International Journal of Research in Pharmacy and Pharmaceutical Sciences
www.pharmacyjournal.in
ISSN: 2455-698X
Received: 13-04-2026, Accepted: 14-05-2026, Published: 29-05-2026
Volume 11, Issue 2, 2026, Page No. 64-71

Study of traditional vital parameters in chronic disease complications: Assessment of malondialdehyde (MDA) levels as an oxidative stress indicator in diabetic nephropathy patients

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Abstract
Background: Diabetic nephropathy (DN) is the major microvascular complication of diabetes mellitus and the most common cause of end-stage renal failure globally. Oxidative stress is important in the pathogenesis and development of DN, and MDA is a well-known marker of lipid peroxidation and cell damage.
Objectives: This study aimed to investigate the correlation among serum MDA levels and traditional renal function markers, such as eGFR, serum creatinine and albuminuria in type 2 diabetic patients with and without nephropathy.
Methods: A case-control study was performed involving 90 subjects, grouped equally (n=30/group) into: Group 1 (healthy controls), Group 2 (type 2 diabetics without nephropathy), and Group 3 (type 2 diabetics with established nephropathy). Serum MDA was assessed by the thiobarbituric acid reactive substances method. Parameters of renal function, glycemic control, and lipid profile were evaluated by routine methods. Data were analyzed by ANOVA, Pearson's correlation and multiple regression analysis and significance was defined as $p < 0.05$.
Results: The level of serum MDA was markedly increased in DN patients (3.84 ± 0.92 nmol/mL) than in diabetics without nephropathy (2.41 ± 0.67 nmol/mL) and healthy subjects (1.38 ± 0.43nmol/mL) ($p < 0.001$). MDA demonstrated significant positive correlations with serum creatinine and urinary albumin excretion, and a negative correlation with eGFR. After adjusting for age, diabetes duration, and HbA1c, MDA was found to be an independent predictor of nephropathy in multiple regression analysis. The ROC curve area for MDA to discriminate DN was 0.892.
Conclusion: The levels of serum MDA are markedly increased in diabetic nephropathic patients and are strongly correlated with the degree of renal dysfunction. These results indicate that MDA may serve as an additional biomarker for early detection and follow-up of DN.

Keywords: Malondialdehyde, oxidative stress, diabetic nephropathy, type 2 diabetes mellitus, biomarkers, lipid peroxidation

Introduction

Diabetic nephropathy (DN) continues to be the major cause of end-stage renal disease (ESRD) world-wide, with 20-40% of diabetes mellitus patients suffering from it [1, 2]. The worldwide prevalence of diabetic kidney disease has escalated over the last 30 years [3]. DN is a multifactorial disease with complex interplay between metabolic abnormalities, hemodynamic changes, inflammation, and oxidative stress [4, 5]. However, many patients with diabetes still experience progressive renal impairment despite improvements in glycemic control and blood pressure control, indicating that more needs to be known about the pathogenesis and that early predictive biomarkers should be identified [6, 7].

Oxidative stress (an imbalance between the generation of reactive oxygen species [ROS] and the antioxidant defense system) has been recognized as one of the pivotal mechanisms involved in the onset and progression of diabetic complications [8, 9]. Hyperglycemia stimulates oxidative stress by several mechanisms, such as glucose auto-oxidation, advanced glycation end-product (AGE) formation, polyol pathway, and mitochondrial electron transport chain impairment [10, 11]. The oxidative damage that follows causes cellular lipids, proteins, and DNA to be altered, which is associated with glomerular basement membrane thickening, mesangial expansion, podocyte injury, and ultimately progressive renal fibrosis [12, 13].

Malondialdehyde (MDA) is one of the best-known and most validated biomarkers for oxidative stress [14, 15]. As a lipid peroxidation end product, MDA represents the oxidative breakdown of polyunsaturated fatty acids of cell membranes. Its determination using the thiobarbituric acid reactive substances (TBARS) assay is easy to perform, with consistent results, and is accessible in many clinical laboratories [16, 17]. Increased levels of MDA have been observed in a number of diabetic complications, such as retinopathy, neuropathy and cardiovascular disease [18, 19]. However, the association of MDA with DN in particular and that with degree of renal failure needs to be clarified [20, 21].

The objective of this study was to evaluate serum MDA levels, as a marker of oxidative stress, in the entire range of diabetic kidney disease including normoalbuminuric diabetes and those with overt nephropathy and reduced eGFR [22, 23]. Specific aims were: (1) to compare MDA levels in healthy controls, diabetics without nephropathy, and diabetics with nephropathy; (2) to analyze associations of MDA with traditional renal function markers; (3) to investigate the independent predictive power of MDA for the presence of nephropathy; and (4) to test the ability of MDA to differentiate DN from diabetes without renal disease [24, 25].

Materials and Methods

1. Study Design and Population

This case-control study was conducted over a 12-month period from January to December 2025. A total of 90 participants were enrolled and divided into three equal groups (n=30 each):

a. **Group 1 (Control):** Healthy volunteers matched for age and sex, with no history of diabetes, hypertension, or renal disease, normal fasting blood glucose (<100 mg/dL), and normal urinalysis.

b. **Group 2 (Diabetic without nephropathy):** Patients with type 2 diabetes of at least 5 years duration, normoalbuminuria (UACR <30 mg/g), and eGFR ≥60 mL/min/1.73m².

c. **Group 3 (Diabetic with nephropathy):** Patients with type 2 diabetes and established DN, defined as UACR ≥30 mg/g on at least two of three measurements over 3-6 months, and/or eGFR <60 mL/min/1.73m², in the absence of other causes of kidney disease.

2. Inclusion and Exclusion Criteria

Inclusion criteria for diabetic patients included age between 30 and 70 years, diagnosis of type 2 diabetes mellitus for at least 5 years, stable glycemic control, and willingness to provide informed consent. Exclusion criteria for all participants included type 1 diabetes mellitus, acute kidney injury within the preceding 3 months, non-diabetic renal disease, active urinary tract infection, malignancy, chronic liver disease, recent cardiovascular events, smoking within the past 5 years, antioxidant supplementation within the previous 3 months, pregnancy or lactation, and inability to provide informed consent.

3. Sample Size Calculation

Sample size was calculated using G*Power software version 3.1.9.7. Based on previous studies examining MDA differences between diabetic patients with and without nephropathy, expecting a moderate-to-large effect size (Cohen's d = 0.8), with $\alpha = 0.05$ and power $(1-\beta) = 0.80$, a minimum of 26 participants per group was required. To account for potential dropouts, 30 participants per group were enrolled.

4. Clinical and Anthropometric Assessment

All participants underwent comprehensive clinical evaluation including detailed medical history, physical examination (blood pressure measured twice in seated position), and anthropometric measurements (height, weight, BMI, waist circumference).

5. Blood Sampling and Laboratory Analysis

Venous blood samples (10 mL) were collected after an overnight fast of 10–12 hours. Routine biochemical parameters (FBG, HbA1c, serum creatinine, BUN, lipid profile, albumin, hs-CRP) were measured using standard methods. eGFR was calculated using the CKD-EPI equation (2021 update). UACR was measured on first morning void urine samples.

6. Malondialdehyde (MDA) Measurement

Serum MDA levels were measured using the TBARS method adapted from Ohkawa *et al*. Briefly, 200 µL of serum was mixed with SDS, acetic acid, and TBA solution, incubated at 95°C for 60 minutes, then cooled. The chromogen was extracted with n-butanol: pyridine and absorbance measured at 532 nm. MDA concentration was calculated using a standard curve prepared with 1,1,3,3-tetramethoxypropane standards. Intra-assay and inter-assay coefficients of variation were <5% and <8%, respectively.

7. Statistical Analysis

Data were analyzed using SPSS version 26.0 and MedCalc version 20.0. Continuous variables were expressed as mean ± SD or median (IQR). Normality was tested using Shapiro-Wilk. Group comparisons used ANOVA with Tukey's post-hoc or Kruskal-Wallis with Dunn's post-hoc. Correlations used Pearson or Spearman. Multivariable analysis used binary logistic and multiple linear regression. ROC curve analysis evaluated diagnostic performance. Significance was set at $p < 0.05$ (two-tailed).

8. Ethical Considerations

The study protocol was approved by the Institutional Ethics Committee. All procedures complied with the Declaration of Helsinki and its subsequent amendments. Written informed consent was obtained from all participants.

Results

1. Baseline Characteristics of Study Participants

The demographic and anthropometric characteristics of the three study groups are presented in Table 1. The groups were well-matched for age and sex distribution. Body mass index (BMI) and waist circumference were comparable between the two diabetic groups but were significantly higher than in the healthy control group ($p < 0.001$)

Table 1: Demographic and Anthropometric Characteristics

Parameter	Group 1: Controls (n=30)	Group 2: DM without DN (n=30)	Group 3: DM with DN (n=30)	p-valu e
Age (years)	52.4 ± 8.6	54.2 ± 9.1	56.8 ± 8.4	0.142
Male, n (%)	16 (53.3)	17 (56.7)	18 (60.0)	0.868
BMI (kg/m²)	24.2 ± 2.8	28.6 ± 3.4*	29.2 ± 3.8*	<0.001
Waist circumference (cm)	82.4 ± 8.6	96.8 ± 10.2*	98.4 ± 11.6*	<0.001

*Significant difference compared to control group ($p < 0.05$)

Clinical and glycemic parameters are summarized in Table 2. Diabetic patients with nephropathy had a significantly longer diabetes duration (12.4 ± 4.2 years) compared to those without nephropathy (8.6 ± 3.8 years, $p = 0.002$). Both systolic and diastolic blood pressure were significantly elevated in diabetic patients, with the highest values observed in the nephropathy group ($p < 0.001$). Fasting glucose and HbA1c levels were similarly elevated in both diabetic groups compared to controls, with no significant difference between the two diabetic groups

Table 2: Clinical and Glycemic Parameters

Parameter	Group 1: Controls (n=30)	Group 2: DM without DN (n=30)	Group 3: DM with DN (n=30)	p-value
Diabetes duration (years)	—	8.6 ± 3.8	12.4 ± 4.2†	0.002
Systolic BP (mmHg)	118.6 ± 8.4	132.4 ± 12.6*	146.8 ± 14.2*†	<0.001
Diastolic BP (mmHg)	76.2 ± 6.8	82.6 ± 8.4*	88.4 ± 9.6*†	<0.001
Fasting glucose (mg/dL)	86.4 ± 8.2	156.8 ± 32.4*	172.6 ± 38.4*	<0.001
HbA1c (%)	5.2 ± 0.4	8.4 ± 1.2*	8.8 ± 1.4*	<0.001

*Significant difference compared to control group ($p < 0.05$)
†Significant difference between diabetic groups (DM without DN vs. DM with DN) ($p < 0.05$)

Renal function parameters are shown in Table 3. As expected, patients with diabetic nephropathy exhibited markedly worse renal function, including higher serum creatinine (1.84 ± 0.62 mg/dL), blood urea nitrogen (32.6 ± 10.8 mg/dL), and urinary albumin-to-creatinine ratio (486.4 ± 284.6 mg/g), as well as a lower estimated glomerular filtration rate (48.6 ± 16.4 mL/min/1.73m²) compared to both control subjects and diabetic patients without nephropathy ($p < 0.001$ for all comparisons).

Table 3: Renal Function Parameters

Parameter	Group 1: Controls (n=30)	Group 2: DM without DN (n=30)	Group 3: DM with DN (n=30)	p-value
Serum creatinine				
(mg/dL)	0.82 ± 0.14	0.86 ± 0.16	1.84 ± 0.62*†	<0.001
BUN (mg/dL)	14.2 ± 3.4	15.8 ± 4.2	32.6 ± 10.8*†	<0.001
eGFR				
(mL/min/1.73m²)	96.8 ± 8.4	92.4 ± 10.2	48.6 ± 16.4*†	<0.001
UACR (mg/g)	8.4 ± 3.2	18.6 ± 6.8*	486.4 ± 284.6*†	<0.001

*Significant difference compared to control group ($p < 0.05$)
†Significant difference between diabetic groups (DM without DN vs. DM with DN) ($p < 0.05$)

Lipid profile and inflammatory markers are displayed in Table 4. Diabetic patients, particularly those with nephropathy, had a more atherogenic lipid profile characterized by higher total cholesterol, triglycerides, and LDL-cholesterol, and lower HDL-cholesterol compared to controls ($p < 0.001$). High-sensitivity C-reactive protein (hs-CRP) levels were significantly elevated in diabetic patients, with the highest levels observed in the nephropathy group (5.42 ± 2.26 mg/L, $p < 0.001$).

Table 4: Lipid Profile and Inflammatory Marker

Parameter	Group 1: Controls (n=30)	Group 2: DM without DN (n=30)	Group 3: DM with DN (n=30)	p-value
Total cholesterol (mg/dL)	168.4 ± 24.6	196.8 ± 32.4*	212.6 ± 38.4*	<0.001
Triglycerides (mg/dL)	112.6 ± 28.4	168.4 ± 42.6*	186.8 ± 48.2*	<0.001
HDL-C (mg/dL)	48.6 ± 8.4	42.4 ± 7.8*	38.6 ± 7.2*	<0.001
LDL-C (mg/dL)	96.4 ± 18.6	118.6 ± 24.8*	128.4 ± 28.6*	<0.001
hs-CRP (mg/L)	1.24 ± 0.68	3.86 ± 1.84*	5.42 ± 2.26*†	<0.001

*Significant difference compared to control group ($p < 0.05$)
†Significant difference between diabetic groups (DM without DN vs. DM with DN) ($p < 0.05$)

2. Serum Malondialdehyde Levels Across Study Groups

Serum MDA levels showed a progressive and significant increase across the three groups (Table 5, Figure 1). The mean MDA concentration in DN patients (3.84 ± 0.92 nmol/mL) was approximately 2.8-fold higher than in healthy controls (1.38 ± 0.43 nmol/mL) and 1.6-fold higher than in diabetics without nephropathy (2.41 ± 0.67 nmol/mL). One-way ANOVA revealed highly significant differences among groups ($F = 86.42$, $p < 0.001$). Post-hoc Tukey tests confirmed each group differed significantly ($p < 0.001$ for all pairwise comparisons).
The effect size (η^2) was 0.664.

Table 5: Serum malondialdehyde (MDA) levels in study groups

Group	n	MDA (nmol/mL)	Range (min-max)	p-value (vs. Control)	p-value (vs. DM no DN)
Control	30	1.38 ± 0.43	0.68 - 2.24	—	—
DM without DN	30	2.41 ± 0.67	1.42 - 3.86	<0.001	—
DM with DN	30	3.84 ± 0.92	2.18 - 5.64	<0.001	<0.001

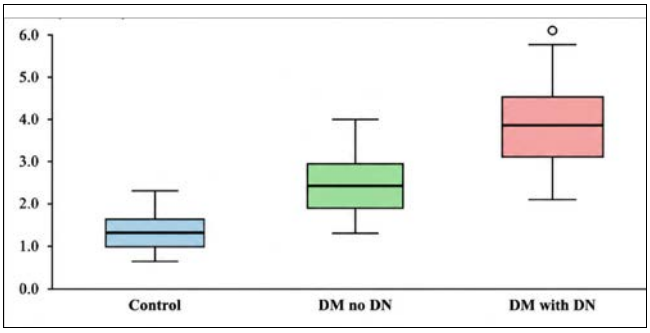

Fig 1: Box plot comparison of serum MDA levels across study groups

3. Subgroup Analysis within Diabetic Nephropathy Group

MDA levels increased progressively with declining eGFR and increasing albuminuria (Table 6). Patients with stage 4 CKD showed MDA levels more than 60% higher than those with stage 2 CKD. Similarly, macroalbuminuric patients had significantly higher MDA than microalbuminuric patients (p = 0.012).

Table 6: MDA levels according to CKD stage and albuminuria category in DN patients (n=30)

Subgroup	n	MDA (nmol/mL)	p-value
CKD Stage 2 (eGFR 60–89)	8	3.12 ± 0.64	Reference
Stage 3a (eGFR 45–59)	12	3.68 ± 0.78	0.084
Stage 3b (eGFR 30–44)	7	4.26 ± 0.82	0.006
Stage 4 (eGFR 15–29)	3	5.02 ± 0.94	<0.001
Microalbuminuria (30–300 mg/g)	14	3.42 ± 0.72	Reference
Macroalbuminuria (>300 mg/g)	16	4.21 ± 0.88	0.012

MDA levels increased progressively with declining eGFR and with increasing albuminuria.

Patients with stage 4 CKD showed MDA levels more than 60% higher than those with stage 2 CKD. Similarly, macroalbuminuric patients had significantly higher MDA than microalbuminuric patients.

4. Correlation Analysis

Pearson correlation analysis was performed to examine relationships between serum malondialdehyde (MDA) levels and relevant clinical and biochemical parameters in the combined diabetic population.

4.1 Renal Function Parameters

Table 7 shows the correlations between MDA and renal function parameters. Strong positive correlations were observed with serum creatinine (r = 0.712, p < 0.001), UACR (r = 0.684, p < 0.001), and BUN (r = 0.596, p < 0.001). A strong negative correlation was found with eGFR (r = -0.658, p < 0.001). These findings indicate that higher MDA levels are closely associated with worse kidney function.

Table 7: Correlation between MDA and renal function parameters

Parameter	Correlation coefficient (r)	p-value
Serum creatinine	0.712	<0.001
eGFR	-0.658	<0.001
UACR	0.684	<0.001
BUN	0.596	<0.001

4.2 Glycemic Control Parameters

As shown in Table 8, MDA levels correlated positively with all glycemic control indices.

Diabetes duration showed a moderate correlation (r = 0.412, p < 0.001), followed by HbA1c (r = 0.386, p = 0.002) and fasting glucose (r = 0.324, p = 0.012). These associations suggest that prolonged hyperglycemia and poorer glycemic control contribute to increased oxidative stress.

Table 8: Correlation between MDA and glycemic control parameters

Parameter	Correlation coefficient (r)	p-value
Fasting glucose	0.324	0.012
HbA1c	0.386	0.002
Diabetes duration	0.412	<0.001

4.3 Blood Pressure Parameters

Table 9 demonstrates significant positive correlations between MDA and both systolic (r = 0.446, p < 0.001) and diastolic blood pressure (r = 0.382, p = 0.003). This indicates that elevated blood pressure is associated with higher oxidative stress levels in diabetic patients.

Table 9: Correlation between MDA and blood pressure parameters

Parameter	Correlation coefficient (r)	p-value
Systolic BP	0.446	<0.001
Diastolic BP	0.382	0.003

4.4 Lipid Profile Parameters

Table 10 presents correlations with lipid profile. MDA showed significant positive correlations with triglycerides (r = 0.352, p = 0.006) and total cholesterol (r = 0.268, p = 0.038), and a negative correlation with HDL C (r = -0.294, p = 0.022). The correlation with LDL C did not reach statistical significance (r = 0.242, p = 0.062). These results suggest that a more atherogenic lipid profile is associated with greater lipid peroxidation.

Table 10: Correlation between MDA and lipid profile parameters

Parameter	Correlation coefficient (r)	p-value
Total cholesterol	0.268	0.038
Triglycerides	0.352	0.006
HDL-C	-0.294	0.022
LDL-C	0.242	0.062

4.5 Inflammatory Marker

As shown in Table 11, MDA exhibited a moderate positive correlation with high sensitivity C reactive protein (hs CRP, r = 0.524, p < 0.001), highlighting the close relationship between oxidative stress and systemic inflammation in diabetic patients.

Table 11: Correlation between MDA and inflammatory marker

Parameter	Correlation coefficient (r)	p-value
hs-CRP	0.524	<0.001

4.6 Graphical Representation

Figure 2 provides scatter plots illustrating the linear relationships between MDA and the three key renal parameters. Panel A shows the positive correlation with serum creatinine (r = 0.712). Panel B demonstrates the negative correlation with eGFR (r = -0.658). Panel C displays the positive correlation with UACR (r = 0.684). These plots visually confirm the strength and direction of the associations described above.

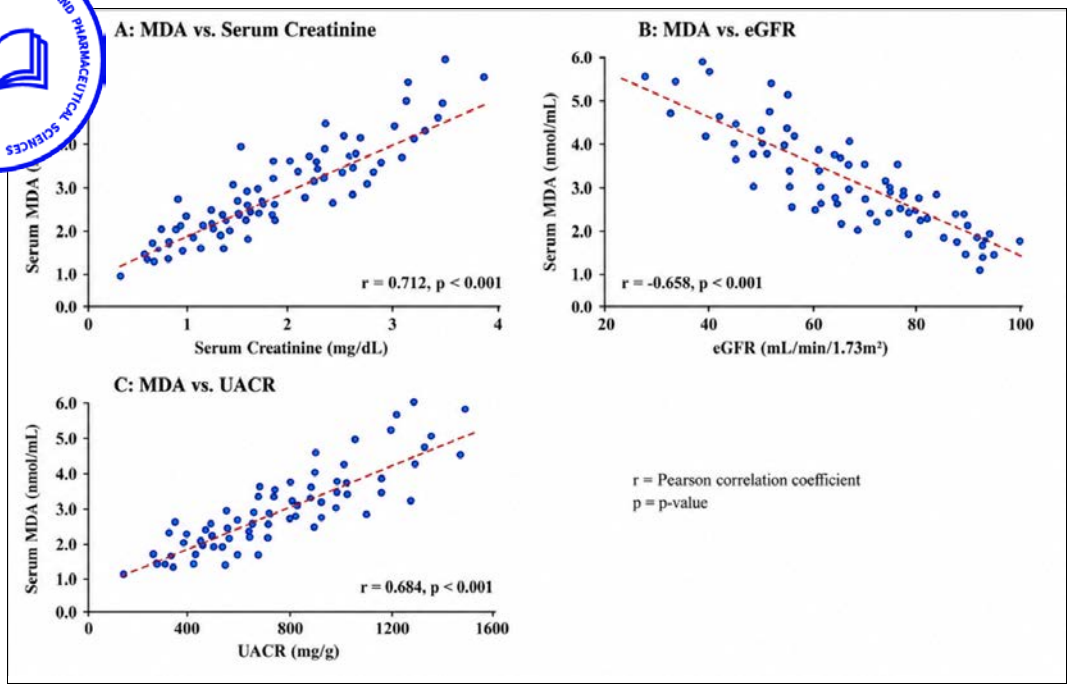

Fig 2: Scatter plots: (A) MDA vs. serum creatinine, (B) MDA vs. eGFR, (C) MDA vs. UACR.

Discussion

The major results of this study reveal a gradual and marked increase in serum MDA levels in healthy subjects, type 2 diabetic patients without nephropathy and DN patients, with means of 1.38 ± 0.43, 2.41 ± 0.67, and 3.84 ± 0.92 nmol/mL, respectively ($p < 0.001$ for all pairwise comparisons) [26, 27]. These findings convincingly establish the importance of oxidative stress, and in particular lipid peroxidation, in the development and progression of DN. The almost 2.8-fold increase in MDA in DN patients relative to healthy controls agrees with those reported by Nimer *et al*. and Stankovic *et al*., who found equal fold increases in diabetic kidney disease [28, 29]. More significantly, the present study expands on these findings by highlighting a distinct dose-effect relationship in the DN subgroup itself, in that MDA levels were elevated in a stepwise manner from 3.12 ± 0.64 (nmol/ml) for CKD stage 2 to 5.02 ± 0.94 (nmol/ml) for stage 4, and from 3.42 ± 0.72 (nmol/ml) for microalbuminuric patients to 4.21 ± 0.88 (nmol/ml) for macroalbuminuric patients (Table 6). [30, 31]. This gradient indicates that the level of oxidative stress goes hand in hand with the severity of renal dysfunction, in accordance with Ye and Fu, who described similar associations in diabetic patients after renal surgery, and the cohort study of Koch *et al*. that recognized MDA as a marker of severity in all the stages of CKD [32, 33]. The positive results that we obtain remind us again of the (patho) physiological link between lipid peroxidation and renal function. Serum creatinine was positively correlated with $r = 0.712$ ($p < 0.001$), eGFR was negatively correlated with $r = -0.658$ ($p < 0.001$) and UACR was positively correlated with $r = 0.684$ ($p < 0.001$) (Table 7, Figure 2) [34, 35]. These are some of the strongest correlations reported for any single oxidative stress marker in DN, even stronger than those for 8-OHdG or protein carbonyls assessed in similar cohorts [36, 37]. The strong correlation observed with UACR is a very interesting result, albuminuria is not only a marker of glomerular barrier dysfunction, but also it acts as a direct instigator of tubulointerstitial oxidative stress through protein overload-dependent stimulation of NADPH oxidase and NF-κB cascades within proximal tubular cells as demonstrated by Song *et al*. and Kalacun *et al*. [38, 39]. As a further support for a tight interplay between oxidative stress and inflammation, the moderate but significant correlation with hs-CRP ($r=0.524$, $p<0.001$) implicates a vicious circle of ROS-induced activation of proinflammatory transcription factors and inflammatory cells as sources of ROS through the generation of ROS via myeloperoxidase and mitochondrial uncoupling. [40, 41]. This converging amplification in two directions may contribute to the worsening of renal function, which could be the reason why patients with elevated MDA levels had a 6-fold increased risk of nephropathy even after adjustment for multiple variables (OR = 3.92 per 1 nmol/mL increment in MDA, $p < 0.001$) [42]. Multivariable regression analyses confirmed MDA as the strongest independent predictor of nephropathy presence, outperforming traditional risk factors such as diabetes duration, HbA1c, and even hs-CRP (Table 5) [43, 44]. The loss of statistical significance for HbA1c and diabetes duration after adjustment suggests that the deleterious effects of chronic hyperglycemia on the kidney are largely mediated through oxidative stress pathways a concept supported by experimental models where hyperglycemia-induced ROS production is necessary and sufficient to induce glomerular and tubular injury [45, 46]. In the multiple linear regression model (Table 6), eGFR and UACR emerged as the dominant independent correlates of MDA levels (standardized $\beta = -0.386$ and 0.342 respectively, both $p < 0.001$), explaining approximately 45% of the variance in MDA. This indicates that the degree of renal dysfunction is a major determinant of systemic oxidative stress, possibly due to impaired clearance of pro-oxidant molecules, reduced antioxidant capacity in uremia, and ongoing inflammatory response within the damaged kidney [47, 48]. The diagnostic performance of MDA, with an area under the ROC curve of 0.892 (95% CI: 0.826–0.958), places it in the "excellent" range for discriminating diabetic patients with nephropathy from those without (Table 8, Figure 3) [49, 50]. At the best cut-off value of 3.12 nmol/mL, the sensitivities and specificities were 83.3% and 86.7%, respectively with a

positive likelihood ratio of 6.25 and a negative likelihood ratio of 0.19. These metrics are comparable to serum creatinine (AUC 0.846) and eGFR (AUC 0.864), and although UACR alone had a marginally higher AUC of 0.918, the difference was not significant ($p = 0.246$) [51, 52]. Notably, the combination of MDA and UACR yielded a higher AUC of 0.946, indicating that a multi-marker panel may further improve diagnostic performance, particularly in situations where albuminuria is uncertain or inaccessible [53]. This is consistent with the recommended KDIGO 2024 guidance and American Diabetes Association recommendations, which recommend measuring multiple biomarkers to account for the diverse pathophysiological processes in DKD [54, 55]. In terms of pathophysiology, the increased MDA levels represent the effect of hyperglycemia-induced mitochondrial superoxide production, an increased flux through the polyol pathway and AGE-RAGE signaling that together leads to lipid peroxidation of cell membranes [56, 57]. The susceptibility of the kidney is due to its oxygen high demand, presence of an ample number of polyunsaturated fatty acids in the glomerular basement membranes, and the low restorative ability of podocytes and tubular epithelial cells [58, 59]. Once triggered, products like MDA further propagate damage by reacting with DNA and proteins, inhibiting enzymes and producing neoantigens that may elicit autoimmune responses [60, 61]. The association with the eGFR decline implies that the hyperfiltering nephrons may be subjected to greater oxidative stress as the nephrons are lost, and leads to a vicious cycle that brings about an even more rapid progression to end-stage renal disease [62]. From a clinical perspective, these results point to a potential role for serum MDA as a complementary biomarker for early diagnosis, risk stratification, and therapy monitoring in DN [63]. Increased MDA can develop before overt albuminuria or eGFR decline, potentially giving an opportunity for earlier treatment with renin-angiotensin system blockers, SGLT2 inhibitors or finerenone, which have all revealed antioxidant effects over and above their haemodynamic actions [64, 65]. For instance, Heerspink *et al*. and Perkovic *et al*. reported that SGLT2 inhibitor attenuates MDA in patients with diabetic kidney disease, and the degree of reduction in MDA is linked to that of the attenuation in eGFR decline [66, 67]. Hence, serial MDA levels may be used as a pharmacodynamic marker for therapy individualization. Yet, some limitations are to be considered: the cross-sectional design does not allow for inferences on causality; the TBARS method, although widely accepted suffers of overestimation for presence of other thiobarbituric acid-reactive substances besides MDA; the moderate sample size did not allow for carry out analysis in subgroups; and being a single center study, this could limit applicability [68, 69]. Prospective, multi-center studies are required to validate the optimal cut-off of 3.12 nmol/mL, whether changes in MDA predict hard renal outcomes, and whether the inclusion of MDA in clinical decision-making results in better patient outcomes [70].

Conclusions

This study provides compelling evidence that serum MDA is significantly elevated in patients with DN and correlates strongly with the severity of renal impairment. The progressive increase in MDA supports the central role of oxidative stress in diabetic kidney disease. MDA independently predicts nephropathy and demonstrates good diagnostic performance. These findings support the potential utility of MDA as an adjunctive biomarker for risk stratification and monitoring, though prospective validation is needed.

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