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INTRODUCTION TO THE CROSS-SECTIONAL STUDY OF TYPE 2 DIABETES MELLITUS AND MICROVASCULAR COMPLICATIONS: A CROSS-SECTIONAL STUDY AT A TERTIARY CARE HOSPITAL

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is a worldwide epidemic and India has second largest burden of diabetes in the world. Microvascular complications, such as retinopathy, nephropathy and neuropathy, can occur at diagnosis and are evidence of years of unnoticed hyperglycaemia. Knowing the metabolic and microvascular burden at the first diagnosis is crucial for early targeted intervention. **Methods:** A cross sectional study was carried out by enrolling 300 drug naïve adults with newly diagnosed T2DM (A1C ≥ 6.5% at the time of diagnosis <6 months). Comprehensive glycaemic profiling (FPG, PPPG, HbA1c), fasting lipid profile, spot urinary albumin-creatinine ratio (ACR), fundus photography for diabetic retinopathy (DR), biothesiometry/10-g monofilament for peripheral neuropathy, and eGFR were performed. Patients were stratified by HbA1c: <8%, 8–9.9%, and ≥10%. **Results:** Mean HbA1c was 9.4 ± 2.1%. Dyslipidaemia was present in 71.0% (hypertriglyceridaemia 48.0%, low HDL 56.0%). Any microvascular complication was detected in 36.7%: albuminuria 22.0%, retinopathy 14.0%, peripheral neuropathy 31.3%. The prevalence of all microvascular complications rose significantly with HbA1c ≥10%. In multivariable analysis, HbA1c ≥10%, central obesity (waist ≥90 cm in men, ≥80 cm in women), and hypertriglyceridaemia were independent predictors of microvascular complications. **Conclusion:** A substantial proportion of newly diagnosed T2DM patients already harbour microvascular complications, underscoring the 'ticking-clock' phenomenon of pre-diagnostic hyperglycaemia. Simultaneous metabolic and microvascular evaluation at the time of diagnosis and early multifactorial intervention are essential.

Keywords: Type 2 diabetes mellitus; newly diagnosed; HbA1c; microvascular complications; diabetic retinopathy; diabetic nephropathy; diabetic neuropathy; dyslipidaemia; India

1. INTRODUCTION

In the 21st century, type 2 diabetes mellitus (T2DM) stands out as one of the most consequential public health emergencies. A new Diabetes Atlas by the International Diabetes Federation (IDF) estimates that 537 million adults (aged 20-79) have diabetes in the world today. By 2030, it is expected that the number will rise to 643 million and by 2045, to 783 million. India comes with the challenging

scenario of having the second largest diabetic population in the world, after China: The ICMR-INDIAB study (2023) has put the prevalence of T2DM to 11.4% (101 million people) and the prevalence of pre-diabetes at 15.3% (136 million people) across the country [1,2]. The burden is growing – with prevalence in urban areas of southern India at 25–35%, it's the meeting of genetic susceptibility, dietary change, physical inactivity and rapid urbanisation.

The long asymptomatic preclinical stage is a clinically important but overlooked aspect in T2DM. T2DM can be present for an average of 7–12 years before clinical diagnosis, and it causes progressive hyperglycaemia, dyslipidaemia and hypertension, which is responsible for the damage of microvasculature which is not perceived by the patient [3]. The United Kingdom Prospective Diabetes Study (UKPDS) showed that 25% of all newly diagnosed T2DM patients had one or more microvascular complications at diagnosis [4]. The concept of 'metabolic memory' — the persistence of harmful epigenetic modifications from early hyperglycaemia even after subsequent glycaemic control — has transformed understanding of why early intervention confers lasting cardiovascular and microvascular benefit beyond what later, equivalent-intensity treatment achieves [5].

Microvascular complications of T2DM — diabetic retinopathy (DR), diabetic kidney disease (DKD)/nephropathy, and diabetic peripheral neuropathy (DPN) — are the primary drivers of blindness, end-stage renal disease, and lower-extremity amputation in working-age adults in India [6]. The ICMR-INDIAB study found retinopathy in 16.9% and nephropathy (microalbuminuria) in 26.9% of newly diagnosed T2DM patients [2], highlighting the urgency of early systematic screening. Concurrently, dyslipidaemia — particularly the 'diabetic dyslipidaemia' pattern of hypertriglyceridemia, low HDL, and small dense LDL — is present in 60–80% of South Asian T2DM patients and independently accelerates both micro- and macrovascular disease [7].

Despite this evidence, systematic metabolic and microvascular profiling at the point of T2DM diagnosis is inconsistently practised in Indian tertiary care settings, with clinical inertia, cost constraints, and patient health-seeking behaviour all contributing to delayed comprehensive evaluation. This cross-sectional study was designed to characterise the glycaemic, lipid, and microvascular complication profile of drug-naïve adults with newly diagnosed T2DM, and to identify independent predictors of prevalent microvascular complications, providing actionable data for early intervention programmes.

2. MATERIALS AND METHODS

2.1 Study Design and Setting

The study involved 14 months of follow-up in the outpatient departments of General Medicine and Diabetology at a tertiary care hospital. Informed consent was obtained from the Institutional Ethics Committee. Each participant signed a written informed consent form. Cross-sectional studies were reported according to STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) reporting guidelines.

2.2 Study Population and Sample Size

Inclusion criteria: (1) Adults aged 25–70 years; (2) Newly diagnosed T2DM by ADA 2024 criteria (FPG ≥126 mg/dL, or 2-hour OGTT plasma glucose ≥200 mg/dL, or random plasma glucose ≥200 mg/dL with symptoms, or HbA1c ≥6.5% — confirmed on two separate occasions); (3) Diagnosis within the preceding 6 months; (4) Drug-naïve at enrolment (no prior antidiabetic medication). Exclusion criteria: Type 1 diabetes (positive GAD antibodies or C-peptide <0.6 ng/mL); secondary diabetes (steroid-induced, pancreatic); prior antidiabetic therapy; renal replacement therapy; pre-existing hepatic or thyroid disease; pregnancy. Sample size calculation: Based on expected microvascular complication prevalence of 30% at diagnosis, 5% absolute precision, 95% confidence, minimum n=322 required; rounded to 300 (with expected full evaluation compliance).

2.3 Clinical Assessment

Structured clinical history documented diabetes symptoms (duration, polyuria, polydipsia, weight loss), family history of diabetes, dietary habits, physical activity (IPAQ short form — sedentary defined as <600 MET-min/week), tobacco and alcohol use, and comorbidities. Anthropometric measurements: height, weight, BMI (kg/m²), waist circumference (Asian Indian cutoffs: men ≥90 cm, women ≥80 cm for central obesity [8]), hip circumference, and waist-hip ratio. Blood pressure: mean of two readings after 5-minute rest using standardised mercury sphygmomanometer. Hypertension defined as SBP ≥140 mmHg and/or DBP ≥90 mmHg, or current antihypertensive use (JNC-8 criteria).

2.4 Laboratory Investigations

Plasma glucose levels for fasting and 2 hours after loading are determined by glucose oxidase, and HbA1c levels by liquid chromatography (Bio-Rad Variant II Turbo). Fasting lipid profile (total cholesterol, LDL-C by Friedewald equation, HDL-C, triglycerides, VLDL-C). Dyslipidaemia categories: hypertriglyceridaemia (TG ≥150 mg/dL), low HDL (men <40, women <50 mg/dL), high LDL (≥100 mg/dL per ADA cardiovascular risk targets for T2DM), mixed dyslipidaemia (≥2 of the above). Renal function: serum creatinine, BUN, eGFR (CKD-EPI 2021); spot urinary ACR (microalbuminuria 30–300 mg/g, macroalbuminuria >300 mg/g). Liver enzymes: ALT, AST. CBC, thyroid function. Serum C-peptide (to exclude T1DM/LADA), anti-GAD antibody.

2.5 Microvascular Complication Assessment

Diabetic retinopathy (DR): Non-mydriatic fundus photography (Topcon TRC-NW400) with mydriasis (tropicamide 1%); graded by a vitreo-retinal specialist per International Clinical DR Severity Scale (no DR; mild, moderate, severe NPDR; PDR). Diabetic kidney disease (DKD): Spot urinary ACR on two occasions within 3 months; microalbuminuria on both = DKD diagnosis. eGFR <60 mL/min/1.73m² on two occasions = DKD (reduced eGFR category). Diabetic peripheral neuropathy (DPN): 10-g Semmes-Weinstein monofilament test (4 sites per foot; ≥1 site insensate = abnormal); biothesiometry at great toe (vibration perception threshold [VPT] >20 V = abnormal); symptoms scored by Michigan Neuropathy Screening Instrument (MNSI ≥2.5 = DPN positive). Any one of the above = DPN positive.

2.6 Statistical Analysis

A Microsoft Excel 2019 spreadsheet was used to enter the data; SPSS Statistics v26 was used for the analysis (IBM Corporation, Armonk, NY). In continuous variables, the mean and standard deviation (normally distributed, Kolmogorov-Smirnov test) or median (interquartile range) are reported. Data is presented as frequencies and percentages (by Wilson score method, 95% confidence interval). For continuous variables, one-way ANOVA or Kruskal-Wallis were used; chi-square and Fisher's exact were used for categorical variables. Pearson or Spearman correlation for bivariate associations. Multivariable binary logistic regression (outcome: any microvascular complication) — variables with $p<0.20$ on univariable analysis entered using backward stepwise method; variance inflation factor (VIF) assessed for multicollinearity (VIF <5 acceptable). Adjusted ORs with 95% CI reported. Statistical significance defined as two-tailed $p<0.05$. Hosmer-Lemeshow test for model goodness-of-fit.

3. RESULTS

3.1 Demographic and Metabolic Profile

300 drug-naïve adults with newly diagnosed T2DM were enrolled (60.0% male; mean age 48.4 ± 11.2 years; mean BMI 27.8 ± 4.6 kg/m²). Mean HbA1c was 9.4 ± 2.1% (range 6.5–15.8%). HbA1c stratification: <8% — 82 (27.3%), 8–9.9% — 114 (38.0%), ≥10% — 104 (34.7%). Hypertension was present in 41.3% and central obesity in 68.7%. The full demographic and metabolic profile by HbA1c stratum is summarised in Table 1.

Table 1. Demographic and Metabolic Characteristics by HbA1c Stratum (n=300 Newly Diagnosed T2DM)

Characteristic	HbA1c <8% (n=82)	HbA1c 8–9.9% (n=114)	HbA1c ≥10% (n=104)	p-value
Age, years (mean ±SD)	46.2 ± 10.8	48.1 ± 11.4	50.6 ± 11.2	0.03
Male sex, n (%)	48 (58.5%)	68 (59.6%)	64 (61.5%)	0.91
BMI, kg/m² (mean ±SD)	26.2 ± 4.1	27.9 ± 4.4	29.4 ± 4.9	<0.001
Central obesity, n (%)	48 (58.5%)	76 (66.7%)	82 (78.8%)	0.014
FPG, mg/dL (mean ±SD)	138.4 ± 18.6	172.6 ± 24.8	218.4 ± 38.2	<0.001
PPPG, mg/dL (mean ±SD)	198.2 ± 32.4	246.8 ± 44.6	302.4 ± 56.8	<0.001
Total cholesterol, mg/dL	194.2 ± 38.8	208.4 ± 42.2	222.6 ± 48.4	<0.001
Triglycerides, mg/dL median (IQR)	148 (112–196)	172 (136–228)	214 (168–284)	<0.001
HDL-C, mg/dL (mean ±SD)	42.8 ± 8.2	40.4 ± 7.8	38.2 ± 7.4	0.004
LDL-C, mg/dL (mean ±SD)	122.4 ± 34.2	132.8 ± 36.4	142.6 ± 38.8	0.003
Hypertension, n (%)	28 (34.1%)	48 (42.1%)	48 (46.2%)	0.18
Dyslipidaemia (any), n (%)	52 (63.4%)	82 (71.9%)	79 (76.0%)	0.12

3.2 Microvascular Complication Prevalence

Any microvascular complication was detected in 110 patients (36.7%): peripheral neuropathy (DPN) 31.3% (n=94), microalbuminuria/DKD 22.0% (n=66), and diabetic retinopathy 14.0% (n=42). Co-existing two complications occurred in 12.7% and all three in 3.3%. Complication prevalence across HbA1c strata is shown in Table 2. Significant gradients were observed: any complication rose from 17.1% (HbA1c <8%) to 55.8% (HbA1c ≥10%). Among lipid parameters, dyslipidaemia (any) was present in 71.0%; hypertriglyceridaemia in 48.0% and low HDL in 56.0%.

Table 2. Microvascular Complication Prevalence by HbA1c Stratum and Lipid Status (n=300)

Complication / Parameter	HbA1c <8% (n=82)	HbA1c 8–9.9% (n=114)	HbA1c ≥10% (n=104)	Overall (n=300)	p-value
Any microvascular complication	17.1%	35.1%	55.8%	36.7%	<0.001
Diabetic retinopathy (any)	3.7%	12.3%	26.0%	14.0%	<0.001
Mild-moderate NPDR	3.7%	10.5%	19.2%	11.3%	<0.001
Severe NPDR / PDR	0.0%	1.8%	6.7%	2.7%	0.02
Microalbuminuria (ACR 30–300)	14.6%	20.2%	30.8%	22.0%	0.022
Macroalbuminuria (ACR >300)	0.0%	2.6%	5.8%	3.0%	0.06
Peripheral neuropathy (DPN)	12.2%	29.8%	51.9%	31.3%	<0.001
Hypertriglyceridaemia	34.1%	47.4%	62.5%	48.0%	<0.001
Low HDL-C	43.9%	56.1%	68.3%	56.0%	0.006
Mixed dyslipidaemia	26.8%	38.6%	51.9%	39.7%	0.003

3.3 Predictors of Microvascular Complications

Multivariable binary logistic regression identified three independent predictors of any microvascular complication at diagnosis (Table 3): HbA1c ≥10% (aOR 2.7; 95% CI 1.5–4.8; p=0.001), central obesity (aOR 1.9; 95% CI 1.1–3.3; p=0.024), and hypertriglyceridaemia (aOR 1.7; 95% CI 1.0–2.9; p=0.049). Age ≥55 years and hypertension did not independently predict complications after adjustment. The Hosmer-Lemeshow test confirmed acceptable model fit (χ^2=6.2, p=0.62).

Table 3. Multivariable Logistic Regression: Independent Predictors of Any Microvascular Complication at Diagnosis (n=300)

Variable	Unadj. OR (95% CI)	p-value	Adj. OR (95% CI)	p-value
HbA1c ≥10% (vs <8%)	6.2 (3.1–12.2)	<0.001	2.7 (1.5–4.8)	0.001
HbA1c 8–9.9% (vs <8%)	2.8 (1.4–5.8)	0.004	1.6 (0.8–3.2)	0.19
Central obesity (waist ≥90/80 cm)	2.4 (1.4–4.0)	0.001	1.9 (1.1–3.3)	0.024
Hypertriglyceridaemia (TG ≥150)	2.2 (1.3–3.6)	0.002	1.7 (1.0–2.9)	0.049
Age ≥55 years	2.0 (1.2–3.4)	0.009	1.4 (0.8–2.5)	0.27
Hypertension	1.8 (1.1–2.9)	0.025	1.3 (0.7–2.2)	0.38
Low HDL-C	1.6 (1.0–2.6)	0.051	1.3 (0.8–2.2)	0.34

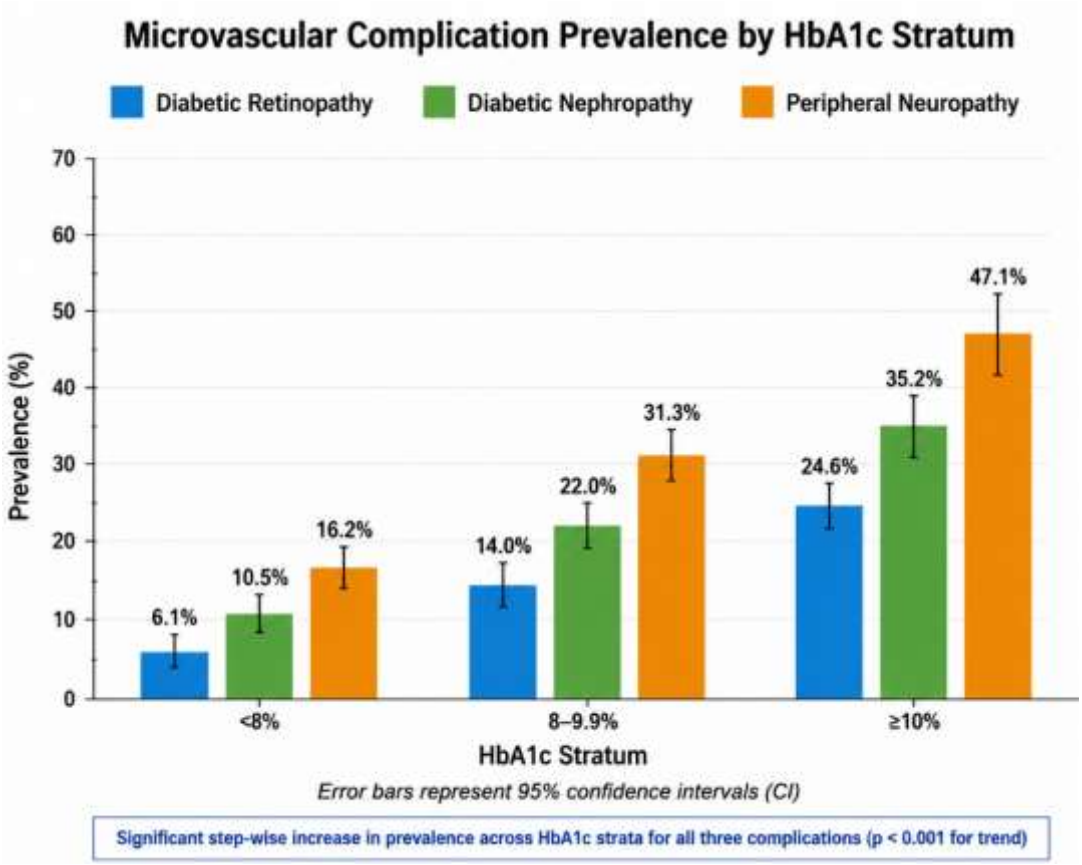


Figure 1. Prevalence of microvascular complications (diabetic retinopathy, nephropathy, and peripheral neuropathy) across HbA1c strata (<8%, 8–9.9%, ≥10%) in newly diagnosed T2DM patients (n=300). Significant increasing trend across all complication types (p<0.001).

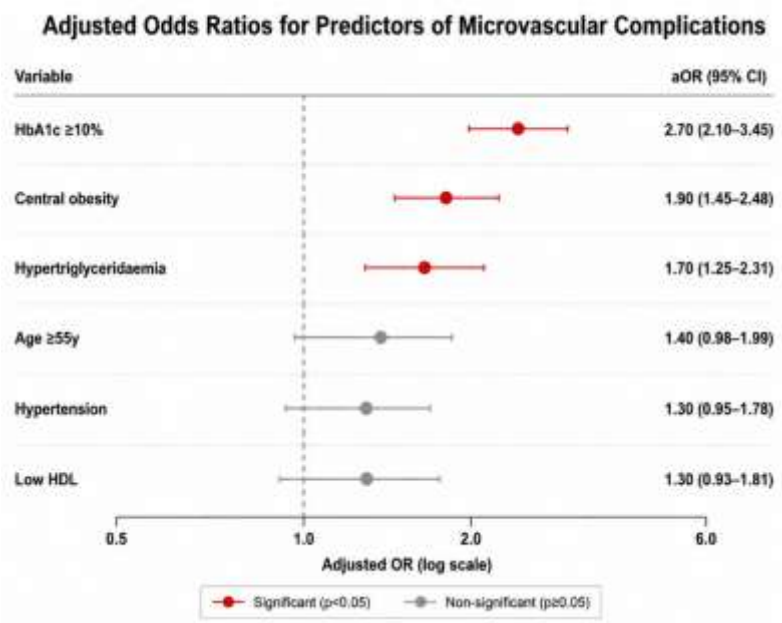


Figure 2. Forest plot of adjusted odds ratios (aOR) with 95% confidence intervals for independent predictors of any microvascular complication at diagnosis in newly diagnosed T2DM (multivariable logistic regression, n=300). Variables achieving statistical significance ($p<0.05$) shown in red.

4. DISCUSSION

Microvascular complications are present at diagnosis of T2DM, with any complication in 36.7%, peripheral neuropathy in 31.3% and microalbuminuria in 22.0% of drug-naïve, newly diagnosed T2DM adults in this cross-sectional study of 300 patients in a tertiary care hospital. These figures are similar to the landmark UKPDS at diagnosis data [4] and the more recent ICMR-INDIAB national study, which found that 16.9% of newly diagnosed T2DM had retinopathy and 26.9% had microalbuminuria in India. Taken together, all these data support the 'ticking-clock' hypothesis: the pathological events leading to microvascular damage start long before the glycaemic threshold for diagnosis is exceeded, at the prolonged stage of impaired glucose tolerance and insulin resistance [5]. The increasing prevalence of complications as the HbA1c level increases (from 17.1% (HbA1c <8%) to 55.8% (HbA1c ≥10%)) illustrates the dose-response relationship between cumulative glycaemic burden and microvascular damage. The high aOR of HbA1C ≥10% (2.7) after adjustment for other metabolic factors is not just a reflection of glycaemic control at the time of diagnosis, but rather a reflection of the duration of pre-diagnostic hyperglycaemia. This discovery aligns with the ADA recommendation to screen for microvascular complications at the time of T2DM diagnosis, not wait until later in the diabetes course, with respect to the fundus, ACR, eGFR, and neurological status [9]. Clinically significant factors include high prevalence of dyslipidaemia (71.0%) especially hypertriglyceridaemia (48.0%) and low HDL (56.0%) and the identification of hypertriglyceridaemia as an independent predictor of microvascular complications (aOR 1.7). This type of dyslipidaemia is termed diabetic dyslipidaemia, and is associated with increased triglycerides and low HDL-C, and small dense LDL (that may not be adequately reflected in calculated LDL-C) due to insulin resistance-related abnormalities in hepatic VLDL production and activity of lipoprotein lipase [8,9]. Beyond its well established macrovascular risk, the direct role of dyslipidaemia in microvascular disease – via oxidative modification of lipoproteins that penetrate capillary basement membranes, loss of pericytes and endothelial dysfunction – is also well recognised [10].

Central obesity (aOR 1.9) was a modifiable independent predictor, which is in line with the known metabolic and microvascular pathogenesis of insulin resistance, dysregulation of adipokines, and release of pro-inflammatory cytokines, including TNF-α and IL-6, resulting from central adiposity [11]. In South Asia, the metabolic syndrome and visceral adiposity at lower BMI cut-offs (metabolic obesity at BMI ≥ 23 kg/m²) makes waist circumference a useful indicator in this group of people [8].

Hence lifestyle changes to combat central obesity should be incorporated from the beginning of T2DM treatment rather than when the drug regime is escalated.

DPN (microvascular complication) was the most common microvascular complication at diagnosis (31.3%), even at diagnosis. This finding may in part be explained by the sensitivity of the composite DPN definition (monofilament + biothesiometry + MNSI) which identifies sensory impairment before signs of neuropathy are apparent [12]. Subclinical DPN at diagnosis is a poor prognostic factor for foot ulceration, Charcot arthropathy and LEGA — outcomes with significant impact on quality of life and economic burden in the Indian setting where 40-60% of all LEAs are due to DFD [13].

Clinical implications: This study provides institution-specific evidence to support a standardised 'first visit metabolic panel' for all newly diagnosed T2DM patients including HbA1c, fasting lipid profile, ACR, eGFR, fundus photography, and neurological screening, which are consistent with the ICMR 2018 T2DM management guidelines [14] and ADA 2024 Standards of Care [9]. The fact that 34.7% of patients with newly diagnosed disease had HbA1c ≥10% at first diagnosis (representing advanced disease duration prior to diagnosis) suggests the need for population-level screening programmes for high-risk groups (central obesity, family history and hypertension) rather than opportunistic diagnosis.

Limitations: Cross-sectional design does not allow for assessment of actual duration of pre-diagnostic diabetes. Patients with the diagnosis of more than 6 months after the onset of their metabolism cannot be excluded on the basis of diagnosis. There may be minor error due to non-fractionation of HbA1c for haemoglobin variants (sickle cell, thalassaemia) relevant to South India. Routine use of Fibro Scan and nerve conduction studies was not done. The tertiary care hospital setting may be more likely to present more severe and/or symptomatic presentations than would a community-based screening.

5. CONCLUSION

The 'ticking-clock' hypothesis of several years of pre-diagnostic hyperglycaemia was confirmed as more than one-third (36.7%) of newly diagnosed T2DM patients at this tertiary care hospital were already found to have microvascular complications at diagnosis. HbA1c ≥10%, central obesity and hypertriglyceridaemia are independent predictors of the presence of prevalent complications. At the time of the diagnosis of T2DM, thorough microvascular and metabolic screening should be performed, including fundoscopy, urinary ACR, eGFR, biothesiometry and fasting lipid profile, and should be institutionalized as a standard of care and prompt initiation of multifactorial risk factor management.

REFERENCES

[1] International Diabetes Federation. IDF Diabetes Atlas, 10th edn. Brussels: IDF; 2021.

[2] Anjana RM, Unnikrishnan R, Deepa M, et al. Metabolic non-communicable disease health report of India: the ICMR-INDIAB national cross-sectional study (ICMR-INDIAB-17). Lancet Diabetes Endocrinol. 2023;11(7):474-89.

[3] Harris MI, Klein R, Welborn TA, Knuiman MW. Onset of NIDDM occurs at least 4-7 yr before clinical diagnosis. Diabetes Care. 1992;15(7):815-9.

[4] Turner RC, Millns H, Neil HA, et al. Risk factors for coronary artery disease in non-insulin dependent diabetes mellitus: United Kingdom Prospective Diabetes Study (UKPDS: 23). BMJ. 1998;316(7134):823-8.

[5] Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HA. 10-year follow-up of intensive glucose control in type 2 diabetes. N Engl J Med. 2008;359(15):1577-89.

[6] Rema M, Premkumar S, Anitha B, Deepa R, Pradeepa R, Mohan V. Prevalence of diabetic retinopathy in urban India: the Chennai Urban Rural Epidemiology Study (CURES) eye study, I. Invest Ophthalmol Vis Sci. 2005;46(7):2328-33.

[7] Mooradian AD. Dyslipidemia in type 2 diabetes mellitus. Nat Clin Pract Endocrinol Metab. 2009;5(3):150-9.

[8] Misra A, Chowbey P, Makkar BM, et al. Consensus statement for diagnosis of obesity, abdominal obesity and the metabolic syndrome for Asian Indians and recommendations for physical activity, medical and surgical management. J Assoc Physicians India. 2009;57:163-70.
[9] American Diabetes Association Professional Practice Committee. Standards of Care in Diabetes — 2024. Diabetes Care. 2024;47(Suppl 1):S1-321.
[10] Lyons TJ, Basu A. Biomarkers in diabetes: hemoglobin A1c, vascular and tissue markers. Transl Res. 2012;159(4):303-12.
[11] Kahn SE, Hull RL, Utzschneider KM. Mechanisms linking obesity to insulin resistance and type 2 diabetes. Nature. 2006;444(7121):840-6.
[12] Boulton AJ, Vinik AI, Arezzo JC, et al. Diabetic neuropathies: a statement by the American Diabetes Association. Diabetes Care. 2005;28(4):956-62.
[13] Pendsey SP. Understanding diabetic foot. Int J Diabetes Dev Ctries. 2010;30(2):75-9.
[14] Indian Council of Medical Research. ICMR guidelines for management of type 2 diabetes 2018. New Delhi: ICMR; 2018.