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ORIGINAL ARTICLE

Reduced Lutein Levels in Elderly Type 2 Diabetics: Implications for Diabetic Kidney Disease Risk

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is considered a widespread metabolic condition associated with morbidity, particularly when complicated by diabetic kidney disease (DKD). Lutein, a natural carotenoid with antioxidant and anti-inflammatory properties, has drawn interest as a potential biomarker in this context. The purpose of this work was to evaluate serum lutein levels among elderly T2DM cases and to investigate its relationship with diabetic kidney disease and relevant metabolic parameters.

Methods: We carried out this case-control study on 63 elderly participants aged ≥65 years (mean age: 69.9 ± 4.5 years) categorized into three groups: healthy controls, T2DM patients without DKD, and T2DM patients with DKD (21 subjects per group). Clinical data, anthropometric measurements, and laboratory tests, involving fasting blood glucose, HbA1c, renal and liver function tests, lipid profile, and serum lutein were collected. Serum lutein levels were assessed using high-performance liquid chromatography coupled with mass spectrometry. Correlation and ROC curve analyses were performed to assess diagnostic performance.

Results: Serum lutein levels differed significantly among groups ($F = 128.237$, $p < 0.001$). Post hoc analysis showed lower levels in both diabetic groups vs. controls ($p1 < 0.001$, $p2 < 0.001$), and in DKD vs. Non-DKD ($p3 = 0.002$). Levels were lowest in the DKD group, followed by non-DKD, and highest in controls. Serum lutein demonstrated high diagnostic accuracy for diabetes. A cutoff ≤0.515 µmol/L identified diabetes without DKD with 95.2% sensitivity, 90.5% specificity, and 92.9% accuracy (AUC = 0.988, $p < 0.001$). For DKD, a cutoff ≤0.36 µmol/L showed 95.2% sensitivity, 81% specificity, and 85.7% accuracy (AUC = 0.961, $p < 0.001$), supporting lutein as a strong stratification biomarker.

Conclusions: Serum lutein levels were significantly reduced in elderly patients with type 2 diabetes, especially those with diabetic kidney disease. Its strong association with glycemic and renal markers suggests that lutein may serve as a useful indicator for early renal involvement in this population.

Keywords: Serum Lutein; Diabetic Kidney Disease; Biomarker; Type 2 Diabetes Mellitus; Elderly.

INTRODUCTION

Elevated blood glucose levels is a hallmark of type 2 diabetes mellitus (T2DM), a chronic metabolic disease that gradually impairs the function of several organs throughout the body and endangers both the duration and quality of life. Over recent years, the global incidence of T2DM has increased substantially. According to estimates from the International Diabetes

Federation, more than 460 million individuals were affected worldwide by the year 2020 [1].

T2DM is largely identified as a disorder of glucose metabolism wherein peripheral insulin resistance plays a pivotal role. This resistance impairs cellular glucose uptake, disrupting energy production and the generation of adenosine triphosphate (ATP), which is essential for normal cellular function [2].

Persistent hyperglycemia over time gives rise to numerous complications, among which diabetic kidney disease (DKD) is a major microvascular consequence. In populations with T2DM, DKD accounts for nearly 20% to 40% of complications and represents a primary etiology of progression to end-stage renal disease [3]. Notably, elderly individuals with T2DM exhibit a greater vulnerability to DKD compared to younger patients. This condition not only contributes significantly to morbidity and mortality in older adults but also imposes substantial socioeconomic strain. Thus, identifying reliable early biomarkers for T2DM and DKD in elderly populations is essential for improving clinical outcomes.

Lutein, an oxygenated carotenoid with well-documented antioxidative and anti-inflammatory actions, has attracted attention in this context [4]. Given that both T2DM as well as DKD are being closely related with higher oxidative stress and chronic inflammation, the biological role of lutein in these conditions warrants investigation [5]. However, the potential link between lutein levels and the occurrence or progression of T2DM and DKD in elderly patients a group with unique metabolic characteristics, increased susceptibility to vascular complications, and age-related changes in renal function remains inadequately understood. Focusing on elderly individuals is particularly important, as they represent a growing population at the highest risk for both diabetes and its renal complications, and may demonstrate distinct biomarker profiles compared to younger patients

We hypothesize that lower serum lutein levels are associated not only with the presence of T2DM in elderly individuals, but also with increased severity of diabetic kidney disease, as reflected by progressively reduced lutein concentrations from healthy controls to diabetics without DKD and to those with DKD. The lack of data on serum lutein levels in this population represents a key research gap. While the association between lutein and diabetic complications has been previously reported, there is limited evidence focusing on elderly patients with T2DM, who have distinct metabolic profiles and a higher risk for DKD. This study hypothesizes that lower serum lutein levels are associated with the presence and severity of T2DM and DKD in elderly individuals, suggesting lutein's potential as an early biomarker. This study aimed to evaluate these correlations and assess the clinical utility of serum lutein as a biomarker for both the diagnosis and stratification of diabetic kidney disease severity in elderly patients

METHODS

We carried out this case-control study at the Internal Medicine Department, Faculty of Medicine, Zagazig University over a period of six months from July 2023 to December 2023, we included 63 participants categorized into three groups: a control group, a diabetic group without DKD (non-DKD), and a diabetic group with DKD.

A total of 63 participants were recruited in the study, with 21 individuals allocated into each of three groups: elderly patients who had type 2 diabetes mellitus and diabetic kidney disease, those with T2DM but without DKD, and a control group. The sample size was calculated based on prior data comparing mean serum lutein levels across these groups (0.38 ± 0.4 vs

0.83 ± 0.86), assuming a power of 80% and a 95% confidence interval using OpenEpi software.

Institutional Review Board (ZU-IRB#11339-3/12/2023) clearance and informed consent were collected and signed from all patients. The Helsinki Declaration, which outlines the standards for research involving human beings, was followed by the researchers in this study.

The study population included elderly cases diagnosed with T2DM, with or without DKD, and were eligible for participation. Subjects were excluded if they declined to participate or had a history of chronic liver disease, chronic kidney disease unrelated to diabetes, malignancy, or autoimmune connective tissue diseases such as systemic lupus erythematosus or rheumatoid arthritis.

Type 2 diabetes mellitus was diagnosed according to the American Diabetes Association (ADA) guidelines [2]. The DKD diagnosis required an albumin-to-creatinine ratio (ACR) ≥30 mg/g in a spot urine sample, confirmed on at least two occasions three to six months apart, or an eGFR <60 mL/min/1.73 m², persisted for at least three months to meet the criteria for chronic kidney disease. [3]. Estimated glomerular filtration rate (eGFR) was calculated for all participants using the [CKD-EPI/MDRD] equation [3].

All participants underwent a detailed medical history assessment, including age, sex, current complaints, medical and surgical history, and family history.

Routine laboratory investigations were conducted for all participants. A complete blood count (CBC)—including hemoglobin white blood cell (WBC) count, red blood cell (RBC) count as well as platelet counts were measured using the Sysmex XN 330 hematology analyzer. Glycemic control was assessed by measuring fasting blood glucose using a glucometer and HbA1c using high-performance liquid chromatography (HPLC) on the Variant II system. Liver enzymes (ALT and AST) and albumin were analyzed on the Abbott Architect C16000 analyzer. Lipid profiles (total cholesterol, HDL, LDL, triglycerides) were measured using enzyme-linked immunosorbent assay (ELISA) kits. Renal function was evaluated using serum creatinine and blood urea nitrogen (BUN) measured with the Roche Cobas 6000 analyzer, and the albumin-to-creatinine ratio was calculated.

Measurement of Serum Lutein Levels:

To measure serum lutein, 5 ml of venous blood was drawn aseptically into sodium citrate tubes (except for CBC, which used EDTA). Plasma was separated by double centrifugation. From each sample, 100 µl of plasma was taken and lysed while kept at 4°C. It was then mixed with 400 µl of methanol that had been prechilled, and the mixture was left to incubate at −80°C for about 8 hours. After that, the samples were centrifuged at 16,000 g for 10 minutes, maintaining the temperature at 4°C throughout the process.

A QTRAP 5500 mass spectrometer (AB SCIEX) and the SCIEX Exion LC AD system were used to detect serum lutein levels utilizing multiple reaction monitoring (MRM). An Agilent Technologies HPLC column (2.7 µm, 30 mm × 3.1 mm) was utilized for the chromatographic separation. Two solvents, acetonitrile and solvent A (0.1 percent formic acid in water), made up the mobile phase. The following linear gradient was implemented at a flow rate of 0.3 ml/min: from 0 to 1 minute, 10% B was administered, then from 1 to 8 minutes, 90% B, and finally, at 9 minutes, 10% B was applied again. Both Q1 and Q3 were set to unit resolution, and 10 µl was the injection volume used.

Statistical analysis:

Quantitative data was presented as mean ± standard deviation (SD), while qualitative variables were represented as numbers and

percentages in the data analysis performed using SPSS version 20.0. Pearson correlation, Student's t-test, Mann-Whitney U-test, Fisher exact test, chi-square test, and total statistical analysis were all part of the package. There were clear associations found by both the univariate logistic regression tests. In order to reliably evaluate clinical, laboratory, and treatment response characteristics, a P-value less than 0.05 was deemed statistically significant.

RESULTS

Table 1 shows non statistically significant variations as regards demographic data among the groups. Gender distribution was similar across groups (χ^2 = 0.127, p = 0.938), with females comprising 47.6% of controls and 53.3% of both diabetic groups. Mean age was slightly higher in diabetic groups but not statistically significant (F = 2.266, p = 0.113).

Table 2 demonstrates significant variations between the studied groups as regards fasting blood glucose (F = 147.001, p < 0.001), HbA1c (F = 261.389, p < 0.001), and HDL cholesterol (F = 4.38, p = 0.017). Post hoc analysis revealed: FBG and HbA1c were significantly higher in both diabetic groups vs. control ($p1$, $p2$ < 0.001), but not between Non-DKD and DKD ($p3$ = 0.143 and 0.084, respectively). HDL was significantly higher in the non-DKD group vs. control ($p1$ = 0.025, $p2$ = 0.013), but not between Non-DKD and DKD ($p3$ = 0.176).

Total bilirubin (KW = 7.391, p = 0.025), was significantly higher in diabetics vs. control ($p1§$ = 0.007; $p2$ = 0.022). Direct bilirubin (KW = 14.095, p < 0.001), significantly higher in diabetics ($p1§$ < 0.001; $p2$ = 0.011). Creatinine (KW = 23.253, p < 0.001), urea (KW = 22.449, p < 0.001), and A/C ratio (KW = 46.578, p < 0.001), all showing significant pairwise differences between each group (control vs. non-DKD, control vs. DKD, and Non-DKD vs. DKD; all p < 0.05) (Table 2).

Table 2 reveals a statistically significant variation in serum lutein levels among the groups (F = 128.237, p < 0.001). Post hoc analysis exhibited significantly lower lutein levels in both diabetic groups compared to controls ($p1$ < 0.001, $p2$ < 0.001), and in DKD compared to non-DKD ($p3$ = 0.002). The lowest serum lutein level was observed among the DKD group, followed by the non-DKD group, with the highest level among the control group.

Estimated glomerular filtration rate (eGFR) differed significantly between the groups, with mean values of 94.3 ± 8.2 ml/min/1.73 m² in controls, 83.1 ± 10.5 ml/min/1.73 m² in the non-DKD diabetic group, and 52.7 ± 7.4 ml/min/1.73 m² in the DKD group (F = 63.714, p < 0.001), indicating progressively reduced renal function from controls to diabetics and most markedly in those with diabetic kidney disease (Table 2).

Table (3) demonstrates statistically significant negative correlations between serum lutein and several laboratory parameters, including fasting blood glucose (r = –0.824, p < 0.001), HbA1c (r = –0.859, p < 0.001), direct bilirubin (r = –0.462, p < 0.001), total bilirubin (r = –0.376, p = 0.002), creatinine (r = –0.487, p < 0.001), urea (r = –0.494, p < 0.001), and A/C ratio (r = –0.787, p < 0.001).

Serum lutein showed high diagnostic accuracy for diabetes. A cutoff of ≤0.515 µmol/L identified diabetes without DKD with 95.2% sensitivity, 90.5% specificity, and 92.9% accuracy (AUC = 0.988, p < 0.001). For diabetes with DKD, a cutoff of ≤0.36 µmol/L yielded 95.2% sensitivity, 81% specificity, and 85.7% accuracy (AUC = 0.961, p < 0.001), making lutein a strong biomarker for diabetes stratification (Table 4, Figure 1).

Table (5) shows a statistically significant negative correlation between A/C ratio and serum lutein (r = –0.787, p < 0.001). A/C ratio also revealed significant positive

correlations with fasting blood glucose (r = 0.617, p < 0.001), HbA1c (r = 0.593, p < 0.001), direct bilirubin (r = 0.44, p < 0.001), total bilirubin (r = 0.328, p = 0.009), creatinine (r = 0.6, p < 0.001), and urea (r = 0.554, p < 0.001).

Table (6) shows that among the variables significantly correlated with A/C ratio, only serum lutein remained an independent predictor in the linear stepwise regression model (β = –341.921, p < 0.001). This indicates that lower serum lutein levels are significantly and independently associated with higher A/C ratios.

Table (1): Comparison between the studied groups regarding demographic data.

	Control group	**Non-DKD group**	**DKD group**	χ^2	**p**
	n=21 (%)	**n=21 (%)**	**n=21 (%)**		
Gender					
Female	10 (47.6%)	11 (53.3%)	11 (53.3%)	0.127	0.938
Male	11 (53.3%)	10 (46.7%)	10 (46.7%)		
	Mean ± SD	**Mean ± SD**	**Mean ± SD**	F	p
Age (year)	68.67 ± 3.44	69.52 ± 5.17	71.52 ± 4.6	2.266	0.113

χ^2 Chi square test, F One way ANOVA test

Table (2): Comparison between the studied groups regarding CBC glycemic lipid profile, liver, kidney function tests and serum lutein.

	Control group	**Non-DKD group**	**DKD group**	**F**	**p**
	Mean ± SD	**Mean ± SD**	**Mean ± SD**		
Hemoglobin (g/dl)	13.2 ± 1.26	12.91 ± 1.35	12.6 ± 1.48	1.132	0.329
eGFR (ml/min/1.73 m²)	94.3 ± 8.2	83.1 ± 10.5	52.7 ± 7.4	63.714	<0.001
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	KW	p
TLC(10^3/mm^3)	6.5(5 – 8.1)	7(6.5 – 8.5)	7(6 – 8.53)	2.939	0.23
Platelet count (10^3/mm^3)	250(178.5 – 360.5)	345(186 – 430)	245(187 – 414.5)	0.971	0.615
FBG (mg/dl)	101.05 ± 6.31	141.86 ± 11.66	147.52 ± 9.98	147.001	<0.001**
Posthoc	P_1 <0.001**	P_2 <0.001**	P_3 0.143		
HbA1c (%)	5.17 ± 0.27	8.52 ± 0.68	8.91 ± 0.69	261.389	<0.001**
Posthoc	P1 <0.001**	P_2 <0.001**	P_3 0.084		
HDL (mg/dl)	42.24 ± 10.9	51.29 ± 9.64	45.71 ± 9.37	4.38	0.017*
Posthoc	P1 0.025*	P_2 0.013*	P_3 0.176		
LDL (mg/dl)	103.38 ± 14.39	106.95 ± 13.67	101.19 ± 15.03	0.86	0.428
Cholesterol (mg/dl)	165.52 ± 19.64	169.57 ± 19.3	165.57 ± 11.67	0.38	0.685

	Control group	Non-DKD group	DKD group	F	p
	Mean ± SD	Mean ± SD	Mean ± SD		
Triglycerides (mg/dl)	60(42 – 79.5)	54(46.5 – 90)	65.5(60.5 – 69.8)	0.02	0.99
Albumin(g/dl)	3.89 ± 0.32	3.83 ± 0.28	3.86 ± 0.38	0.144	0.866
T bilirubin (mg/dl)	0.43(0.34 – 0.57)	0.6(0.44 – 0.85)	0.57(0.49 – 0.72)	7.391	0.025*
Pairwise	$P_1^{\S}$ 0.007*	P_2 0.022*	P_3 0.893		
D bilirubin (mg/dl)	0.25(0.21 – 0.36)	0.36(0.26 – 0.44)	0.41(0.36 – 0.47)	14.095	<0.001**
Pairwise	$P_1^{\S}$ <0.001**	P_2 0.011*	P_3 0.255		
ALT (U/l)	28(20 – 33)	32(21 – 37)	33(27.3 – 39)	3.869	0.145
AST (U/L)	25(16.5 – 34)	21(14 – 29)	24(19.3 – 28.8)	1.51	0.47
Creatinine (mg/dl)	0.78(0.75 – 0.89)	0.98(0.81 – 1.05)	1.1(0.98 – 1.36)	23.253	<0.001**
Pairwise	$P_1^{\S}$ <0.001**	P_2 0.012*	P_3 0.02*		
Urea (mg/dl)	10(8 – 14)	12(11 – 16)	17.5(14 – 21)	22.449	<0.001**
Pairwise	$P_1^{\S}$ <0.001**	P_3 0.004*	P_4 <0.001**		
A/C ratio	11(9.5 – 14)	16(12.5 – 19)	351(224.3–533.8)	46.578	<0.001**
Pairwise	$P_1^{\S}$ <0.001**	P_2 0.024*	P_3 <0.001**		
Serum lutein	0.905 ± 0.222	0.389 ± 0.075	0.231 ± 0.078	128.237	<0.001**
Post hoc	P_1 <0.001**	P_2 <0.001**	P_3 0.002*		

F One way ANOVA test, KW Kruskal Wallis test , IQR interquartile range , p1 p for independent sample t test comparing diabetic patients versus control group , $P_1^{\S}$ p for Mann Whitney t test comparing diabetic patients versus control group , p2 difference between control group and diabetic non-DKD groups, p3 difference between non-DKD and DKD groups, *p<0.05 is statistically significant, **p≤0.001 is statistically highly significant, CBC: Complete Blood Count, WBCs: White Blood Cells, TLC: Total Leukocyte Count, FBG: Fasting Blood Glucose, HbA1c: Hemoglobin A1c (Glycated Hemoglobin), HDL: High-Density Lipoprotein, LDL: Low-Density Lipoprotein, ALT: Alanine Aminotransferase, AST: Aspartate Aminotransferase, T bilirubin: Total Bilirubin, D bilirubin: Direct Bilirubin, A/C ratio: Albumin-to-Creatinine Ratio, DKD: Diabetic Kidney Disease, SD: Standard Deviation, IQR: Interquartile Range, g/dl: grams per deciliter, mg/dl: milligrams per deciliter, U/l: units per liter

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Table (3): Correlation between serum lutein and laboratory parameters of studied patients.

	R	p
Hemoglobin (g/dl)	0.185	0.146
TLC (10^3/mm^3)	-0.246¥	0.052
Platelet count (10^3/mm^3)	-0.045¥	0.728

	R	p
FBG (mg/dl)	**-0.824**	**<0.001****
HbA1c (%)	**-0.859**	**<0.001****
HDL (mg/dl)	-0.226	0.075
LDL (mg/dl)	0.031	0.811
Cholesterol (mg/dl)	-0.038	0.766
Triglycerides (mg/dl)	-0.071¥	0.582
Albumin(g/dl)	0.001	0.999
T bilirubin (mg/dl)	***-0.376***¥	***0.002****
D bilirubin (mg/dl)	**-0.462**¥	**<0.001****
ALT (U/l)	-0.161¥	0.209
AST (U/L)	0.148¥	0.247
Creatinine (mg/dl)	**-0.487**¥	**<0.001****
Urea (mg/dl)	**-0.494**¥	**<0.001****
A/C ratio	**-0.787**¥	**<0.001****

*p<0.05 is statistically significant , **p≤0.001 is statistically highly significant , r Pearson correlation coefficient, ¥Spearman rank correlation coefficient

WBCs: White Blood Cells, TLC: Total Leukocyte Count, FBG: Fasting Blood Glucose, HbA1c: Hemoglobin A1c (Glycated Hemoglobin), HDL: High-Density Lipoprotein, LDL: Low-Density Lipoprotein, ALT: Alanine Aminotransferase, AST: Aspartate Aminotransferase, T bilirubin: Total Bilirubin, D bilirubin: Direct Bilirubin, A/C ratio: Albumin-to-Creatinine Ratio, DKD: Diabetic Kidney Disease, SD: Standard Deviation, IQR: Interquartile Range, g/dl: grams per deciliter, mg/dl: milligrams per deciliter, U/l: units per liter, R: Pearson or Spearman correlation coefficient, p: p-value (statistical significance).

Table (4): Performance of serum lutein in diagnosis of diabetes with and without diabetic kidney disease.

Diagnosis of diabetes without diabetic kidney disease							
Cutoff	**AUC**	**Sensitivity**	**Specificity**	**PPV**	**NPV**	**Accuracy**	**p**
≤0.515	0.988	95.2%	90.5%	90.9%	95%	92.9%	<0.001**
Diagnosis of diabetes with diabetic kidney disease							
≤0.36	0.961	95.2%	81%	71.4%	97.1%	85.7%	<0.001**

**p≤0.001 is statistically highly significant , AUC area under curve, PPV positive predictive value, NPV negative predictive value

Table (5): Correlation between A/C ratio and laboratory parameters of studied patients.

	r	p
Hemoglobin (g/dl)	0.185	0.146
TLC (10^3/mm^3)	0.116	0.366
Platelet count (10^3/mm^3)	0.054	0.674
FBG (mg/dl)	**0.617**	**<0.001****
HbA1c (%)	**0.593**	**<0.001****
HDL (mg/dl)	0.041	0.747
LDL (mg/dl)	-0.059	0.648
Cholesterol (mg/dl)	-0.035	0.782
Triglycerides (mg/dl)	0.043	0.74
Albumin(g/dl)	-0.054	0.673
T bilirubin (mg/dl)	**0.328**	**0.009***
D bilirubin (mg/dl)	**0.44**	**<0.001****
ALT (U/l)	0.188	0.141
AST (U/L)	-0.085	0.507
Creatinine (mg/dl)	**0.6**	**<0.001****
Urea (mg/dl)	**0.554**	**<0.001****
Serum lutein	**-0.787**	**<0.001****

*p<0.05 is statistically significant , **p≤0.001 is statistically highly significant, r Pearson correlation coefficient, ¥Spearman rank correlation coefficient TLC: Total Leukocyte Count, FBG: Fasting Blood Glucose, HbA1c: Hemoglobin A1c (Glycated Hemoglobin), HDL: High-Density Lipoprotein, LDL: Low-Density Lipoprotein, ALT: Alanine Aminotransferase, AST: Aspartate Aminotransferase, T bilirubin: Total Bilirubin, D bilirubin: Direct Bilirubin, A/C ratio: Albumin-to-Creatinine Ratio, DKD: Diabetic Kidney Disease, SD: Standard Deviation, IQR: Interquartile Range, g/dl: grams per deciliter, mg/dl: milligrams per deciliter, U/l: Units per Liter, r: Pearson correlation coefficient, R: Spearman correlation coefficient, p: p-value (indicates statistical significance),

Table (6): Linear stepwise regression analysis for factors associated with A/C ratio.

	Unstandardized Coefficients		Standardized Coefficients	t	p	95.0% Confidence Interval	
	β	Std. Error	Beta			Lower	Upper
(Constant)	313.014	45.607		6.863	<0.001**	221.818	404.210
serum lutein	-341.921	75.947	-.499	-4.502	<0.001**	-493.786	-190.057

**p≤0.001 is statistically highly significant

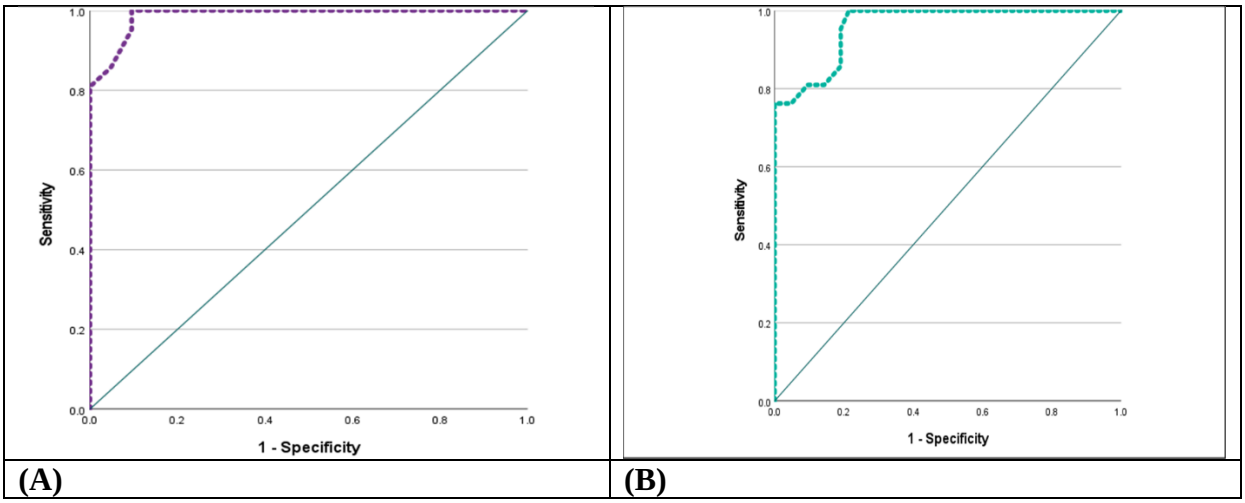

Figure (1): ROC curve showing Performance of serum lutein in diagnosis of: (A) diabetes without diabetic kidney disease (B) diabetes with diabetic kidney disease.

DISCUSSION

Our findings support and extend previous literature by specifically analyzing an elderly cohort, applying advanced quantification techniques, and establishing clinically relevant cut-offs for serum lutein that may facilitate earlier detection and risk stratification of DKD in this high-risk group. This contributes new data relevant for personalized nephrology care in aging populations.

Lutein, which is a naturally found oxygen-rich carotenoid, was known for its antioxidant as well as anti-inflammatory effects. In both type 2 diabetes mellitus and diabetic kidney disease, ongoing inflammation and oxidative stress were strongly linked to the disease process and were believed to contribute to their development and progression [6].

In the present study, demographic analysis across the groups did not reveal significant differences in sex distribution, with females representing nearly half of participants in all groups. The mean age was slightly higher in diabetic patients particularly those with DKD than controls, but the difference was not statistically meaningful. These findings align with the clinical understanding that DKD tends to manifest more commonly with longer diabetes duration and advancing age.

This trend was supported by findings from Gheith et al. [7] who noted that the incidence of diabetic nephropathy increases substantially after 10 years of diabetes, peaking between 10 and 20 years, and then declining thereafter. Notably, individuals with diabetes of over two decades who have not yet developed DKD are at relatively low risk of a later onset.

In addition, Chentli et al. [8] observed that complications of diabetes are more commonly encountered in older individuals, with cardiovascular disease being particularly prevalent due to the combination of aging and diabetes-associated early-onset atherosclerosis. Other complications such as vision impairment and dementia, including Alzheimer's disease, are also more common in elderly diabetic patients.

As for hematologic parameters, non-significant variations were revealed among the groups in hemoglobin levels, white blood cell counts, or platelet counts. These observations differ from results reported by Narjis et al. [9] who found that certain

components of the complete blood count, including leukocyte and hemoglobin levels, were altered in diabetic patients, especially in those with complications. They proposed that elevated WBC levels may reflect underlying chronic inflammation, potentially contributing to the development and progression of diabetes-related complications.

In our study, both glycemic control and lipid parameters showed significant variations among the examined groups. Fasting blood glucose and glycosylated hemoglobin levels were markedly elevated in diabetic individuals compared to controls, with the highest values noted in the group with diabetic kidney disease. The differences were statistically significant (FBG: $F = 147.001$, $p < 0.001$; HbA1c: $F = 261.389$, $p < 0.001$), and post-hoc analysis confirmed significant disparities between diabetic patients and controls, though not between the DKD and non-DKD diabetic subgroups.

Interestingly, high-density lipoprotein levels were found to be significantly elevated in the diabetic groups ($F = 4.38$, $p = 0.017$), while other lipid profile components—LDL, total cholesterol, and triglycerides did not show significant group differences. Triglyceride levels were consistent across all groups ($KW = 0.02$, $p = 0.99$).

The increased FBG and HbA1c levels observed among diabetic patients, especially those with DKD, are consistent with the chronic hyperglycemic state attributed to insulin resistance and β-cell dysfunction—two hallmark features of T2DM pathophysiology [10,11]. However, the similarity in glycemic indices between the DKD and non-DKD diabetic groups may suggest that glycemic levels alone do not reliably predict DKD progression. Instead, they are likely to contribute to ongoing oxidative stress and inflammatory processes that ultimately damage renal structures [12].

An unexpected finding was the elevation of HDL in diabetic patients. This could reflect the impact of therapeutic measures, such as statin administration or dietary and lifestyle modifications, which are commonly employed in diabetes care to reduce cardiovascular risk [13].

Supporting our findings, Shurraw et al. [14] investigated the link between glycemic control and long-term outcomes in a large cohort of diabetic individuals with chronic kidney disease. They found that elevated HbA1c levels were significantly and independently associated with increased mortality and progression to end-stage renal disease (ESRD), regardless of baseline kidney function. Their data reinforces the critical role of sustained hyperglycemia in worsening renal and systemic outcomes in T2DM.

In the current study, the assessment of liver and kidney function parameters revealed notable findings. There were no notable differences in serum albumin, ALT, or AST levels between the different groups studied. However, both total and direct bilirubin levels showed a significant increase in diabetic participants, especially those diagnosed with DKD ($KW = 7.391$, $p = 0.025$ for total bilirubin; $KW = 14.095$, $p < 0.001$ for direct bilirubin). Also, with all p-values dropping below 0.001, the DKD group had significantly higher levels of kidney function markers, such as serum creatinine, blood urea nitrogen (urea), and the albumin-to-creatinine ratio. These findings reinforce the presence of compromised renal function among DKD patients, as expected in the natural progression of diabetic microvascular complications.

Although some experimental evidence suggests that lutein can induce heme oxygenase-1 and potentially increase bilirubin as an adaptive antioxidant response, the higher bilirubin levels

observed in our diabetic groups with low lutein are likely due to the combined effects of diabetes-related metabolic disturbances, subclinical hepatic dysfunction (such as NAFLD), and impaired renal excretion. Therefore, the relationship between serum lutein and bilirubin in clinical populations may not be directly linear, and elevated bilirubin in this context reflects complex metabolic and organ-specific alterations beyond the influence of lutein alone [6].

Our observations are consistent with findings reported by Anzar et al. [15] who explored the role of lutein and zeaxanthin in individuals with T2DM and DKD, as well as other metabolic conditions. Their clinical study confirmed the safety of these carotenoids in terms of liver and renal markers and demonstrated a beneficial role in glycemic control. Although minor increases in bilirubin and urea levels were noted in the lutein-treated group, the overall hepatic and renal function remained within acceptable clinical limits. Importantly, the study highlighted a potential stabilizing effect of lutein supplementation on HbA1c and kidney function, further supporting its utility in metabolic health management.

Our study demonstrated that serum lutein concentrations were significantly reduced in diabetic patients compared to controls, with the lowest levels found in those with diabetic kidney disease (DKD) ($F = 128.237$, $p < 0.001$). Post-hoc analysis confirmed a statistically significant decline across all groups, including diabetic patients with and without DKD ($p = 0.002$). These findings suggest a progressive reduction in serum lutein as renal function deteriorates in the context of diabetes.

The observed depletion of serum lutein in diabetic and particularly DKD patients may be attributed to elevated oxidative stress and chronic inflammation—key features of both conditions. As lutein acts to neutralize reactive oxygen species, increased oxidative burden likely accelerates its consumption. Additionally, renal impairment may disrupt lutein metabolism and clearance, further exacerbating its reduction. This pattern highlights the possible utility of serum lutein as a biomarker for oxidative burden and DKD progression [16,17].

Our findings were in line with those of Sanlier et al. [6] who found significantly lower serum lutein levels among elderly individuals with T2DM and DKD, with notable differences between DKD and non-DKD diabetic subgroups ($p < 0.001$). Similarly, Ahn and Kim [18] reported decreased serum and retinal lutein concentrations in individuals with diabetes, supporting the association between systemic lutein depletion and diabetic metabolic stress.

Hu et al. [19] also contributed valuable data on carotenoids in chronic kidney disease (CKD). Their study found that elevated serum levels of multiple carotenoids, including lutein and zeaxanthin—were significantly correlated with reduced all-cause mortality among CKD patients. These findings underscore the potential protective roles of dietary carotenoids in renal disease.

Furthermore, our analysis revealed significant negative correlations between serum lutein and various markers of glycemic control and renal function: fasting blood glucose ($r = –0.824$, $p < 0.001$), HbA1c ($r = –0.859$, $p < 0.001$), total and direct bilirubin ($r = –0.376$ and $–0.462$, respectively), creatinine ($r = –0.487$), urea ($r = –0.494$), and albumin-to-creatinine ratio ($r = –0.787$); all p-values were < 0.001, except for total bilirubin ($p = 0.002$). No significant associations were found between lutein and hemoglobin, lipid fractions, or liver enzymes, reinforcing that lower lutein primarily reflects poor glycemic and renal indices rather than hepatic or hematologic alterations.

This correlation profile aligns with that of Sanlier et al. [6], who reported inverse relationships between serum lutein and parameters such as body mass index, fasting glucose, HbA1c, triglycerides, and urinary albumin-to-creatinine ratio, while identifying a positive association with HDL cholesterol.

Our results showed that serum lutein demonstrated strong diagnostic potential for both diabetic patients without kidney disease and those with diabetic kidney disease (DKD). ROC curve analysis yielded an area under the curve (AUC) of 0.988 ($p < 0.001$) for detecting diabetes without DKD, and 0.961 ($p < 0.001$) for identifying DKD among diabetics. A cutoff of ≤0.515 μmol/L for diabetes without DKD provided high sensitivity (95.2%) and specificity (90.5%), with an overall accuracy of 92.9%. For DKD detection, a cutoff of ≤0.36 μmol/L gave 95.2% sensitivity and 81% specificity, with an accuracy of 85.7%.

These findings are consistent with results reported by Sanlier et al. [6], who observed that serum lutein levels could effectively distinguish between healthy individuals, T2DM patients, and those with DKD. The reported AUC values were 0.880 and 0.779, respectively, with cut-off points identified at 0.433 μmol/L and 0.197 μmol/L. Both results were statistically significant, with p-values less than 0.001 [7].

In this study, the albumin-to-creatinine ratio showed a positive correlation with several metabolic and kidney-related markers. These included fasting blood glucose ($r = 0.617$, $p < 0.001$), HbA1c ($r = 0.593$, $p < 0.001$), total bilirubin ($r = 0.328$, $p = 0.009$), direct bilirubin ($r = 0.44$, $p < 0.001$), serum creatinine ($r = 0.6$, $p < 0.001$), and urea ($r = 0.554$, $p < 0.001$). Interestingly, serum lutein was found to have a strong negative correlation with the A/C ratio ($r = –0.787$, $p < 0.001$). On the other hand, no significant correlations were observed between the A/C ratio and hemoglobin levels, liver enzymes, or lipid parameters.

These results align with previous findings by Amelia et al. [19]. who evaluated the utility of A/C ratio as an early marker for diabetic nephropathy and found significant relationships between higher A/C levels and markers of poor glycemic control such as HbA1c and fasting glucose. Similar associations between A/C ratio and renal dysfunction in diabetes have been observed in other studies as well [20].

In our regression analysis, serum lutein emerged as a significant independent predictor of the A/C ratio. A reduction in lutein levels was strongly associated with increased albuminuria ($\beta = –341.921$, $p < 0.001$), with a standardized beta coefficient of –0.499 and 95% CI from –493.786 to –190.057.

The strong inverse relationship between serum lutein and the A/C ratio in DKD patients is likely due to lutein's antioxidative and anti-inflammatory effects. By neutralizing reactive oxygen species (ROS) and suppressing nuclear factor kappa B (NF-κB), lutein contributes to the protection of renal cells—especially podocytes—thereby preserving the glomerular filtration barrier. Additionally, lutein supports endothelial integrity and metabolic balance, which are critical in reducing microvascular injury and proteinuria. In contrast, lower lutein availability may aggravate oxidative damage, inflammatory cascades, and glomerular permeability, leading to a higher A/C ratio and progression of nephropathy [21-23].

Although the study provided valuable insights, there were a few limitations worth noting. To begin with, the sample size was somewhat limited, which might affect how broadly the results can be applied. Also, because the study had a cross-sectional design, it wasn't possible to draw clear conclusions about cause and effect between

serum lutein levels and the progression of DKD. Factors like diet and lifestyle, which could have an impact on lutein levels, weren't taken into account. NAFLD was not specifically screened for or excluded. As NAFLD is prevalent among elderly patients with T2DM and can independently affect liver enzymes and bilirubin levels, its presence may have confounded some of our findings regarding hepatic and metabolic markers. Lastly, the laboratory data were based on single time-point measurements, which may not accurately represent long-term metabolic or kidney function.

CONCLUSIONS

Serum lutein levels were significantly reduced in elderly patients with type 2 diabetes, especially those with diabetic kidney disease. Its strong association with glycemic and renal markers suggests that lutein may serve as a useful indicator for early renal involvement in this population.

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REFERENCES

1. Cho NH, Shaw JE, Karuranga S, Huang Y, da Rocha Fernandes JD, Ohlrogge AW, et al. IDF diabetes atlas: global estimates of diabetes prevalence for 2017 and projections for 2045. Diabetes Res Clin Pract. 2018;138:271–3.
2. International Diabetes Federation. IDF Diabetes Atlas, 10th ed. Brussels, Belgium: International Diabetes Federation; 2021.
3. Zhang L, Long J, Jiang W, Shi Y, He X, Zhou Z, et al. Trends in chronic kidney disease in China. N Engl J Med. 2016;375(9):905–6.
4. Kijlstra A, Tian Y, Kelly ER, Berendschot TT. Lutein: more than just a filter for blue light. Prog Retin Eye Res. 2012;31(4):303–15.
5. Folli F, Corradi D, Fanti P, Davalli A, Paez A, Giaccari A, et al. The role of oxidative stress in the pathogenesis of type 2 diabetes mellitus micro- and macrovascular complications: avenues for a mechanistic-based therapeutic approach. Curr Diabetes Rev. 2011;7(5):313.
6. Sanlier N, Gökcen BB, Sahin G. A review of the effects of some carotenoids on the complications of diabetes mellitus and its mechanisms. Nutrients. 2024;16(1):88.
7. Gheith O, Farouk N, Nampoory N, Halim MA, Al-Otaibi T. Diabetic kidney disease: worldwide difference of prevalence and risk factors. J Nephropharmacol. 2016;5(1):49.
8. Chentli F, Azzoug S, Mahgoun S. Diabetes mellitus in elderly. Indian J Endocrinol Metab. 2015;19(6):744–52.
9. Narjis M, Noreen M, Safi SZ, Ilahi NE, Alomar SY, Alkhuriji AF. Cross talk between complete blood count and progression of type 2 diabetes mellitus. J King Saud Univ Sci. 2021;33(6):101492.
10. Cernea S, Dobreanu M. Diabetes and beta cell function: from mechanisms to evaluation and clinical implications. Biochem Med (Zagreb). 2013;23(3):266–80.
11. Cohrs CM, Panzer JK, Drotar DM, Enos SJ, Kipke N, Chen C, et al. Dysfunction of persisting β cells is a key feature of early type 2 diabetes pathogenesis. Cell Rep. 2020;31(1):107469.
12. Jha JC, Chow BS, Cooper ME. Diabetes and kidney disease: role of oxidative stress. Antioxid Redox Signal. 2016;24(12):1271–85.
13. Kingwell BA, Chapman MJ, Kontush A, Miller NE. HDL-targeted therapies: progress, failures and future. Nat Rev Drug Discov. 2014;13(6):445–56.
14. Shurraw S, Hemmelgarn B, Lin M, Majumdar SR, Klarenbach S, Manns B, et al. Association between glycemic control and adverse outcomes in people with diabetes mellitus and chronic kidney disease: a population-based cohort study. Arch Intern Med. 2011;171(21):1920–7.
15. Anzar C, Joseph M, Sundaram R, Mathew J, Mathew J, George S, et al. Safety assessment of lutein and zeaxanthin supplementation and its effects on blood glucose levels, kidney functions, liver functions and bone health—a randomized, double-blind, placebo-controlled clinical study. medRxiv. 2023:2023.09.22.23295947.
16. Kijlstra A, Tian Y, Kelly ER, Berendschot TT. Lutein: more than just a filter for blue light. Prog Retin Eye Res. 2012;31(4):303–15.
17. Ahn YJ, Kim HJ. Lutein as a modulator of oxidative stress-mediated inflammatory diseases. Antioxidants. 2021;10(9):1448.
18. Hu Y, Cai X, Zhang N, Wang Y, Li Y, Wang Y, et al. Relation between dietary carotenoid intake, serum concentration, and mortality risk of CKD patients among US adults: national health and nutrition examination survey 2001–2014. Front Med. 2022;9:871767.
19. Amelia R, Sari DK, Muzasti RA, Fujiati II, Wijaya H. Early detection of diabetic nephropathy based on albumin creatinine ratio (ACR) in type 2 diabetes

mellitus patients in Medan, Indonesia. Fam Med Prim Care Rev. 2021;23(2):123–7.
20. Dorajoo SR, Ng JSL, Goh JHF, Lim SC, Lee J, Sabanayagam C, et al. HbA1c variability in type 2 diabetes is associated with the occurrence of new-onset albuminuria within three years. Diabetes Res Clin Pract. 2017;128:32–9.
21. Fatani AJ, Al-Rejaie SS, Parmar MY, Al-Shabanah OA, Al-Harbi NO, Al-Hosaini KA, et al. Lutein attenuates diabetic-induced renal damage via inhibiting oxidative and nitrosative stresses. Progr Nutr. 2017;19:57–65.
22. Kumar Pasupulati A, Chitra PS, Reddy GB. Advanced glycation end products mediated cellular and molecular events in the pathology of diabetic nephropathy. Biomol Concepts. 2016;7(5–6):293–309.
23. Leyane TS, Jere SW, Houreld NN. Oxidative stress in ageing and chronic degenerative pathologies: molecular mechanisms involved in counteracting oxidative stress and chronic inflammation. Int J Mol Sci.2022;23(13):7273.

Citation

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