach may improve early risk stratification and facilitate timely preventive and therapeutic interventions in patients with T2DM and CAD.

KEYWORDS: Type 2 diabetes mellitus; Coronary artery disease; Urinary albumin-to-creatinine ratio; Serum nitrite; High-sensitivity C-reactive protein; Atherogenic Index of Plasma; Endothelial dysfunction; Cardiorenal risk.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance, progressive pancreatic β-cell dysfunction and persistent hyperglycaemia, resulting in disturbances of carbohydrate, lipid and protein metabolism. It is one of the fastest-growing non-communicable diseases worldwide and is a major contributor to premature morbidity and mortality because of its microvascular and macrovascular complications. According to the 11th International Diabetes Federation (IDF) Diabetes Atlas, approximately 589 million adults aged 20–79 years were living with diabetes globally in 2024, and this number is projected to increase to 853 million by 2050. India has the second largest diabetic population worldwide, with approximately 89.8 million adults affected in 2024, which is expected to

increase to 156.7 million by 2050 [1]. The nationwide ICMR–INDIAB study further demonstrated that diabetes, prediabetes, obesity, hypertension and dyslipidaemia have reached epidemic proportions across India, emphasizing the enormous cardiometabolic burden and the urgent need for early identification of vascular complications [2]. Persistent hyperglycaemia initiates multiple metabolic disturbances including oxidative stress, advanced glycation end-product (AGE) formation, chronic inflammation and endothelial dysfunction, ultimately predisposing individuals to cardiovascular and renal complications [3–5].

Among the chronic complications of T2DM, coronary artery disease (CAD) remains the leading cause of morbidity and mortality, accounting for nearly two-thirds of deaths among patients with diabetes. Individuals with T2DM have approximately a two- to four-fold higher risk of developing CAD than the general population because prolonged hyperglycaemia accelerates atherosclerosis through endothelial dysfunction, oxidative stress, vascular inflammation and atherogenic dyslipidaemia [3–6]. Hyperglycaemia promotes activation of the AGE–RAGE signalling pathway, increases reactive oxygen species production, reduces nitric oxide bioavailability and enhances expression of pro-inflammatory cytokines, thereby accelerating vascular smooth muscle proliferation, plaque instability and thrombosis [5,6]. Consequently, patients with diabetes frequently develop diffuse, multivessel coronary artery disease with poorer clinical outcomes than non-diabetic individuals. These observations underscore that T2DM and CAD are not isolated disorders but interconnected manifestations of systemic vascular dysfunction, providing the biological basis for investigating biomarkers that simultaneously reflect metabolic disturbance, endothelial injury and inflammation [5,6].

Beyond accelerating coronary atherosclerosis, the metabolic and vascular abnormalities associated with T2DM also profoundly affect the renal microcirculation, giving rise to the concept of the cardiovascular–kidney–metabolic (CKM) continuum (cardiorenal continuum), in which cardiovascular and renal dysfunction share common pathophysiological mechanisms. Persistent hyperglycaemia, oxidative stress, endothelial dysfunction, chronic low-grade inflammation and activation of the renin–angiotensin–aldosterone system (RAAS) collectively impair glomerular endothelial integrity, disrupt the endothelial glycocalyx, induce podocyte injury and increase glomerular permeability, resulting in albumin leakage into the urine. Consequently, patients with concomitant T2DM and CAD are particularly susceptible to progressive renal injury because systemic endothelial dysfunction and diffuse atherosclerosis simultaneously compromise both coronary and renal microvasculature. Recent clinical studies have demonstrated that albuminuria is not merely a marker of diabetic kidney disease but also an indicator of generalized vascular injury and an independent predictor of adverse cardiovascular and renal outcomes in patients with diabetes. Furthermore, increasing urinary albumin excretion has been associated with accelerated decline in renal function, higher incidence of chronic kidney disease and increased cardiovascular mortality, even in the absence of overt renal impairment. These observations highlight the close interaction between cardiovascular disease and renal injury and emphasize the importance of identifying biomarkers capable of detecting renal involvement in this high-risk population [7–13].

Urinary albumin-to-creatinine ratio (UACR) has emerged as a simple, reliable and non-invasive biomarker for assessing glomerular injury by correcting urinary albumin excretion for variations in urine concentration using urinary creatinine. Persistent hyperglycaemia, systemic inflammation and endothelial dysfunction promote disruption of the glomerular filtration barrier through glycocalyx degradation, endothelial cell injury and podocyte dysfunction, leading to increased urinary albumin excretion. Consequently, elevated UACR reflects increased glomerular permeability and renal microvascular injury before substantial nephron loss occurs. Recent clinical studies have further demonstrated that increased albuminuria is not confined to diabetic kidney disease but also represents generalized vascular dysfunction associated with adverse cardiovascular outcomes. In a prospective cohort study, Nazarzadeh et al. demonstrated that elevated urinary albumin-to-creatinine ratio was independently associated with increased risks of chronic kidney disease progression, cardiovascular events and all-cause mortality among individuals with diabetes [10]. Similarly, Koye et al. reported that albuminuria remained a strong determinant of kidney disease progression and cardiovascular complications despite improvements in glycaemic control, emphasizing its importance as a marker of ongoing microvascular injury [11]. Furthermore, recent evidence suggests that even modest elevations in albuminuria are associated with diffuse endothelial dysfunction and systemic vascular injury rather than isolated renal pathology, highlighting the clinical relevance of UACR in patients with concomitant T2DM and CAD [12-14].

Although urinary albumin-to-creatinine ratio reflects renal involvement, the development and progression of renal injury in patients with concomitant Type 2 Diabetes Mellitus and Coronary Artery Disease is driven by multiple interconnected pathophysiological mechanisms rather than isolated glomerular damage. Endothelial dysfunction, persistent inflammation, hyperglycaemia and atherogenic dyslipidaemia interact synergistically to accelerate vascular injury within both the coronary and renal microcirculation. Serum nitrite, a stable oxidative metabolite of nitric oxide, serves as an indirect marker of nitric oxide bioavailability, and reduced serum nitrite concentrations indicate impaired endothelial nitric oxide synthesis, a hallmark of endothelial dysfunction in diabetes and atherosclerosis. Simultaneously, elevated high-sensitivity C-reactive protein (hs-CRP) reflects chronic low-grade systemic inflammation, which contributes to endothelial activation, vascular remodelling and progression of atherosclerotic lesions. Persistent fasting hyperglycaemia further amplifies oxidative stress through activation of the AGE–RAGE pathway, while dyslipidaemia characterized by elevated triglycerides, increased low-density lipoprotein cholesterol and reduced high-density lipoprotein cholesterol accelerates lipid deposition and plaque instability. Recent clinical investigations have consistently demonstrated that endothelial dysfunction, inflammation and adverse cardiometabolic profiles are closely associated with both albuminuria and cardiovascular risk in patients with diabetes, suggesting that these biomarkers represent complementary rather than independent pathways of vascular injury [5, 15-17]. Therefore, simultaneous evaluation of UACR together with serum nitrite, hs-CRP, fasting plasma glucose and lipid profile may provide a more comprehensive understanding of renal

involvement and systemic vascular dysfunction in patients with T2DM and CAD than assessment of a single biomarker alone.

Despite substantial advances in understanding the individual roles of albuminuria, endothelial dysfunction, inflammation and cardiometabolic abnormalities in diabetes and coronary artery disease, these biomarkers have predominantly been investigated independently. Consequently, their integrated relationship in patients with concomitant Type 2 Diabetes Mellitus and Coronary Artery Disease remains insufficiently characterized, particularly in the Indian population where the burden of diabetes and cardiovascular disease continues to increase. A comprehensive biomarker approach may improve understanding of the complex interactions linking renal involvement, endothelial dysfunction, inflammation and metabolic abnormalities in this high-risk group. Therefore, the present study was undertaken to perform an integrated assessment of urinary albumin-to-creatinine ratio with endothelial, inflammatory and cardiometabolic biomarkers in patients with Type 2 Diabetes Mellitus and Coronary Artery Disease, in order to characterize their combined biomarker profile and explore their potential role in understanding renal involvement in diabetic coronary artery disease.

MATERIALS AND METHODS

Study Design and Setting

The present cross-sectional observational study was conducted in the Department of Biochemistry in collaboration with the Departments of General Medicine and Cardiology at MGM Medical College and Hospital, Kamothe, Navi Mumbai, Maharashtra, India. The study was carried out from 2024 to 2025.

The study was designed to assess urinary albumin-to-creatinine ratio as an early marker of renal and systemic vascular injury and to evaluate its association with endothelial, inflammatory, glycaemic and lipid-related cardiometabolic biomarkers in patients with type 2 diabetes mellitus and coronary artery disease.

Study Population

The sample size was estimated using one-way ANOVA for four independent groups with a significance level of 5% ($\alpha = 0.05$), statistical power of 80% and an assumed effect size (Cohen's *f*) of 0.20. The minimum required sample size was approximately 70 participants per group. After accounting for possible incomplete data and sample loss, the final sample size was fixed at 75 participants per group, giving a total of **300 participants** with aged 30–75 years.

- Group I – Healthy controls: Apparently healthy individuals without type 2 diabetes mellitus, coronary artery disease, hypertension or known renal disease.
- Group II – T2DM: Patients with established type 2 diabetes mellitus without clinical or documented coronary artery disease.
- Group III – CAD: Patients with angiographically confirmed coronary artery disease without type 2 diabetes mellitus.
- Group IV – T2DM with CAD: Patients with type 2 diabetes mellitus and documented coronary artery disease.

Diagnostic Criteria: Type 2 diabetes mellitus was diagnosed on the basis of documented medical history, use of glucose-lowering medication or fulfilment of accepted biochemical diagnostic criteria, including one or more of the following:

- Fasting plasma glucose ≥126 mg/dL, Two-hour plasma glucose ≥200 mg/dL during an oral glucose tolerance test, HbA1c ≥6.5%, or Random plasma glucose ≥200 mg/dL in a patient with classical symptoms of hyperglycaemia.

Coronary artery disease was diagnosed through Angiographically documented coronary artery stenosis by cardiologist.

Inclusion Criteria: Group I: Healthy Controls: Adults aged 30–75 years, Normal fasting plasma glucose and HbA1c, No history of diabetes mellitus, coronary artery disease, chronic kidney disease or hypertension, No acute or chronic inflammatory disorder. Willingness to provide written informed consent.

Group II: Type 2 Diabetes Mellitus: Adults aged 30–75 years, established type 2 diabetes mellitus, Absence of documented coronary artery disease, Stable clinical condition at the time of recruitment, Willingness to participate in the study.

Group III: Coronary Artery Disease: Adults aged 30–75 years, Documented coronary artery disease, No previous diagnosis of diabetes mellitus, Fasting plasma glucose and HbA1c below the diagnostic threshold for diabetes, Stable clinical condition at the time of enrolment.

Group IV: Type 2 Diabetes Mellitus with Coronary Artery Disease: Adults aged 30–75 years, established type 2 diabetes mellitus, documented coronary artery disease, Stable clinical condition, Willingness to provide written informed consent.

Exclusion Criteria: Type 1 diabetes mellitus, Acute myocardial infarction or acute coronary syndrome within the preceding three months, Known chronic kidney disease with an estimated glomerular filtration rate below 30 mL/min/1.73 m², Nephrotic syndrome, glomerulonephritis, polycystic kidney disease or other established primary renal disorders, Urinary tract infection, haematuria or urinary calculi, Acute febrile illness or active infection. Autoimmune disease, chronic inflammatory disorder or malignancy, Severe hepatic dysfunction, Congestive cardiac failure, Pregnancy or lactation, Recent major surgery or trauma, Current menstruation at the time of urine collection, Vigorous physical exercise within 24 hours before sample collection, Long-term corticosteroid or immunosuppressive therapy, Incomplete clinical data or inadequate blood or urine specimen, haematuria, menstruation, fever and recent vigorous exercise were excluded because these conditions can cause transient elevation of urinary albumin excretion and may lead to misclassification of albuminuria.

Sample Collection: Participants were instructed to fast overnight for 8–12 hours. On the following morning, approximately 8–10 mL of venous blood was collected under aseptic precautions. The blood was distributed as: 2 mL in a fluoride-oxalate tube for estimation of fasting plasma glucose, 2 mL in an EDTA tube for estimation of HbA1c, 4–6 mL in a plain or serum-separator tube for estimation of serum creatinine, lipid profile, high-sensitivity C-reactive protein and serum nitrite. Samples collected in plain tubes were allowed to clot and were centrifuged at approximately 3,000 revolutions per minute for 10 minutes. Serum was separated immediately and analysed on the same day wherever possible. Samples

intended for batch analysis were aliquoted into labelled tubes and stored at an appropriate temperature according to the stability requirements of the assay. Repeated freeze–thaw cycles were avoided.
Urine Sample Collection: A clean-catch, first-morning, midstream urine sample was collected in a sterile, dry, leak-proof container (spot urine sample). A first-morning specimen was preferred because it reduces the effect of hydration, physical activity and diurnal variation on urinary albumin excretion.
Participants were instructed to: Avoid vigorous physical exercise for at least 24 hours before collection, Collect the urine sample before breakfast, avoid collection during menstruation, Report fever, symptoms of urinary tract infection or visible blood in urine, and follow standard clean-catch collection instructions.
Urine samples were visually inspected and subjected to routine urine examination. Samples showing significant haematuria, pyuria or evidence of urinary tract infection were excluded. Urine samples were mixed gently, centrifuged if visibly turbid and analysed promptly. When immediate analysis was not possible, aliquots were stored under validated refrigerated or frozen conditions.

Biochemical Parameters

Renal and Urinary Biomarkers: Urinary albumin, Urinary creatinine, Urinary albumin-to-creatinine ratio
Endothelial Biomarker: Serum nitrite as an indirect marker of nitric oxide bioavailability
Inflammatory Biomarker: High-sensitivity C-reactive protein
Glycaemic and Cardiometabolic Biomarkers: Fasting plasma glucose, Glycated haemoglobin, Total cholesterol, Triglycerides, High-density lipoprotein cholesterol, Low-density lipoprotein cholesterol, Very-low-density lipoprotein cholesterol, Non-HDL cholesterol, The Atherogenic Index of Plasma (AIP) is a widely used marker of cardiovascular risk and is calculated from triglycerides (TG) and HDL cholesterol (HDL-C).

Formula: AIP-$\log_{10}$ (Tg/HDL-C)
Interpretation of AIP

AIP Value	Cardiovascular Risk
< 0.11	Low risk
0.11–0.21	Intermediate risk
> 0.21	High risk

Analytical Methods

Parameter	Specimen	Analytical method
Fasting plasma glucose	Fluoride plasma	Glucose oxidase–peroxidase method or hexokinase method
HbA1c	EDTA whole blood	High-performance liquid chromatography or NGSP-certified immunoturbidimetric method
Total cholesterol	Serum	Cholesterol oxidase–peroxidase method
Triglycerides	Serum	Glycerol phosphate oxidase–peroxidase method
HDL cholesterol	Serum	Direct homogeneous enzymatic method
LDL cholesterol	Serum	Direct homogeneous method or Friedewald calculation, where applicable
Urinary albumin	Urine	Immunoturbidimetric method
Urinary creatinine	Urine	Kinetic Jaffé or enzymatic method
hs-CRP	Serum	High-sensitivity immunoturbidimetric method
Serum nitrite	Serum	Griess reaction

All routine biochemical parameters were analysed using a fully automated VITROS 5600, clinical chemistry analyser, according to the reagent manufacturer's instructions.
Statistical Analysis on SPSS 25. A two-tailed p-value of <0.05 was considered statistically significant. Continuous variables were expressed as mean ± standard deviation when normally distributed and as median with interquartile range when non-normally distributed. Categorical variables were presented as frequencies and percentages.
Comparisons among the four groups were performed using: One-way analysis of variance for normally distributed continuous variables, ANOVA when the assumption of homogeneity of variance was violated, Chi-square test for categorical variables. The study protocol was reviewed and approved by the Institutional Ethics Committee of MGM Medical College, Kamothe, Navi Mumbai.
Written informed consent was obtained from every participant before enrolment. Participant confidentiality was maintained by assigning a unique study identification number. Participation was voluntary, and participants were permitted to withdraw from the study at any stage without affecting their medical care.

RESULTS

Table No. 1. Comparison of Fasting Plasma Glucose, hs-CRP and Serum Nitrite Concentration (Indirect Marker of Nitric Oxide Bioavailability), and UACR Between Healthy Controls, T2DM, CAD and CAD with T2DM Patients

Parameter	Healthy Controls	T2DM (n =75)	CAD (n =75)	CAD with T2DM	P-value

	(n =75)			(n =75)	
Age	53.75 ± 6.35	54.75 ± 6.12a	54.15 ± 4.23b,d	55.75 ± 3.53c,e,f	0.100 NS
Fasting Plasma Glucose (mg/dL)	82.9±8.21	188.23±25.6a*	90.12±10.3b,d-*	269.4±25.8c*,e*,f**	<0.01
hs-CRP (mg/L)	0.85±0.42	4.6±1.52a*	7.09±2.61b*,d*	11.01±1.3c*,e*, f*	<0.01
Serum Nitrite (NO_2^-) (µmol/L)	34.46±6.32	28.12±7.49a*	17.12±4.36b*,d-*	12.46±2.13c*,e-*,f-**	<0.01
UACR, mg/g	8.6 ± 2.3	20.31 ± 3.2a*	22.6 ± 2.6b*,d	31.21 ± 6.4c*,e-*,f*	< 0.01

Table No. 2: Comparison of Lipid Profile Among Healthy Controls, T2DM, CAD and CAD with T2DM

Parameters	Control	T2DM	CAD	T2DM+CAD	F value	P value
T. Cholesterol (mg/dl)	147.7±15.6	212.1±17.1a*	223.6±10.1b*, d*	238.2±15.4c***, e* f*	546.47	<0.01S
TG (mg/dl)	98.4±22.2	164.5±18.3 a*	188.2±20.9b**, d	201.6±11.7 c**, e*, f	449.56	<0.01S
HDL-C (mg/dl)	56.8±4.85	48.01±5.6a*	38.5±2.5b*, d*	37.6±1.6 c**, e*, f	384.82	<0.01S
LDL-C (mg/dl)	71.22±10.21	131.19±16.7a*	147.46±15.2b*, d*	160.28±13.5c*, e**, f*	123.542	<0.01S
VLDL-C (mg/dl)	19.68±3.5	32.90±4.6a*	37.64±6.5b*, d	40.32±3.8c*, e*, f	449.56	<0.01S
Non-HDL-C (mg/dl)	90.90±36.2	164.09±28.4a*	185.10±32.5b*, d*	200.60±31.6c*, e*, f	753.20	<0.01S
AIP	0.10±0.01	0.2±0.1a*	0.62±0.08b**,d*	0.72±0.02c**,e*,f	553.26	<0.01S

Values are expressed as Mean ±SD, p*≤0.05 significant, p**≤0.01 highly significant with 95 % CI and a, b, c, d, e, & f without asteric shows non-significant difference.

Table no. 1 and 2 shows a) Comparison of lipid profile in control to T2DM, b) Comparison of control to CAD, c) Comparison of control to T2DM with CAD, d) Comparison of T2DM to CAD, e) Comparison of T2DM to T2DM with CAD and f) Comparison of CAD to T2DM with CAD.

Table No. 3: Correlation of HbA1c, Atherogenic Index, hs-CRP and Serum Nitrite with UACR

Parameter	Pearson correlation coefficient (r)	P value	Interpretation
HbA1c (%)	0.61	<0.01	Strong positive correlation
Atherogenic Index of Plasma (AIP)	0.64	<0.01	Moderate to strong positive correlation
hs-CRP (mg/L)	0.76	<0.01	Strong positive correlation
Serum Nitrite (NO_2^-, µmol/L)	−0.71	<0.01	Strong negative correlation

DISCUSSION

In the present study, we observed a gradual worsening in metabolic, inflammatory, endothelial and renal biomarkers (table no. 1) from healthy controls to patients with T2DM, CAD and T2DM with CAD. Patients with concomitant T2DM and CAD had highest fasting plasma glucose, hs-CRP and UACR and lowest serum nitrite levels, showing that chronic hyperglycaemia, inflammation, endothelial dysfunction and renal microvascular injury coexist and interact in the development of diabetic cardiovascular disease. These findings corroborate the concept of the cardiorenal continuum, in which metabolic disturbances impact concomitantly coronary, renal and systemic microvasculature, and not as isolated pathological processes.

The mean age of the healthy control, T2DM, CAD, and T2DM with CAD groups was 53.75±6.35, 54.75±6.12, 54.15±4.23, 55.75±3.53 years, respectively, with no statistically significant difference between the groups (p=0.100). This age matching reduced the influence of age as a potential confounding variable as advancing age is independently associated with endothelial dysfunction, arterial stiffness, oxidative stress and declining renal function. Therefore, the differential pattern of biochemical biomarkers is more likely due to the disease status rather than physiological changes related to aging, which contributes to the internal validity of the study. Fasting plasma glucose was significantly different

between the four groups ($p<0.001$). Healthy controls (82.9±8.21 mg/dL) and patients with isolated CAD (90.12±10.3 mg/dL) had glucose concentrations in the non-diabetic range, whereas patients with T2DM (188.23±25.6 mg/dL) and especially those with T2DM and CAD (269.4±25.8 mg/dL) had significantly higher fasting glucose concentrations, indicating poor glycaemic control and a greater metabolic burden in the combined disease group. Persistent hyperglycaemia is the initiating event in the development of diabetic vascular complications. Increased intracellular glucose stimulates mitochondrial superoxide production and activation of multiple biochemical pathways including the polyol pathway, protein kinase C pathway and hexosamine pathway, and promotes formation of advanced glycation end products (AGEs). AGEs bind to their receptor (RAGE) and activate nuclear factor-κB (NF-κB), which leads to up-regulation of pro-inflammatory cytokines, adhesion molecules and oxidative enzymes. These molecular events together lead to endothelial activation, vascular smooth muscle cell proliferation, oxidative stress and accelerated atherosclerosis and eventually to both microvascular and macrovascular complications of diabetes [6,18].

One of the primary consequences of oxidative stress generated by hyperglycemia is the decreased availability of nitric oxide. Excess superoxide interacts rapidly with nitric oxide to create peroxynitrite, therefore lowering physiologically active nitric oxide and oxidising tetrahydrobiopterin (BH4), an important co-factor of endothelial nitric oxide synthase (eNOS). Oxidation of BH4 results in uncoupling of eNOS, which causes the enzyme to produce more superoxide than nitric oxide, propagating oxidative stress and endothelial dysfunction [19,20]. Hyperglycaemia contributes to the simultaneous metabolic and vascular abnormalities and hence offers the molecular foundation for the gradual inflammatory activation, endothelial dysfunction, dyslipidaemia and renal damage as seen in the later analyses of the present study.

In the present investigation, hs-CRP levels were found to increase from healthy controls (0.85±0.42 mg/L) to patients with T2DM (4.6±1.52 mg/L), CAD (7.09±2.61 mg/L) and T2DM with CAD (11.01±1.30 mg/L), with significant differences across the groups ($p<0.001$). The pattern is consistent with a steady enhancement in systemic inflammatory activity with increasing cardiometabolic disease burden. The low hs-CRP levels among healthy controls indicate no major metabolic or vascular inflammation. In contrast, the high levels among T2DM and CAD indicate active activation of the inflammatory cascade.

Chronic low-grade inflammation is now recognized as a basic characteristic of both diabetes and atherosclerosis. Insulin resistance in T2DM patients causes adipose tissue dysfunction, resulting in increased secretion of inflammatory cytokines, mainly interleukin-6 and tumour necrosis factor-α . Interleukin-6 induces hepatic synthesis of C-reactive protein, making hs-CRP a sensitive marker of systemic inflammation [21]. By contrast, CAD is characterized by chronic vascular inflammation in atherosclerotic lesions with activated endothelial cells, macrophages and vascular smooth muscle cells that release cytokines and proteolytic enzymes that drive plaque growth and instability [22].

The heightened levels of hs-CRP in patients with simultaneous T2DM and CAD shows that metabolic inflammation and vascular inflammation may synergize to produce a higher inflammatory burden than each condition alone. Habib et al. published similar findings, showing significantly greater hs-CRP concentrations in diabetic patients with CAD compared to non-diabetic CAD patients, indicating the role of systemic inflammation in accelerating cardiovascular disease in individuals with diabetes [23]. Moreover, Festa et al. demonstrated that inflammatory indicators were positively linked with albuminuria and cardiovascular risk factors, supporting the role of inflammation as a major biological link between renal and cardiovascular damage [24]. Thus, the significantly higher levels of hs-CRP in the present study further emphasize the role of chronic inflammation as a major contributor to diabetic cardiovascular disease.

The serum nitrite concentrations decreased progressively in the study groups with a value of 34.46±6.32 µmol/L in healthy control subjects, 28.12±7.49 µmol/L in T2DM, 17.12±4.36 µmol/L in CAD and 12.46±2.13 µmol/L in patients with T2DM and CAD ($p<0.001$). Serum nitrite is a persistent oxidative product of nitric oxide, and these findings indicate progressive impairment of nitric oxide bioavailability and deteriorating endothelial dysfunction.

Nitric oxide is an important regulator of vascular homeostasis, mediating vasodilatation, inhibition of platelet aggregation, leukocyte adhesion, vascular smooth muscle proliferation and oxidative modification of lipoproteins [26]. Therefore, decreased availability of nitric oxide is an early marker of endothelial dysfunction and directly involved in the development of atherosclerosis. Serum nitrite levels were decreased in patients with T2DM which is consistent with earlier studies that demonstrated reduced endothelial nitric oxide generation in diabetes. Ghosh et al. showed lower serum nitric oxide concentrations in patients with T2DM than in healthy individuals, while Tessari et al. observed a significant decrease in nitric oxide synthesis in patients with type 2 diabetes, especially in those with diabetic nephropathy [27,28]. The greater decline found in patients with CAD reflects the greater degree of endothelial damage associated with established coronary atherosclerosis. Oxidative stress has been shown to induce endothelial nitric oxide synthase uncoupling with reduced nitric oxide synthesis and increasing endothelial dysfunction (Janaszak-Jasiecka et al., [29]). Likewise, Habib et al., reported changed endothelial nitric oxide synthase activity in individuals with diabetes exacerbated by coronary artery disease, further validating the disturbance of nitric oxide signalling in diabetic cardiovascular disease [30]. The lowest serum nitrite content in individuals with simultaneous T2DM and CAD is a reflection of significant endothelial dysfunction due to the combined impact of persistent metabolic disorders and developed coronary atherosclerosis. These findings, together with the gradual rise in hs-CRP, suggest that inflammation and endothelial dysfunction occur in parallel during illness progression and are mutually reinforcing mechanisms contributing to vascular injury, not independent clinical processes.

In the present investigation, a substantial progressive increase in UACR was seen in the study groups from 8.6±2.3 mg/g in healthy controls to 20.31±3.2 mg/g in patients with T2DM, 22.6±2.6 mg/g in patients with CAD and 31.21±6.4 mg/g in patients with combined T2DM and CAD ($p<0.001$). These data suggest that rising cardiometabolic disease burden is associated with progressive renal microvascular injury. They further support the notion that albuminuria is a marker of widespread rather than isolated renal vascular damage. UACR in healthy controls was within normal limits (<30 mg/g)

while patients with T2DM and CAD had considerably higher UACR levels, albeit below the usual threshold for moderately elevated albuminuria. By comparison, the mean UACR in individuals with simultaneous T2DM and CAD was greater than 30 mg/g, i.e., clinical albuminuria. The finding shows that having diabetes and coronary artery disease together leads to faster progression of kidney impairment than having either illness by itself. Albuminuria is a classic early manifestation of diabetic kidney disease and signals a perturbation of the glomerular filtration barrier before a considerable reduction in glomerular filtration rate is seen. Mohandes et al. reported that diabetic kidney disease originates from numerous molecular perturbations, including podocyte injury, glomerular basement membrane malfunction and progressive renal fibrosis that ultimately led to increased urine albumin excretion [31]. Increased UACR is thus an early marker of renal injury and can identify patients at increased risk of developing kidney disease. The slightly increased UACR in patients with isolated CAD as compared to those with T2DM suggests that albuminuria is also a reflection of systemic vascular injury associated with atherosclerosis. Urinary albumin excretion was shown to be independently associated with angiographically documented coronary artery disease by Tuttle et al. [32] and albuminuria was shown to independently predict cardiovascular events, heart failure and all-cause mortality in subjects with and without diabetes by Gerstein et al. [13]. These findings suggest that albuminuria is a measure of widespread vascular dysfunction rather than merely a symptom of diabetic nephropathy.

Mild increases in UACR are also confirmed in recent investigations as having prognostic relevance. Lin et al. [33] revealed that modest elevated UACR was independently linked with increased cardiovascular mortality in patients with coronary artery disease. Similarly, Gao et al. showed that higher UACR predicted cardiovascular and all-cause mortality in patients with diabetes and preexisting atherosclerotic cardiovascular disease [34]. Zeng et al. also showed UACR increment as an independent predictor of major adverse cardiovascular events and mortality in individuals with type 2 diabetes mellitus even in the range of normal albuminuria [35]. These findings are quite similar with the present study where gradual increases in UACR paralleled worsening metabolic and cardiovascular disease severity. These data together imply that UACR is not just a sign of renal involvement but also an integrated marker of cardiorenal risk. The progressive increase throughout the study groups reinforces the importance of UACR as a simple, affordable and clinically relevant biomarker for early identification of T2DM and CAD patients at greater risk of both renal disease progression and unfavourable cardiovascular events. The present investigation showed a sequential deterioration of lipid markers (table no. 2) from healthy controls to the patients of T2DM, CAD and T2DM with CAD. Total cholesterol, triglycerides, LDL-C, VLDL-C, non-HDL-C and AIP increased considerably in all the study groups while HDL-C decreased progressively ($p<0.01$). The most prominent dyslipidaemia was found in patients with simultaneous T2DM and CAD, demonstrating that the combination of diabetes and existing coronary artery disease significantly worsens anomalies in lipid metabolism.

Diabetic dyslipidaemia is characterized by hypertriglyceridaemia, elevated triglyceride-rich lipoproteins, increased concentrations of small dense LDL particles and reduced HDL-C. These abnormalities are mainly due to insulin resistance which increases hepatic influx of free fatty acids and synthesis of very-low-density lipoproteins, decreases lipoprotein lipase activity, and impairs HDL metabolism. This results in the evolution of a highly atherogenic lipid profile in T2DM patients which accelerates CAD leading to adverse cardiovascular outcomes. Current findings are in line with the American Diabetes Association Standards of Care and the 2023 ESC Guidelines, which both recognize diabetic dyslipidaemia as a major contributor to cardiovascular morbidity and mortality [36,4]. The progressive increase in non-HDL-C observed in the present study further supports the presence of an increased atherogenic lipoprotein burden. Non-HDL-C contains all the cholesterol in lipoproteins that are considered atherogenic, including VLDL, intermediate-density lipoproteins and remnant particles, in addition to LDL-C. Thus, non-HDL-C has become an important therapeutic target and predictor of cardiovascular risk, especially in patients with diabetes and hypertriglyceridaemia [36].

The stepwise increase in UACR correlated with the worsening lipid abnormalities observed in the present study, suggesting that dyslipidaemia and renal injury commonly occur in patients with advanced cardiometabolic disease. Similar results have been reported by Zeng et al. and Ruilope et al. who demonstrated that albuminuria is strongly associated with adverse lipid abnormalities and independently predicted cardiovascular events, progression of diabetic kidney disease and all-cause mortality [35,37]. Thus, simultaneous evaluation of lipid profile and UACR provides a more complete assessment of cardiorenal risk than either biomarker alone.

The Atherogenic Index of Plasma (AIP) also increased progressively from healthy controls (0.10 ± 0.01) to patients with T2DM (0.20 ± 0.10), CAD (0.62 ± 0.08) and T2DM with CAD (0.72 ± 0.02) indicating worsening atherogenic dyslipidaemia with increasing disease severity. AIP, defined as $\log_{10}$(TG/HDL-C), represents the ratio of circulating triglycerides to protective HDL cholesterol and is an indirect marker of small dense LDL particles. Therefore, elevated AIP is a composite marker for residual cardiovascular risk beyond standard lipid measures.

The progressive increase of AIP in the present study is consistent with the results of Qin et al. who showed that high AIP was an independent predictor for adverse cardiovascular outcomes in patients with type 2 diabetes who underwent percutaneous coronary intervention [38]. The highest AIP in patients with concomitant T2DM and CAD reflects the additive effects of insulin resistance and advanced coronary atherosclerosis on lipid metabolism. These findings imply that AIP could be an easy, inexpensive and potentially useful clinical marker to identify diabetic patients with a particularly high cardiovascular risk and may provide additional prognostic information when combined with the interpretation of conventional lipid parameters.

The present study showed a significant positive correlation (table no. 3) of UACR with HbA1c ($r = 0.61$), Atherogenic Index of Plasma (AIP) ($r = 0.64$) and hs-CRP ($r = 0.76$) and a significant negative correlation with serum nitrite ($r = -0.71$) ($p < 0.01$ for all). These findings show that progressive deterioration of glycaemic control, atherogenic dyslipidaemia, systemic inflammation and endothelial function are closely associated with increasing renal microvascular injury in patients with T2DM and CAD. The robust associations of UACR with multiple cardiometabolic biomarkers are

consistent with a role for UACR as an integrated indicator of generalized vascular dysfunction rather than a marker of renal injury alone.

The observed correlations are consistent with previous clinical studies. Zeng et al. showed that higher UACR in patients with type 2 diabetes mellitus was independently associated with major adverse cardiovascular events and all-cause mortality, suggesting that albuminuria could be a marker of cardiovascular and renal risk [35]. And the American Diabetes Association Standards of Care recognise persistent hyperglycaemia as a key driver of progression to diabetic kidney disease [36] and the 2023 ESC Guidelines highlight that diabetic dyslipidaemia markedly increases cardiovascular and cardiorenal risk [4]. In addition, the strong inverse correlation between serum nitrite and UACR in the present study is consistent with the work of Förstermann and Münzel and Li and Förstermann that showed that reduced nitric oxide bioavailability secondary to endothelial nitric oxide synthase dysfunction contributes to both endothelial injury and progressive vascular complications in diabetes and atherosclerosis [19,20].

A major strength of the present study is the integrated evaluation of urinary albumin-to-creatinine ratio with endothelial, inflammatory and cardiometabolic biomarkers in a single cohort of healthy controls, patients with T2DM, CAD and concomitant T2DM with CAD. In previous studies, these biomarkers have been mainly studied in isolation, whereas the current study demonstrates their complementary relationship in different stages of cardiometabolic disease. The progressive increase in fasting plasma glucose, hs-CRP, atherogenic lipid parameters, AIP and UACR and the progressive decline in serum nitrite provide evidence of a coordinated deterioration in metabolic control, inflammation, endothelial function and renal integrity.

From a clinical perspective, simultaneous assessment of fasting plasma glucose, lipid profile, AIP, hs-CRP, serum nitrite and UACR offers a comprehensive and practical approach for evaluating cardiorenal risk using routinely available laboratory investigations. Integration of these biomarkers may facilitate earlier identification of high-risk patients, improve risk stratification and support timely implementation of preventive and therapeutic strategies aimed at reducing cardiovascular and renal complications. Nevertheless, the findings should be interpreted in the context of the cross-sectional study design, and further large-scale prospective multicentre studies are required to validate the prognostic utility and clinical applicability of this integrated multimarker approach.

CONCLUSION

The present study demonstrated that patients with type 2 diabetes mellitus and coronary artery disease exhibit significant alterations in metabolic, inflammatory, endothelial and renal biomarkers compared with healthy controls. The coexistence of T2DM and CAD was associated with the highest fasting plasma glucose, hs-CRP and UACR levels and the lowest serum nitrite concentration, indicating a synergistic interaction between chronic hyperglycaemia, systemic inflammation, endothelial dysfunction and renal microvascular injury.

Persistent hyperglycaemia promotes oxidative stress and inflammatory signalling, resulting in reduced nitric oxide bioavailability and progressive endothelial dysfunction, which contribute to both atherosclerosis and increased glomerular permeability. Although UACR is the standard clinical biomarker for the detection and monitoring of diabetic kidney disease, and also reflects generalized endothelial dysfunction and systemic vascular injury. Therefore, the combined assessment of fasting plasma glucose, hs-CRP, serum nitrite and UACR provides a comprehensive evaluation of the interconnected metabolic, inflammatory, endothelial and renal abnormalities in patients with T2DM and CAD.

These findings suggest that the integrated use of these biomarkers may improve early identification of patients at increased cardio-renal risk and facilitate timely implementation of preventive and therapeutic strategies aimed at reducing cardiovascular and renal complications. Further large-scale prospective studies are warranted to validate the prognostic utility of this multimarker approach for risk stratification and long-term clinical outcomes.

Limitations

This was a single-centre, cross-sectional study with a relatively small sample size. Serum nitrite was used as an indirect marker of nitric oxide bioavailability, and UACR was measured only once. Further large, prospective multicentre studies are required to validate these findings.

Acknowledgements

The authors sincerely thank the Department of Biochemistry, Department of General Medicine and Department of Cardiology of MGM Medical College and Hospital, Kamothe, Navi Mumbai, Maharashtra, India, for their continuous support and cooperation during the conduct of this study. The authors are grateful to all the study participants for their voluntary participation. The technical assistance provided by the laboratory staff of the Central Clinical Biochemistry Laboratory is also gratefully acknowledged.

Conflict of Interest

The authors declare that they have no conflict of interest.

Funding

Self-funded project

REFERENCES

1. Magliano DJ, Boyko EJ, editors. IDF Diabetes Atlas. 11th ed. Brussels, Belgium: International Diabetes Federation; 2025.

2. Anjana RM, Deepa M, Pradeepa R, Mahanta J, Narain K, Das HK, et al. Prevalence of diabetes and prediabetes in 31 states and union territories of India: findings from the ICMR–INDIAB population-based cross-sectional study. *Lancet Diabetes Endocrinol*. 2023;11(7):474–489.
3. American Diabetes Association Professional Practice Committee. 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes—2025. Diabetes Care. 2025;48(Suppl 1):S27-S49.
4. Marx N, Federici M, Schütt K, Müller-Wieland D, Ajjan RA, Antunes MJ, et al.; ESC Scientific Document Group. 2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes. Eur Heart J. 2023;44(39):4043-4140.
5. Dri E, Romanello M, Stasi A, De Zorzi M, Da Porto A, Cattin L, et al. Inflammatory mediators of endothelial dysfunction: molecular mechanisms and therapeutic implications. Life (Basel). 2023;13(6):1420.
6. Paul S, Ali A, Katare R. Molecular complexities underlying the vascular complications of diabetes mellitus: a comprehensive review. J Diabetes Complications. 2020;34(8):107613.
7. Alicic RZ, Cox EJ, Neumiller JJ, Tuttle KR. Incretin drugs in diabetic kidney disease: biological mechanisms and clinical evidence. *Nat Rev Nephrol*. 2022;18(4):227–244.
8. de Boer IH, Khunti K, Sadusky T, et al. Diabetes management in chronic kidney disease: a consensus report by the American Diabetes Association (ADA) and Kidney Disease: Improving Global Outcomes (KDIGO). *Diabetes Care*. 2022;45(12):3075–3090.
9. Matsushita K, Coresh J, Sang Y, et al. Estimated glomerular filtration rate, albuminuria and adverse kidney and cardiovascular outcomes: an updated collaborative meta-analysis. *Lancet Diabetes Endocrinol*. 2023;11:567–579.
10. Nazarzadeh M, Bidel Z, Canoy D, et al. Albuminuria and risks of kidney failure, cardiovascular disease, and mortality in diabetes: a prospective population-based cohort study. *Diabetes Care*. 2022;45(11):2678–2686.
11. Koye DN, Magliano DJ, Nelson RG, Pavkov ME. The global epidemiology of diabetes and kidney disease. *Nat Rev Nephrol*. 2023;19(2):73–84.
12. Lee YH, Kim SR, Han KD, et al. Urine albumin-to-creatinine ratio within the normal range predicts chronic kidney disease in patients with type 2 diabetes. *Front Endocrinol (Lausanne)*. 2022;13:864562.
13. Gerstein HC, Mann JF, Yi Q, Zinman B, Dinneen SF, Hoogwerf B, et al. Albuminuria and risk of cardiovascular events, death, and heart failure in diabetic and nondiabetic individuals. JAMA. 2001;286(4):421-426.
14. Lambers Heerspink HJ, Gansevoort RT. *Albuminuria Is an Appropriate Therapeutic Target in Patients with CKD: The Pro View*. Clin J Am Soc Nephrol. 2015;10(6):1079-1088.
15. Lee MMY, Petrie MC, McMurray JJV, Sattar N. The cardiovascular–kidney–metabolic syndrome: pathophysiology and clinical implications. *Nat Rev Cardiol*. 2023;20:635–654.
16. Brown E, Heerspink HJL, Cuthbertson DJ, Wilding JPH. SGLT2 inhibitors and the cardiorenal continuum in type 2 diabetes: mechanisms and clinical evidence. *Lancet Diabetes Endocrinol*. 2023;11:415–426.
17. Mach F, Baigent C, Catapano AL, Koskinas KC, Casula M, Badimon L, et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. Eur Heart J. 2020;41(1):111-188.
18. González P, Lozano P, Ros G, Solano F. Hyperglycemia and oxidative stress: an integral, updated and critical overview of their metabolic interconnections. Int J Mol Sci. 2023;24(11):9352.
19. Förstermann U, Münzel T. Endothelial nitric oxide synthase in vascular disease: from marvel to menace. Circulation. 2006;113(13):1708-14. doi:10.1161/CIRCULATIONAHA.105.602532. PMID: 16585403.
20. Li H, Förstermann U. Uncoupling of endothelial NO synthase in atherosclerosis and vascular disease. Curr Opin Pharmacol. 2013;13(2):161-7.
21. Zatterale F, Longo M, Naderi J, Raciti GA, Desiderio A, Miele C, et al. Chronic adipose tissue inflammation linking obesity to insulin resistance and type 2 diabetes. Front Physiol. 2020;10:1607.
22. Libby P. Inflammation in atherosclerosis—No longer a theory. Clin Chem. 2021;67(1):131-142.
23. Habib SS, Kurdi MI, Al Aseri ZA. Serum high-sensitivity C-reactive protein and lipoprotein(a) levels: a comparison between diabetic and non-diabetic patients with coronary artery disease. Med J Malaysia. 2011;66(2):113-116
24. Festa A, D'Agostino R Jr, Howard G, Mykkänen L, Tracy RP, Haffner SM. Inflammation and microalbuminuria in nondiabetic and type 2 diabetic subjects: the Insulin Resistance Atherosclerosis Study. Kidney Int. 2000;58(4):1703-10.
25. Pearson TA, Mensah GA, Alexander RW, et al. Markers of inflammation and cardiovascular disease: application to clinical and public health practice: a statement for healthcare professionals from the Centers for Disease Control and Prevention and the American Heart Association. Circulation. 2003;107(3):499-511.
26. Carlström M, Weitzberg E, Lundberg JO. Nitric oxide signaling and regulation in the cardiovascular system: recent advances. Pharmacol Rev. 2024;76(6):1038-1062.
27. Tessari P, Cecchet D, Cosma A, et al. Nitric oxide synthesis is reduced in subjects with type 2 diabetes and nephropathy. Diabetes. 2010;59:2152-9.
28. Ghosh A, Sherpa ML, Bhutia Y, Pal R, Dahal S. Serum nitric oxide status in patients with type 2 diabetes mellitus in Sikkim. Int J Appl Basic Med Res. 2011;1:31-5.
29. Janaszak-Jasiecka A, Płoska A, Wierońska JM, et al. Endothelial dysfunction due to eNOS uncoupling: molecular mechanisms as potential therapeutic targets. Cell Mol Biol Lett. 2023;28(1):21.
30. Habib SS, Al-Regaiey KA, Al-Khlaiwi T, Habib SM, Bashir S, Al-Hussain F, et al. Serum inducible and endothelial nitric oxide synthase in coronary artery disease patients with type 2 diabetes mellitus. Eur Rev Med Pharmacol Sci. 2022;26(10):3695-3702.

31. Mohandes S, Doke T, Hu H, Mukhi D, Dhillon P, Susztak K. Molecular pathways that drive diabetic kidney disease. J Clin Invest. 2023;133(4):e165654.
32. Tuttle KR, Puhlman ME, Cooney SK, Short R. Urinary albumin and insulin as predictors of coronary artery disease: an angiographic study. Am J Kidney Dis. 1999;34:918-25.
33. Lin X, Song W, Zhou Y, Gao Y, Wang Y, Wang Y, et al. Elevated urine albumin creatinine ratio increases cardiovascular mortality in coronary artery disease patients with or without type 2 diabetes mellitus: a multicenter retrospective study. Cardiovasc Diabetol. 2023;22(1):203.
34. Gao F, Zhou Y, Liu Y, Chen S, Chen L, Fang Y, et al. Effect of urinary albumin creatinine ratio on cardiovascular morbidity and mortality in diabetes patients with atherosclerotic disease. Diabetes Metab Syndr Obes. 2023;16:819-828.
35. Zeng C, Liu M, Zhang Y, Deng S, Xin Y, Hu X. Association of urine albumin-to-creatinine ratio with cardiovascular outcomes in patients with type 2 diabetes mellitus. J Clin Endocrinol Metab. 2024;109(4):1080-1093.
36. American Diabetes Association Professional Practice Committee. *Standards of Care in Diabetes—2025*. Diabetes Care. 2025;48(Suppl 1):S1-S350.
37. Ruilope LM, Ortiz A, Lucia A, Miranda B, Alvarez-Llamas G, Barderas MG, Volpe M, Ruiz-Hurtado G, Pitt B. Prevention of cardiorenal damage: importance of albuminuria. Eur Heart J. 2023;44(13):1112-1123.
38. Qin Z, Zhou K, Li Y, Cheng W, Wang Z, Wang J, et al. The atherogenic index of plasma plays an important role in predicting the prognosis of type 2 diabetic subjects undergoing percutaneous coronary intervention: results from an observational cohort study in China. Cardiovasc Diabetol. 2020;19(1):23.