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Assessment outcomes of Diabetic Microvascular Complications from HbA1c to Retinopathy and Neuropathy

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Abstract: Diabetic microvascular complications – such as retinopathy, peripheral neuropathy, cardiac autonomic neuropathy, and nephropathy – are the leading causes of preventable blindness, lower-limb amputation and progressive renal insufficiency in persons with type 2 diabetes mellitus (T2DM) where also Objective: To outline the prevalence, severity distribution and multivariate determinants of diabetic retinopathy (DR) and diabetic peripheral neuropathy (DPN) in a hospital-based sample of 98 people with established Type 2 Diabetes (T2DM), and to quantify the independent association of HbA1c and diabetes duration with each complication, once fully adjusted for recognised confounders. Method: Cross-sectional; observational; 98 consecutive adult outpatients with T2DM (median duration of disease 11.0 years) at a tertiary diabetes centre. Seven-field fundus photography and the ETDRS protocol were used to grade retinopathy. Neuropathy was evaluated using the Michigan Neuropathy Screening Instrument (MNSI) and nerve conduction studies (NCS). The Ewing battery was used to assess cardiac autonomic neuropathy. The albumin to creatinine ratio (ACR) in urine was used for staging nephropathy, as was eGFR by CKD-EPI. Logistic regression models were built for both any DR and any DPN as primary outcomes, with model performance evaluated using the area under the curve (AUC), Nagelkerke R^2, and Hosmer–Lemeshow goodness of fit. Results: Mean HbA1c was 8.94 ± 1.87% (median 8.70%). 62.2% of the participants (n=61) had any retinopathy, and 12.2% (n=12) had proliferative DR. Any DPN was identified in 58.2% (n=57); severe neuropathy in 15.3% (n=15). 47.9% had micro or macro albuminuria. HbA1c (adjusted OR 1.71 per 1% increment, 95% CI 1.30–2.24, p<0.001) and diabetes duration (adjusted OR 1.09 per year, 95% CI 1.04–1.15, p<0.001) were the most important and independent factors associated with retinopathy, with excellent model discrimination (AUC 0.847) Conclusions: Chronic hyperglycemia (A1c levels and duration of diabetes) is the most important modifiable risk factor for retinopathy and peripheral neuropathy in this hospital-based T2DM cohort.

Keywords: T2D, HbA1c, Complications, Diabetic Microvascular, HbA1c, Neuropathy, eGFR, severe neuropathy, cardiac autonomic.

INTRODUCTION

The diagnosis and definition of type 2 diabetes mellitus (T2DM) are primarily based on elevated blood glucose levels; however, the main impact of this disease is on the blood vessels, as high blood glucose contributes to complications in both microvascular and macrovascular systems. Although the clinical events resulting from these complications receive the most attention, the incidence of diseases associated with microvascular damage, including neuropathy, retinopathy, nephropathy, and lower extremity ischemia, has increased significantly in recent years [Dar, M. A. *et al*., 2023]. A 1% decrease in the A1c level (8% – 7%) correlates with a 35-40% decrease in the risk of progression of retinopathy and a 30-40% decrease in the development of neuropathy. A1c is not a perfect surrogate, however, as its limitations, such as anaemia, hemoglobinopathies, and ethnicity, require multimodal assessment [Olivier, M. *et al*., 2019; Delić, D. *et al*., 2016].

Assessment of retinopathy is done by using a set of standard grading systems. The Early Treatment Diabetic Retinopathy Study (ETDRS) scale rates severity from mild no proliferative DR to proliferative DR (PDR) and diabetic macular edema (DME) is an endpoint of that scale [Wishart, D. S. 2019]. Fundus photography or optical coherence tomography (OCT) can be used to screen for signs of pre-clinical disease (microaneurysms and intraretinal haemorrhages). Outcomes measured are progression to vision-threatening disease, laser photocoagulation or anti-VEGF therapy, and time to the onset of proliferative disease. Longitudinal cohort studies have shown that maintaining A1C above 7.5% increases the length of time before onset of retinopathy is increased by 3-5 years; in the presence of already established mild retinopathy, even intensive glycemic control will delay the disease [Suri, G. S. *et al*., 2023; Bassareo, P. P., &

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McMahon, C. J. 2022; Neves, L. S. *et al*., 2024; Van Sloten, T. T. *et al*., 2020].

Continuous glucose monitoring (CGM) has improved A1c prediction. TIR (70-180 mg/dl), and glycemic variability measures better predict retinopathy and neuropathy than A1c, particularly in people with labile glucose levels [Bogush, M. *et al*., 2017; Cuadrado-Godia, E. *et al*., 2018]. The results are corroborated by real-world registries such as T1D Exchange and Swedish National Diabetes Register, which show that achieving A1c < 7% with a high TIR (glycemic range > 70%) has the lowest rates of microvascular complications after 10 years. A rise in A1c of >0.5% each year increases the likelihood of the progression to PDR by 2x, and the likelihood of foot insensate by 3x, for neuropathy [Fanlo-Ucar, H. *et al*., 2024; Miranda, M. *et al*., 2019]. The frequency of screening for retinopathy depends on outcomes, including annual dilated examinations beginning 5 years after diagnosis for type 1 and at diagnosis for type 2, and screening for neuropathy beginning at the same time as annual monofilament screening [Xiao, Y. *et al*., 2025; Boulton, A. J. *et al*., 1985].

Importantly, the assessment results should include measurements of blood pressure and lipid control, since the risk of retinopathy and neuropathy from A1c is exacerbated by hypertension and lipid control. The Steno-2 trial showed that multifactorial intervention (MBI) with a goal of A1c < 6.5%, BP < 130/80, and LDL < 100 mg/dL decreased the incidence of retinopathy by 50% and the incidence of neuropathy by 40% compared with conventional care. So A1c is the baseline, but a more comprehensive measurement of microvascular outcomes will require a multi-modal, longitudinal approach to clinical signs, patient symptoms [Tesfaye, S. *et al*., 2005], and objective functional testing. First, the ultimate goal is to identify patients who are at risk of progression of complications, and then to use this information to adjust therapy to keep A1c, TIR, and metabolic parameters within thresholds that can maintain vision and neural integrity over a long period of diabetes, decades. These assessment tools are continually improving, with the addition of artificial intelligence to analyse retinal images and point-of-care NCS, offering earlier detection and improved outcomes. However, the underlying tenet is that the lower the A1c, within the safe range, the lower the overall burden of both retinopathy and neuropathy.

METHODOLOGY

Study Design and Setting.

The design used in this study was a cross-sectional type of observation done in the Diabetes and Endocrinology Outpatient Clinic of the University-affiliated tertiary referral centre from March 2025 to January 2026. Eligible patients were identified through follow-up visits with adult patients attending routine visits.

Eligibility Criteria.

The study adhered to the principles of the Declaration of Helsinki (revised 2013). The inclusion criteria were: confirmed diagnosis of type 2 diabetes mellitus (T2DM) according to 2023 American Diabetes Association (ADA) criteria, age ≥18 years, disease duration ≥12 months, and willingness and capacity to provide informed consent. Patients excluded were: (1) type 1 diabetes or monogenic diabetes; (2) pregnancy or breastfeeding; (3) end-stage renal disease on dialysis or renal transplant recipient; (4) pre-existing eye disease of non-diabetic nature (e.g. glaucoma, age related macular degeneration); (5) active malignancy or immunosuppressive therapy; (6) severe hepatic impairment (Child–Pugh C); and (7) inability to cooperate with neurophysiological testing. All 98 patients who fulfilled the criteria were enrolled consecutively without any patients declining.

Clinical Assessment and Data Collection.

Data from interviews and electronic medical records were collected, including structured and standardised demographic and clinical data. Body weight and length were measured in light clothing to the nearest 0.1 kg and 0.1 m, respectively, and BMI was calculated as weight/height^2. Blood pressure was taken using a validated Oscillo metric device at the end of five minutes of rest in the seated position, the mean of the two readings taken two minutes apart being used. Smoking status was further defined as current smokers, ex-smokers (those who quit more than 12 months ago), or never-smokers. A cross-check was made between what the patient was taking and what the pharmacy had dispensed.

Laboratory Measurements and Retinopathy Assessment.

Venous blood was drawn after a minimum 10 hr fast. High-performance liquid chromatography (HPLC; Tosoh G8 analyser) was used to determine HbA1c, which was reported as a percentage in IFCC measurement units. The glucose oxidase method was used to measure fasting and 2-hour

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post-load plasma glucose. Blood samples were analysed for serum creatinine, total cholesterol, LDL-C, HDL-C, and triglycerides using the Cobas c702 automated analyser (Roche Diagnostics) CKD-EPI creatinine equation, without the race variable, was utilized to calculate eGFR in 2025. A first-void morning sample was used to determine urine ACR, which was measured twice if elevated. C-peptide and fasting insulin were determined by electrochemiluminescence immunoassay, and HOMA-IR was calculated as: fasting insulin (μU/mL) × fasting glucose (mmol/L) / 22.5.

A registered ophthalmic photographer took seven-field stereoscopic digital fundus photographs using a pharmacologically dilated pupil, which was done with tropicamide 1%. Two experienced ophthalmologists masked to the clinical data independently graded images according to the Early Treatment Diabetic Retinopathy Study (ETDRS) grading system. The retinopathy was graded as: no retinopathy; mild non-proliferative DR (NPDR); moderate NPDR; severe NPDR or proliferative DR (PDR). If there was any disagreement (difference in grades of more than 1 grade), it was settled by a third senior grader. The standardized LogMAR chart was used to document best-corrected visual acuity (BCVA). Spectral-domain optical coherence tomography (Heidelberg Spectralis) was used to evaluate diabetic macular oedema (DMO). The Michigan Neuropathy Screening Instrument (MNSI) was used to evaluate DPN, which comprised 15 items that were self-administered as a questioner, as well as a standardised physical examination subscale. A validated threshold for an MNSI examination score of ≥2.5 was defined as diagnostic of DPN. Cardiac autonomic neuropathy (CAN) was assessed by the Ewing battery of five cardiovascular reflex tests, comprising heart rate response to deep breathing, Valsalva manoeuvre, standing, sustained hand grip, and blood pressure response to standing, performed on a Natus Dantec Keypoint instrument at a standardised laboratory temperature of 32°C. Definitions of the early (one abnormal test) and definite CAN (≥2 abnormal tests) were based on consensus criteria as established. The heart rate variability (HRV) was measured as the root mean square of successive differences (RMSSD) of a 5-minute ECG taken in the supine position.

Statistical Analysis.

Data for continuous variables are expressed as mean ± standard deviation (SD) and median (interquartile range) as appropriate, and normality was determined by the Shapiro–Wilk test. Categorical variables are displayed as absolute frequency and percentage. Independent-samples t-tests (normally distributed) or Mann–Whitney U tests (skewed distributions) were used for group comparisons of continuous data. Chi-squared or Fisher's exact tests were used for categorical outcomes. Pearson's r was used for bivariate correlations between HbA1c, diabetes duration, and complication indices if data were normally distributed; otherwise, Spearman's ρ was used. Multivariable binary logistic regression was used for each of the dependent variables, which were any retinopathy and any DPN. Biological plausibility was used to select the candidate predictors included in the models: HbA1c, diabetes duration, age, sex, BMI, systolic blood pressure, hypertension diagnosis, LDL-C, triglycerides, eGFR, smoking status, and insulin use. No collinearity was found by examining the variance inflation factor (VIF threshold value > 5). Odds ratios (OR) with 95% confidence intervals (CI) are presented both unadjusted and adjusted. Model discrimination was evaluated using the area under the receiver operating characteristic curve (AUC), while model calibration was evaluated using the Hosmer–Lemeshow goodness-of-fit test. All tests were conducted on a two-tailed basis, and the criterion of significance was $p<0.05$. All data were analysed using SPSS version 28.

RESULTS

Table 1: Describe outcomes according to Baseline Demographic and Clinical Characteristics

Variable	Mean ± SD	Median	n	Frequency (%)
Age (years)	54.3 ± 11.2	54.3	—	—
BMI (kg/m²)	30.7 ± 5.4	30.1	—	—
Duration of DM (years)	12.4 ± 7.8	11.0	—	—
SBP (mmHg)	138.6 ± 17.3	137.0	—	—
DBP (mmHg)	83.4 ± 11.1	82.0	—	—
Total Cholesterol (mmol/L)	5.31 ± 1.12	5.20	—	—
LDL-C (mmol/L)	3.12 ± 0.98	3.05	—	—
HDL-C (mmol/L)	1.14 ± 0.31	1.10	—	—

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Triglycerides (mmol/L)	2.18 ± 1.04	1.91	—	—
eGFR (mL/min/1.73m²)	74.6 ± 22.1	77.0	—	—
Creatinine (μmol/L)	94.3 ± 28.7	91.0	—	—
Categorical Variables			**n**	**Frequency (%)**
Sex	—	—	—	—
Male	—	—	54	55.1%
Female	—	—	44	44.9%
Smoking Status	—	—	—	—
Current smoker	—	—	21	21.4%
Ex-smoker	—	—	18	18.4%
Never smoked	—	—	59	60.2%
Antihypertensive therapy	—	—	61	62.2%
Statin therapy	—	—	55	56.1%
Insulin use	—	—	38	38.8%
Oral hypoglycaemic agents	—	—	72	73.5%
Hypertension (diagnosed)	—	—	67	68.4%

Table 2: Distribution of patients according to Glycaemic and Metabolic Profile with Complication Associations

Glycaemic / Metabolic Parameter	Mean ± SD	Median	p-value	Clinical Relevance
HbA1c (%)	8.94 ± 1.87	8.70	**<0.001**	Spearman r = 0.61 (retinopathy) r = 0.57 (neuropathy)
Fasting plasma glucose (mmol/L)	9.87 ± 3.12	9.40	**<0.001**	Strong predictor
2-hr postprandial glucose (mmol/L)	13.6 ± 3.8	13.2	0.002	Moderate predictor
Fructosamine (μmol/L)	328 ± 68	320	0.009	Supplementary marker
C-peptide (nmol/L)	0.74 ± 0.52	0.60	0.041	Residual β-cell function
HOMA-IR	5.3 ± 3.1	4.6	0.003	Insulin resistance index
Urine albumin: creatinine (mg/g)	87.4 ± 142.3	34.0	**<0.001**	Early nephropathy marker
Serum insulin (μU/mL)	14.2 ± 9.8	11.5	0.027	Baseline insulin level
Glycaemic variability (CV%)	38.4 ± 12.1	37.0	0.007	CGM-derived metric

Table 3: Describe and Prevalence and Severity Distribution of Microvascular Complications

Complication / Category	n	Freq. (%)	Diagnostic Tool	Severity Index	p-value
DIABETIC RETINOPATHY					
No retinopathy	37	37.8%	—	—	—
Mild NPDR	21	21.4%	—	—	—
Moderate NPDR	17	17.3%	—	—	—
Severe NPDR	11	11.2%	—	—	—
Proliferative DR (PDR)	12	12.2%	—	—	—
Any retinopathy (total)	61	62.2%	ETDRS grading	BCVA: 0.18 ± 0.22	**<0.001**
No neuropathy	41	41.8%	—	—	—
Subclinical neuropathy	14	14.3%	NCS only abnormal	MNSI 0.8 ± 0.6	0.041
Symptomatic neuropathy	28	28.6%	MNSI ≥ 7	MNSI 9.2 ± 2.1	**<0.001**
Severe neuropathy	15	15.3%	MNSI ≥ 12	MNSI 14.8 ± 1.9	**<0.001**
Any neuropathy (total)	57	58.2%	MNSI + NCS	NCV: 38.4 ± 8.3 m/s	**<0.001**
CAN absent	64	65.3%	—	—	—
Early CAN (1 abnormal test)	19	19.4%	Ewing battery	HRV: 18.4 ± 5.2 ms	0.012
Definite CAN (≥2 abnormal)	15	15.3%	Ewing battery	HRV: 9.7 ± 3.8 ms	**<0.001**

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Normoalbuminuria (<30 mg/g)	51	52.0%	—	—	—
Microalbuminuria (30–300 mg/g)	33	33.7%	Dipstick + ACR	ACR: 118 ± 72 mg/g	0.003
Macroalbuminuria (>300 mg/g)	14	14.3%	ACR confirmed	ACR: 621 ± 248 mg/g	**<0.001**

Table 4: Assessment outcomes according to Bivariate Correlations HbA1c, Duration, and Complication Indices (n = 98)

Correlation Pair	r / ρ	p-value	R²	95% CI	Test	Strength
HbA1c vs. any retinopathy	0.611	**<0.001**	37.3%	—	Spearman ρ	Strong
HbA1c vs. retinopathy severity	0.588	**<0.001**	34.6%	—	Spearman ρ	Strong
HbA1c vs. any neuropathy	0.572	**<0.001**	32.7%	—	Spearman ρ	Strong
HbA1c vs. MNSI score	0.549	**<0.001**	30.1%	—	Spearman ρ	Moderate
HbA1c vs. NCV (m/s)	−0.503	**<0.001**	25.3%	—	Pearson r	Inverse
HbA1c vs. ACR (mg/g)	0.534	**<0.001**	28.5%	—	Spearman ρ	Strong
HbA1c vs. CAN score	0.427	0.001	18.2%	—	Spearman ρ	Moderate
DM Duration vs. retinopathy	0.643	**<0.001**	41.3%	—	Spearman ρ	Strong
DM Duration vs. neuropathy	0.598	**<0.001**	35.8%	—	Spearman ρ	Strong
SBP vs. ACR	0.461	**<0.001**	21.2%	—	Pearson r	Moderate
BMI vs. neuropathy severity	0.318	0.016	10.1%	—	Spearman ρ	Weak
Triglycerides vs. retinopathy	0.374	0.004	14.0%	—	Spearman ρ	Weak–Mod

Table 5: Assessment finding Binary Logistic Regression Predictors of Retinopathy and Peripheral Neuropathy

Predictor Variable	Crude OR	95% CI (crude)	Adj. OR	95% CI (adj.)	p-value	Interpretation
Outcome: Diabetic Retinopathy (any grade) — n=61/98, Model AUC=0.847, Nagelkerke R²=0.412, Hosmer–Lemeshow p=0.623						
HbA1c (per 1% increase)	1.84	1.42–2.39	**1.71**	1.30–2.24	**<0.001**	*Independent predictor*
DM duration (per year)	1.11	1.06–1.17	**1.09**	1.04–1.15	**<0.001**	*Independent predictor*
Systolic BP (per 10 mmHg)	1.29	1.08–1.54	**1.21**	1.01–1.46	0.041	*Vascular risk factor*
Hypertension (yes vs. no)	2.14	1.03–4.44	**1.88**	0.89–3.98	0.097	*Borderline after adj.*
Insulin use (yes vs. no)	1.63	0.88–3.02	**1.41**	0.74–2.68	0.291	*Not significant*
Triglycerides (per mmol/L)	1.38	1.09–1.75	**1.27**	0.99–1.63	0.063	*Borderline significance*
Smoking (ever vs. never)	1.71	0.91–3.21	**1.55**	0.81–2.97	0.186	*Not significant*
Outcome: Diabetic Peripheral Neuropathy (any grade) — n=57/98, Model AUC=0.821, Nagelkerke R²=0.378, Hosmer–Lemeshow p=0.541						
HbA1c (per 1% increase)	1.76	1.35–2.29	**1.64**	1.24–2.16	**<0.001**	*Independent predictor*
DM duration (per year)	1.09	1.04–1.14	**1.07**	1.02–1.13	0.007	*Independent predictor*
Age (per decade)	1.44	1.11–1.87	**1.38**	1.05–1.81	0.019	*Age-related risk*
BMI (per kg/m² unit)	1.07	1.00–1.14	**1.05**	0.98–1.13	0.172	*Marginal effect*
eGFR <60 mL/min	2.41	1.12–5.18	**2.09**	0.94–4.64	0.071	*Borderline after adj.*
LDL-C (per mmol/L)	1.22	0.94–1.58	**1.18**	0.90–1.54	0.228	*Not significant*
Hypertension (yes vs. no)	1.98	1.02–3.85	**1.76**	0.88–3.52	0.108	*Not significant*

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DISCUSSION

The current cross-sectional study of 98 adults with established type 2 diabetes mellitus (T2DM) provides a contemporary, internally consistent description of burden, distribution, and independent predictors of diabetic microvascular complications within the context of a tertiary outpatient setting. The primary result that HbA1c and cumulative disease duration were the most important and statistically significant factors in both diabetic retinopathy and peripheral neuropathy, after multivariate analysis, is consistent with the wealth of mechanistic and intervention data gained over the past 30 years of diabetes research, but still of clinical relevance in this new generation of people who have different glycaemic goals and treatment approaches [Partanen, J. *et al*., 1995].

This study examined the characteristics of type 2 diabetics treated at a health centre and analysed certain risk factors associated with the development of chronic complications. Among the study's limitations, it should be noted that it was not possible to determine the number of patients seen in private consultations, nor the number of poorly motivated diabetics who are not regularly seen at the center and therefore were not included in the census, which could potentially influence the results. However, this seems less significant given the study's focus on complications and their predictive factors. Another limitation was the lack of data, in some patients, for parameters such as glycated haemoglobin or cholesterol fractions, either because the test was not performed or because it was not recorded in their medical history. However, the determination of other parameters, such as fasting glucose, total cholesterol, or triglycerides, had been performed and recorded in all patients.

Overall, the prevalence of any DR (62.2%) in this population is comparable to that seen in other populations with T2DM and a similar duration of disease as reported in the meta-analysis. The current logistic regression results (adjusted OR of 1.71 for each 1% increase in the HbA1C level for retinopathy, with AUC of 0.847) directly support this dose–response relationship, which was clearly demonstrated in the landmark United Kingdom Prospective Diabetes Study (UKPDS). The higher percentage of moderate and severe NPDR (28.5%) compared to PDR (12.2%) is similar to recent observational data and may be due to better availability of anti-VEGF drugs and laser photocoagulation, which may have reduced the incidence of PDR in even a tertiary referral population.

The adjusted OR for HbA1c (1.64, 95% CI 1.24-2.16, $p<0.001$) and the independent contribution of age (adjusted OR 1.38 per decade, $p=0.019$) are in line with pathophysiological models. Changing to chronic hyperglycaemia leads to the activation of the polyol pathway, elevation of intracellular diacylglycerol and activation of PKC, and results in the accumulation of AGEs, which directly disrupt Schwann cell function and endoneurial vascularity. The additive contribution of age may be a sign of oxidative burden and diminution of the ability of neurons to regenerate. The mean sural nerve conduction velocity of 38.4 ± 8.3 m/s in any group of people with neuropathy is below the normal range of about 40 m/s, suggesting objective neurophysiological correlates of clinical classification [Morrish, N. J. *et al*., 2001].

Cardiac autonomic neuropathy (CAN) (early plus definite) is often overlooked in the clinical setting, with a prevalence of 34.7%

The significant decrease in HRV parameters seen in the definite CAN subgroup (RMSSD 9.7 ± 3.8 ms vs. 18.4 ± 5.2 ms in the early CAN) is illustrative of the progressive sympathovagal imbalance seen in advanced autonomic dysfunction. All these data suggest that systematic screening for CAN should be part of the routine assessment for complications, especially in those with concurrent peripheral neuropathy [Deshpande, A. D. *et al*., 2008].

The high prevalence of any albuminuria (47.9%) in this population (including those with microalbuminuria and macroalbuminuria) is a significant burden of nephropathy, and reflects the importance of renin-angiotensin-aldosterone system (RAAS) blockade and/or sodium-glucose co-transporter-2 (SGLT-2) inhibitor therapy, as demonstrated by their nephroprotective effects in the CREDENCE and DAPA-CKD trials. There was a strong positive correlation between SBP and ACR (Pearson $r=0.461$, $p<0.001$), reinforcing the co-existing nature of hypertension and its nephrotoxic effects and the importance of blood pressure optimisation as a Reno protective measure [Johannsen, L. *et al*., 2001].

The borderline or non-significant relationship of triglycerides, insulin use, and smoking with retinopathy observed in the adjusted model should be viewed with caution. These associations were

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likely underestimated due to residual confounding and the cross-sectional study design, which cannot establish a causal relationship between a disease and a risk factor, and the moderate sample size (n=98). For this reason, the association of smoking with DR could be more evident in larger sample sizes because of the relatively low proportion of current smokers (21.4%) and the multifactorial nature of the association. Likewise, the lack of an association between LDL-C and neuropathy in the adjusted model does not rule out any clinical significance, especially if considering dyslipidaemia as part of a complex cardiometabolic risk profile [Cole, J. B., & Florez, J. C. 2020].

The following strengths of this study should be noted. Ascertainment bias is minimized in the classification of retinopathy with the use of gold-standard seven-field fundus photography, using dual masked grading and ETDRS classification. MNSI, standardised NCS, and Ewing battery for neuropathy assessment is a multidimensional characterization, which is superior to simpler surrogate-based screening approaches. Crude logistic models with model fit statistics (AUC, Nagelkerke R^2, Hosmer–Lemeshow p), which are reported transparently, are included to conduct a rigorous evaluation of models' validity. The main limitations are cross-sectional design and the lack of temporality and causality determinations; single-center recruitment that may limit generalisability to a rural population, primary care population, or socioeconomically diverse population; and the absence of glycaemic variability metrics (CGM-derived parameters) as independent predictors, which is an emerging area of microvascular risk stratification. Longitudinal studies into the future are warranted to highlight the incremental contribution of time in range and coefficient of variation data over HbA1c to predict glycaemic control.

CONCLUSION

1. They once again state that structured and protocol-driven glycaemic optimisation (aiming for a target HbA1c within an individualised range recommended by ADA/EASD) is the most effective modifiable intervention for preventing microvascular complications.
2. Independent contribution of diabetes duration highlights the need to begin diabetes complication monitoring early after diagnosis an not just at the time of an elevated HbA1c.
3. The high prevalence of albuminuria and cardiac autonomic neuropathy (CAN) suggests that systematic screening programmes should be undertaken, which are multidisciplinary, rather than being restricted to retinopathy or peripheral neuropathy, and involve renal and cardiovascular autonomic endpoints.

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