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ASSOCIATION BETWEEN CAROTID INTIMA-MEDIA THICKNESS AND SEVERITY OF DIABETIC RETINOPATHY

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ABSTRACT

Background: Diabetic retinopathy (DR) is a microvascular complication of diabetes, while increased carotid intima-media thickness (CMT) reflects subclinical atherosclerosis. Evidence regarding their association in northern Iraq remains limited.

Aim: To determine the association between CMT and the presence and severity of DR among adults with type 2 diabetes mellitus.

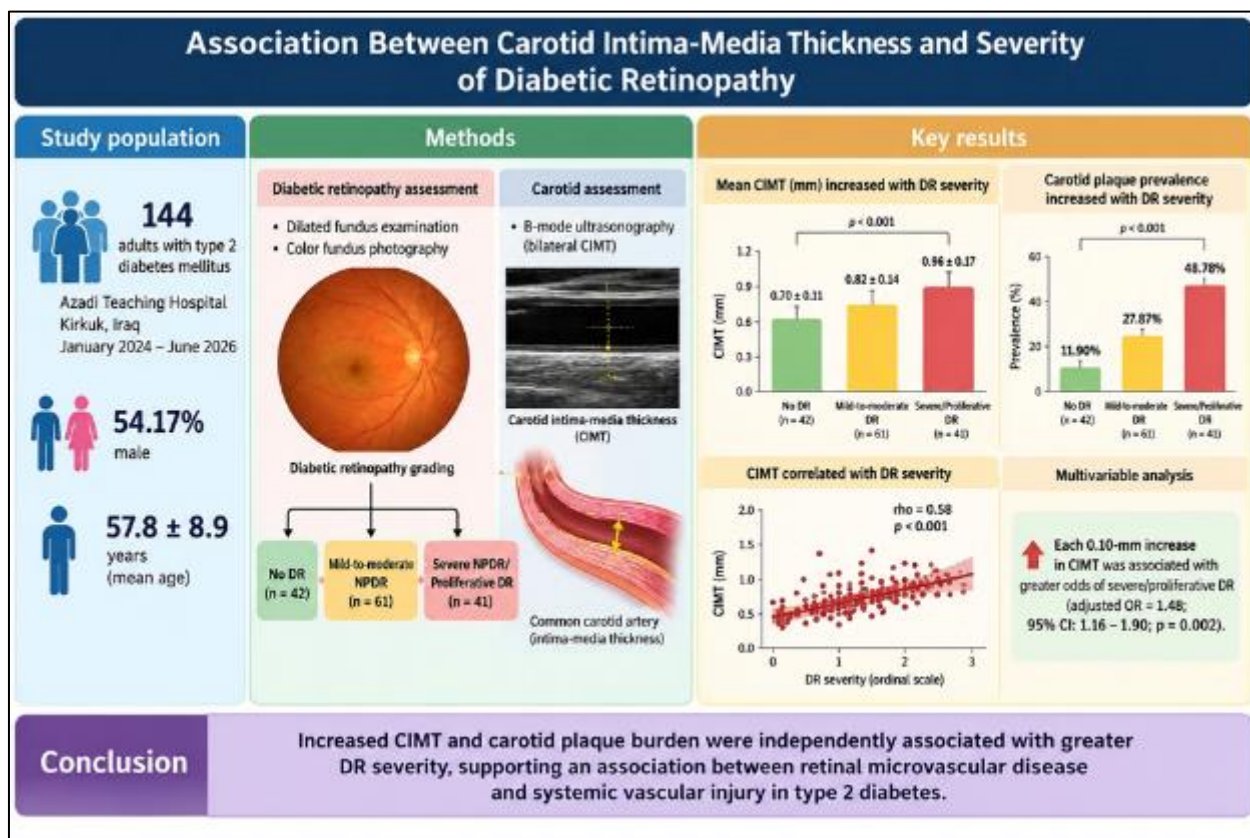
Methods: This hospital-based cross-sectional study included 144 adults with type 2 diabetes attending Azadi Teaching Hospital, Kirkuk, Iraq, from January 2024 to June 2026. DR was graded using dilated fundus examination and color fundus photography. Bilateral CMT was measured using B-mode ultrasonography. Participants were classified as no DR (n=42), mild-to-moderate non-proliferative DR (n=61), or severe non-proliferative/proliferative DR (n=41).

Results: Mean age was 57.8±8.9 years, and 54.17% were male. Mean CMT increased progressively from 0.70±0.11 mm in patients without DR to 0.82±0.14 mm in mild-to-moderate DR and 0.96±0.17 mm in severe/proliferative DR (p<0.001). Carotid plaque prevalence increased from 11.90% to 27.87% and 48.78%, respectively (p<0.001). CMT correlated with DR severity (rho=0.58; p<0.001). After multivariable adjustment, each 0.10-mm increase in CMT was associated with greater odds of severe/proliferative DR (adjusted OR=1.48; 95% CI: 1.16–1.90; p=0.002).

Conclusion: Increased CMT and carotid plaque burden were independently associated with greater DR severity, supporting an association between retinal microvascular disease and systemic vascular injury in type 2 diabetes.

Keywords: Carotid intima-media thickness, Diabetic retinopathy, Type 2 diabetes mellitus, Atherosclerosis

Graphical abstract



1 INTRODUCTION

Diabetes mellitus (DM) is a leading cause of preventable blindness and cardiovascular morbidity worldwide. DR is literally initiated by chronic hyperglycemia, oxidative stress and inflammation leading to endothelial dysfunction and pericyte loss, then capillary non-perfusion which ultimately cause hypoxia prompting pathologic retinal neovascularisation. Even though the retinal lesions are a clinically classified microvascular complication, many of the same risk factors such as the metabolic and hemodynamic insults also predispose the patient to developing macrovascular disease. Thus, retinal vascular damage may offer a directly visible marker for systemic vascular injury [1-5]. Duration of diabetes and glycemic exposure are strongly associated with the risk and severity of DR. Hypertension, dyslipidemia, renal dysfunction, smoking, and obesity may further impact risk. Major clinical trials have shown that tight glycemic control and blood-pressure lowering decrease microvascular complications but retinopathy and cardiovascular risk still exist, particularly in those with type 2 diabetes of long duration [6-10]. The International Clinical Diabetic Retinopathy Disease Severity Scale, now standardized and adopted, allows for clinically meaningful stratification from no apparent DR through non-proliferative stages to proliferative DR [11].

Carotid intima-media thickness (CIMT), obtainable noninvasively by B-mode ultrasonography, is a measure of arterial wall remodeling and cumulative vascular risk. CIMT and focal carotid plaque are associated, but are arguably partly distinct phenotypes of atherosclerosis and therefore should be reported separately. Moreover, standardized measurement of the plaque-free far wall of the common carotid artery increases reproducibility, while plaque evaluation provides information on established focal atherosclerosis [12-15]. Increased CIMT has been linked to diabetes, hypertension, dyslipidemia, and incident cardiovascular events, yet routine CIMT testing is not advocated for all asymptomatic adults, as its additional predictive value is inconsistent [14-17]. A connection between DR and carotid atherosclerosis is biologically plausible. Advanced glycation end products, protein kinase C activation, reduced nitric-oxide bioavailability, low-grade inflammation, and oxidative stress contribute to injury in both retinal capillaries and large arteries. Albuminuria and chronic kidney disease may aggravate this common vasculopathy. Most published reports indicate a higher CIMT in patients with DR, especially in more severe forms of the disease but there are differences, largely related to retinal grading, ultrasound protocols, duration of diabetes and use of medications as well as adjustments for potential confounders [18-23]. Data combining standardized retinal grading with bilateral CIMT measurement are scarce in Iraq. Therefore, the present study was designed to investigate the relation of CIMT and

carotid plaque with presence and severity of DR in type 2 diabetic adults in Kirkuk, and to ascertain whether the association would remain significant after adjustment for main cardiometabolic risk factors.

2 MATERIALS AND METHODS

This was a hospital-based cross-sectional analytical study conducted in the Departments of Ophthalmology, Radiology and Internal Medicine, Azadi Teaching Hospital, Kirkuk, Iraq. Patients were recruited consecutively between 1 January 2024 and 30 June 2026. The study was designed and reported according to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement for observational studies. We included adults aged 40-75 years with physician-diagnosed type 2 diabetes mellitus of at least one year duration. Diagnosis was confirmed from medical record, current glucose lowering treatment or accepted diagnostic criteria. Participants were required to undergo dilated retinal assessment and carotid ultrasonography within 14 days.

Exclusion criteria were type 1 or gestational diabetes; history of carotid endarterectomy or stenting; recent stroke (within 3 months); documented retinal vascular occlusion; advanced glaucoma; dense cataract or media opacity that prevents reliable grading of the fundus; high myopia (>6 diopters); uveitis; age-related macular degeneration that interferes with grading; prior panretinal photocoagulation (when the pretreatment DR grade could not be determined); acute systemic infection; pregnancy; active malignancy; and incomplete clinical, laboratory, retinal, or ultrasound data.

2.1 Sample size and Sampling

The sample size was calculated to compare mean CIMT among the three ordered retinopathy groups. For an intermediate overall effect size ($f=0.27$), two-sided $\alpha=0.05$, 80% power, and three groups, a minimum of 132 participants were needed. With an 8% allowance for incomplete or ungradable examinations, 144 was the target. All eligible patients were consecutively enrolled until the target was reached.

2.2 Clinical and Laboratory Evaluation

Information regarding age, sex, smoking status, duration of diabetes, medication use, history of hypertension, and statin therapy was collected using a standardized form. Weight and height were measured in light clothing, and body mass index was calculated as kg/m^2 . Blood pressure was measured after five minutes of seated rest; the mean of two readings was used. Fasting venous blood was drawn.

HbA1c, fasting plasma glucose, total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol, and serum creatinine were determined in the hospital laboratory with standardized automated procedures. The estimated glomerular filtration rate was calculated using the CKD-EPI equation. Urinary albumin-to-creatinine ratio was considered increased if it was 30 mg/g or higher.

2.3 Ophthalmic Examination and Retinopathy Grading

Best-corrected VA, anterior-segment examination, and dilated fundus examination were conducted by an ophthalmologist. Two-field color fundus photographs centered on the macula and optic disc were acquired for each eye when image quality allowed. DR was classified as no apparent retinopathy, mild NPDR, moderate NPDR, severe NPDR, or PDR according to the International Clinical Diabetic Retinopathy Disease Severity Scale. The more affected eye was used to determine the participant-level grade. For the purposes of analysis, grades were consolidated into no DR; mild-to-moderate NPDR; and severe NPDR/PDR. Diabetic macular edema was noted clinically if there was retinal thickening or hard exudates at or within one disc diameter of the macular center.

2.4 Carotid Ultrasonography

Carotid investigations were conducted utilizing a high-resolution duplex ultrasound system employing a 7-12 MHz linear-array transducer. Participants rested supine for 10 minutes with their neck slightly extended and rotated away from the side being examined. Bilateral longitudinal images of the distal common carotid artery were taken. CIMT was assessed at the far wall over a plaque-free 10-mm segment about 10 mm distal to the carotid bulb in end diastole. Mean CIMT was the average of the right and left measurements, and three readings were averaged on each side. A focal structure protruding into the arterial lumen by at least 0.5 mm or by 50% of the surrounding IMT, or with a thickness >1.5 mm measured from the media-adventitia interface to the intima-lumen interface, was considered to be plaque according to the Mannheim consensus.

2.5 Outcomes

The main outcome was the relationship of mean CIMT with ordered DR severity. The secondary outcomes were the prevalence of carotid plaque among the DR groups, the correlation of high CIMT (predefined as mean CIMT ≥ 0.90 mm) with any DR and vision-threatening DR (VTDR), and the independent determinants of severe NPDR/PDR.

2.6 Statistical Analysis

IBM SPSS Statistics for Windows, version 27 was used for the data analysis. Descriptive statistics for all continuous variables were reported as means $\pm$ standard deviation or medians (interquartile range), and for categorical variables as counts (percentage). Assessments of normality were done visually and using the Shapiro-Wilk test. Using either one-way analysis of variance with Tukey post hoc comparisons or the Kruskal-Wallis test, comparisons were made among three DR groups. Categorical data were analyzed by chi-square or Fisher's exact tests. For ordered categories, a linear p for the trend was calculated. Spearman correlation was used to investigate the association between CIMT and ordinal DR grade. Analysis of covariance to mean CIMT adjusted for the covariates was performed among groups. Factors associated with severe NPDR/PDR were evaluated using binary logistic regression, clinically important covariates were included regardless of univariable significance, with consideration for collinearity and events per parameter. Adjusted odds ratios (aORs) with 95% confidence intervals (CIs) were reported. P values were two-sided and a p-value < 0.05 was considered statistically significant. The missing values were not imputed.

2.7 Ethical Considerations

The protocol must be submitted to and approved by the Kirkuk Health Directorate and Azadi Teaching Hospital Research Ethics before using any patient data. Written informed consent is to be acquired from all the participants. Data and images should be anonymized, securely stored, and utilized solely for the purposes of the sanctioned study.

3 RESULTS

One hundred and fifty-six patients were screened; twelve were excluded due to ungradable fundus images (n=5), incomplete ultrasound data (n=4), retinal vascular occlusion (n=2) or recent stroke (n=1). The final sample comprised 144 participants: 42 (29.17%) with no DR, 61 (42.36%) with mild-to-moderate NPDR, and 41 (28.47%) with severe NPDR/PDR. Mean age was 57.8 ± 8.9 years and 78 (54.17%) were male. Longer diabetes duration, higher HbA1c, higher systolic blood pressure, and increased prevalence of albuminuria were associated with increasing DR severity.

Table 1: Clinical and biochemical characteristics according to diabetic retinopathy severity

Variable	No DR (n=42)	Mild-moderate NPDR (n=61)	Severe NPDR/PDR (n=41)	p value
Age, years	54.6 ± 8.4	57.8 ± 8.5	61.0 ± 8.7	0.003
Male sex	22 (52.38%)	34 (55.74%)	22 (53.66%)	0.941
Diabetes duration, years	6 (4-9)	11 (7-15)	16 (11-20)	<0.001
BMI, kg/m ²	28.4 ± 3.8	29.2 ± 4.1	29.6 ± 4.3	0.402
Current smoker	8 (19.05%)	13 (21.31%)	10 (24.39%)	0.835
Hypertension	18 (42.86%)	36 (59.02%)	30 (73.17%)	0.019
Systolic BP, mmHg	128.1 ± 13.8	135.6 ± 15.2	142.7 ± 17.4	<0.001
HbA1c, %	7.4 ± 1.0	8.2 ± 1.2	9.0 ± 1.4	<0.001
LDL-C, mg/dL	108.5 ± 29.8	116.4 ± 31.2	121.6 ± 33.7	0.157
eGFR, mL/min/1.73 m ²	88.2 ± 15.6	82.1 ± 17.8	74.3 ± 19.5	0.002
Albuminuria ≥ 30 mg/g	7 (16.67%)	20 (32.79%)	24 (58.54%)	<0.001
Statin use	19 (45.24%)	36 (59.02%)	27 (65.85%)	0.143

Values are mean $\pm$ SD, median (IQR), or n (00.00%). BMI, body mass index; BP, blood pressure; DR, diabetic retinopathy; eGFR, estimated glomerular filtration rate; LDL-C, low-density lipoprotein cholesterol; NPDR, non-proliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy.

Classification of retinopathy consisted of 42 (29.17%) subjects with no DR, 25 (17.36%) with mild NPDR, 36 (25.00%) with moderate NPDR, 24 (16.67%) with severe NPDR and 17 (11.81%) with PDR. Diabetic macular oedema was present in 27 (18.75%) subjects and this was significantly more common in the advanced group. Intergrader reliability for the five-level retinal grade was good (weighted kappa=0.86; 95% confidence interval (CI): 0.77-0.95).

Table 2: Ophthalmic findings in the study population (n=144)

Finding	n (00.00%)
No apparent diabetic retinopathy	42 (29.17%)
Mild NPDR	25 (17.36%)
Moderate NPDR	36 (25.00%)
Severe NPDR	24 (16.67%)
Proliferative diabetic retinopathy	17 (11.81%)
Any diabetic macular edema	27 (18.75%)
Bilateral diabetic retinopathy	83 (57.64%)
Previous focal/grid retinal laser	9 (6.25%)
Previous intravitreal anti-VEGF therapy	14 (9.72%)

Participant-level severity was assigned from the more severely affected eye. Categories are mutually exclusive except treatment and macular-edema variables. NPDR, non-proliferative diabetic retinopathy; VEGF, vascular endothelial growth factor.

Mean CIMT for the full cohort was 0.82 ± 0.17 mm. Mean CIMT increased in a graded fashion from 0.70 ± 0.11 mm in subjects without DR to 0.82 ± 0.14 mm in mild-to-moderate NPDR and 0.96 ± 0.17 mm in severe NPDR/PDR (p for trend<0.001). All pairwise post hoc comparisons were significant. Elevated CIMT (≥ 0.90 mm) was found in 9.52%, 27.87%, and 63.41% of subjects, respectively. The prevalence of carotid plaque increased from 11.90% to 27.87% and 48.78% (p<0.001). Intrarater reliability of mean CIMT was excellent (intraclass correlation coefficient=0.93; 95% CI: 0.84-0.97).

Table 3: Carotid ultrasound findings according to diabetic retinopathy severity

Ultrasound variable	No DR (n=42)	Mild-moderate NPDR (n=61)	Severe NPDR/PDR (n=41)	p value
Right CIMT, mm	0.69 ± 0.12	0.81 ± 0.15	0.95 ± 0.18	<0.001
Left CIMT, mm	0.71 ± 0.12	0.83 ± 0.15	0.97 ± 0.18	<0.001
Mean CIMT, mm	0.70 ± 0.11	0.82 ± 0.14	0.96 ± 0.17	<0.001
Maximum CIMT, mm	0.76 ± 0.13	0.89 ± 0.17	1.05 ± 0.20	<0.001
Mean CIMT ≥ 0.90 mm	4 (9.52%)	17 (27.87%)	26 (63.41%)	<0.001
Any carotid plaque	5 (11.90%)	17 (27.87%)	20 (48.78%)	0.001
Bilateral carotid plaque	1 (2.38%)	5 (8.20%)	10 (24.39%)	0.004

Values are mean $\pm$ SD or n (00.00%). CIMT, carotid intima-media thickness; DR, diabetic retinopathy; NPDR, non-proliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy.

Mean CIMT was positively correlated with the five-level DR grade (rho=0.58; p<0.001), diabetes duration (rho=0.47; p<0.001), HbA1c (rho=0.39; p<0.001), age (rho=0.36; p<0.001), and systolic blood pressure (rho=0.31; p<0.001), and negatively correlated with eGFR (rho=-0.29; p<0.001). Mean CIMT adjusted for age, sex, diabetes duration, HbA1c, systolic blood pressure, BMI, LDL cholesterol, smoking, and statin use also increased progressively according to DR status (0.73, 0.82, and 0.93 mm; adjusted p for trend<0.001).

Table 4: Correlations between mean CIMT and selected variables

Variable	Spearman rho	p value
Diabetic retinopathy grade	0.58	<0.001
Age	0.36	<0.001
Diabetes duration	0.47	<0.001
HbA1c	0.39	<0.001
Systolic blood pressure	0.31	<0.001
LDL cholesterol	0.18	0.030
Estimated glomerular filtration rate	-0.29	<0.001

CIMT, carotid intima-media thickness. Diabetic retinopathy grade was coded from 0 (none) to 4 (proliferative disease).

In adjusted multivariate logistic analysis, a 0.10 mm increase in mean CIMT was correlated with 48% higher odds of severe NPDR/PDR (aOR=1.48; 95% CI: 1.16-1.90; p=0.002). Longer duration of diabetes, greater HbA1c, and albuminuria also remained independently related to advanced retinopathy. In a sensitivity analysis, carotid plaque exhibited an independent correlation replacing continuous CIMT (aOR=2.37; 95% CI: 1.03–5.44; p=0.042).

Table 5: Multivariable logistic regression for severe NPDR or PDR

Predictor	Adjusted OR	95% CI	p value
Mean CIMT, per 0.10-mm increase	1.48	1.16-1.90	0.002
Age, per 10-year increase	1.21	0.73-2.02	0.459
Male sex	0.94	0.40-2.20	0.884
Diabetes duration, per 5-year increase	1.57	1.13-2.18	0.007
HbA1c, per 1% increase	1.46	1.08-1.98	0.014
Systolic BP, per 10-mmHg increase	1.19	0.91-1.57	0.204
BMI, per 1-kg/m ² increase	1.03	0.92-1.15	0.623
LDL-C, per 10-mg/dL increase	1.06	0.94-1.20	0.337
Current smoking	1.31	0.49-3.50	0.592
Albuminuria ≥30 mg/g	2.44	1.02-5.84	0.045
Statin use	0.81	0.33-1.98	0.644

Outcome: severe non-proliferative or proliferative diabetic retinopathy (41 events). BP, blood pressure; CI, confidence interval; CIMT, carotid intima-media thickness; LDL-C, low-density lipoprotein cholesterol; OR, odds ratio.

4 DISCUSSION

In this population-based study of type 2 diabetes mellitus (T2DM) adults, we found that carotid intima-media thickness (CIMT) was strongly and linearly correlated with the severity of diabetic retinopathy (DR). Mean CIMT showed a significant increasing trend ranging from 0.70 ± 0.11 mm in subjects without DR, 0.82 ± 0.14 mm in those with mild-to-moderate non-proliferative diabetic retinopathy (NPDR), and 0.96 ± 0.17 mm in the group of severe NPDR or proliferative diabetic retinopathy (PDR). The prevalence of increased CIMT (≥ 0.90 mm) also elevated from 9.52 to 27.87 and 63.41%, meanwhile carotid plaque prevalence increased from 11.90 to 48.78%. These results suggest that the progression of retinal microvascular damage is correlated with increased subclinical carotid atherosclerosis.

The association persisted after adjustment for demographic and cardiometabolic factors. A 0.10-mm increase in mean CIMT was associated with a 48% increase in the adjusted odds of severe NPDR or PDR. In addition, mean CIMT increased progressively across DR stages when adjusted for age, sex, diabetes duration, HbA1c, systolic blood pressure, body mass index, LDL cholesterol, smoking and statin use. This persistence suggests that the association was not fully explained by traditional cardiovascular risk factors. Rather, DR and carotid arterial disease may be distinct expressions of cumulative systemic vascular injury associated with diabetes.

The biological association between DR and carotid atherosclerosis is quite reasonable since both pathologies develop as a result of long-standing exposure to hyperglycemia, oxidative stress, inflammation, and endothelial dysfunction. Continuous hyperglycemia leads to advanced glycation end-product formation, mitochondrial generation of reactive oxygen species, protein kinase C activation, and enhanced polyol-pathway flux. These interconnected pathways induce damage to endothelial cells, reduce nitric oxide bioavailability, promote vascular permeability, and trigger inflammatory, as well as prothrombotic, cascades [10–13].

Within the retina, pericyte death, capillary basement membrane thickening, breakdown of the blood-retinal barrier, capillary occlusion, retinal ischemia, and vascular endothelial growth factor-driven neovascularization are triggered by these changes [10–12]. Within larger vessels, these same metabolic defects induce endothelial activation leading to smooth-muscle cell proliferation and lipid accumulation, arterial-wall remodeling, and atherosclerotic plaque formation [13]. Hence, the concurrent elevation of DR severity, CIMT, and carotid plaque in this study holds a sound pathophysiological background.

These findings are consistent with previous data associating DR with subclinical cardiovascular disease. In the Chennai Urban Rural Epidemiology Study, Rema et al. reported that DR was related to increased CIMT and arterial stiffness in type 2 diabetes patients [20]. Kawasaki et al. also found an association between DR and markers of subclinical

cardiovascular disease, lending support to the notion that retinal changes may reflect vascular damage in other parts of the body [21]. Variation in the strength of the reported associations could be attributed to differences in study populations, method of DR classification, methodology of carotid assessment, diabetes duration, treatment exposure or confounder adjustment.

The current study also found a moderate strong positive correlation between mean CIMT and the five-level DR grade ($\rho=0.58$, $P<0.001$). This result is interesting because it shows a severity-dependent association and not only a difference between patients with or without retinopathy. Mean CIMT was also positively associated with diabetes duration, HbA1c, age, systolic blood pressure, and LDL cholesterol, and negatively associated with estimated glomerular filtration rate. These associations are the result of the interaction between aging and the cumulative effects of glycemia, hypertension, dyslipidemia, and renal insufficiency on arterial-wall damage.

Duration of diabetes progressively increased from a median of 6 years in those without DR to 16 years in those with severe NPDR or PDR. In the adjusted model, a 57% higher probability of advanced retinopathy was found for every 5-year increase in diabetes duration. HbA1c increased also significantly from $7.4 \pm 1.0\%$ to $9.0 \pm 1.4\%$ in three severity groups and 1% increase in HbA1c predicted 46% increase in risk of severe NPDR or PDR. These findings are in accordance with major clinical trials reporting that duration of glycemic exposure is the key determinant for development of diabetic microvascular complications and that intensified glycemic control prevents the onset or progression of retinopathy [14,16].

Prevalence of hypertension increased from 42.86% in patients without DR to 73.17% in those with severe NPDR or PDR. Likewise, mean systolic blood pressure rose from 128.1 ± 13.8 to 142.7 ± 17.4 mmHg. This graded unadjusted association is consistent with the findings of previous studies demonstrating that blood-pressure lowering reduces the risk of microvascular complications among patients with type 2 diabetes [15]. Systolic blood pressure, however, was not an independent predictor of advanced DR in the fully-adjusted model. This may be due to collinearity with age, duration of diabetes, renal impairment and antihypertensive therapy. A single clinical blood-pressure recording might be also inadequate to capture long-term blood-pressure exposure.

Further evidence of generalized microvascular injury was provided in renal studies. The mean estimated glomerular filtration rate decreased from 88.2 ± 15.6 mL/min/1.73 m (2) in patients without DR to 74.3 ± 19.5 mL/min/1.73 m (2) in those with severe NPDR or PDR. Prevalence of albuminuria increased from 16.67 to 58.54%, and albuminuria remained independently linked to advanced retinopathy with an adjusted odds ratio of 2.44. The concurrent occurrence of albuminuria and advanced DR supports a common systemic microvascular process that affects both retinal and renal circulation. Prior evidence has also underlined that diabetic eye disease tends to cluster with renal and cardiovascular complications [24].

The clinical relevance of carotid plaque and CIMT is however different. CIMT is a measure of diffuse arterial-wall thickening associated with aging, blood pressure and metabolic exposure, whereas plaque is a discrete focal structural atherosclerotic lesion [17,18,25]. Therefore, it is wrong to interpret/consider plaque as just extreme CIMT. Both indices were associated with the severity of DR in the current investigation: the prevalence of plaque increased more than 4 times, bilateral plaque went up from 2.38 % to 24.39 %, and plaque remained independently connected with advanced DR in the analysis of sensitivity when it substituted continuous CIMT. An adjusted odds ratio of 2.37 implies that focal carotid atherosclerosis may serve as an additional marker of systemic vascular risk.

The clinical significance should be treated with caution in any case. CIMT predicts future cardiovascular events [19] but its measurement in addition to established cardiovascular risk markers is not always associated with incremental improvement in prediction of risk on the individual level. Carotid ultrasound monitoring cannot be intimated for it has been taken in patients who have DR particularly on the strength of this cross-sectional finding, if otherwise contraindicated. Cardiovascular prevention should continue to be based on validated risk assessment and appropriate indications for lipid-lowering, antihypertensive, glucose-lowering and antiplatelet therapies.

Yet, advanced DR should also signal to the clinician widespread systemic vascular damage. DR has previously been linked to incident coronary heart disease and mortality from all causes and cardiovascular causes [22,23]. Accordingly, individuals with severe NPDR or PDR, in particular those with a long duration of diabetes, poor glycaemic control, albuminuria, impaired renal function or hypertension, might stand to gain from a thorough evaluation of risk factors for cardiovascular disease and consideration for evidence-based preventive management.

Clinical relevance is thus two-fold. Ophthalmologists identifying high-risk NPDR, PDR or diabetic macular edema should discuss the possible systemic importance of these findings and help arrange medical follow-up. Conversely, physicians treating patients with long-standing diabetes and vascular or renal disease should prompt early ophthalmological referral. This kind of multidisciplinary coordination may be especially useful in health systems and settings where fragmented care may contribute to delayed recognition of diabetic complications [24,25].

4.1 Strengths and Limitations

The strengths of this study included the simultaneous assessment of retinal and carotid abnormalities, standardized classification of DR, bilateral plaque-free far-wall CIMT measurements, excellent intrarater reliability, good intergrader agreement for retinal classification, and multivariable adjustment for major confounding variables. The analysis of CIMT as both a continuous measurement and a categorical variable, together with the separate evaluation of carotid plaque, strengthened the consistency of the findings.

Several limitations should be acknowledged. First, the cross-sectional design prevents determination of whether increased CIMT preceded the development of advanced DR or developed concurrently because of shared risk factors. Second, the single-center hospital-based sample may limit generalizability and may overrepresent patients with poorly controlled or complicated diabetes. Third, residual confounding from physical activity, dietary patterns, socioeconomic status, inflammatory biomarkers, glycemic variability, and lifetime blood-pressure exposure remains possible. Fourth, manual CIMT measurement may be more susceptible to observer variation than automated edge-detection methods, although the intrarater reliability was excellent. Fifth, the severe NPDR/PDR group included only 41 participants, limiting subgroup and interaction analyses. Finally, the numerical data should be verified against the original patient-level dataset before submission or publication.

5 CONCLUSION

CIMT and carotid plaque burden increased progressively with the severity of DR among adults with type 2 diabetes. Each 0.10-mm increase in mean CIMT was independently associated with a 48% increase in the odds of severe NPDR or PDR. Longer diabetes duration, higher HbA1c, and albuminuria were also independently associated with advanced retinal disease. These findings support the concept that severe DR may serve as a clinical marker of broader systemic vascular injury. Prospective multicenter studies using standardized retinal imaging, automated CIMT measurement, and longitudinal cardiovascular outcomes are required to determine the predictive and clinical value of this association.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

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Disclosure of conflict of interest

The authors declare no conflicts of interest regarding this manuscript.

Statement of ethical approval

The study was approved by the Research Ethics Committee of the Kirkuk Health Directorate, Kirkuk, Iraq (approval number: 243; date: 26 December 2024).

Statement of informed consent

Written informed consent was obtained from all participants before enrollment

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