

# High Prevalence of Additional Cardiovascular Risk Factors in Eastern-Indian Young Adults with Type 2 Diabetes Mellitus

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## Abstract

**Background and Aims:** The American Diabetes Association recommends statin therapy for young type 2 diabetes mellitus (T2DM) adults only if one additional cardiovascular (CV) risk factor coexists. The data regarding CV risk factors in young Indian T2DM adults is limited. Hence, we assessed the prevalence of CV risk factors in young adults with T2DM from eastern India. **Methods:** In this cross-sectional study, diabetic medical health check records of eastern-Indian T2DM patients performed between March 2018 and March 2019 were retrospectively reviewed and the relevant data of T2DM patients ( $n = 3564$ ) including CV risk factors [serum LDL-cholesterol of  $\geq 100$  mg/dL, hypertension ( $>140/90$  mmHg), smoking, chronic kidney disease (eGFR of  $<60$  ml/min), microalbumin to creatinine ratio of  $\geq 30$   $\mu\text{g}/\text{mg}$ , and obesity/overweight (body mass index  $\geq 23$   $\text{kg}/\text{m}^2$ )] were analysed. **Results:** There were 3280 T2DM patients from eastern India and 679 (20.7%) were  $\leq 40$  years of age. Overweight/obesity (74.3%) and serum LDL-cholesterol of  $\geq 100$  mg/dL (69.2%) were the two most common additional CV risk factors. At least one additional CV risk factor was present in 576 (95.36%) patients, whereas at least two additional CV risk factors were present in 409 (67.7%) patients. At least one non-obesity/overweight CV risk factor was present in 472 (78.1%) patients. **Conclusions:** The study demonstrates a high prevalence of additional CV risk factors in young eastern-Indian adults with T2DM. Hence, there is a need for an intensive approach to managing the CV risk factors in young Indian adults with T2DM.

**Keywords:** Cardiovascular risk, LDL-cholesterol, obesity, statin, type 2 diabetes mellitus, young adults

## INTRODUCTION

Type 2 diabetes mellitus (T2DM) is one of the most common chronic diseases, and its prevalence is increasing exponentially in India.<sup>[1]</sup> In a recent study, it was reported that the age at the onset of T2DM was 15 years earlier in India than in the United Kingdom (UK). The decreasing age at onset of T2DM in India has markedly increased the prevalence of T2DM in Indian young adults.<sup>[2]</sup> T2DM is associated with an increased risk of cardiovascular disease (CVD) and cardiovascular (CV) mortality. CVD is more frequent and occurs at an earlier age in Asian Indians than in Caucasians.<sup>[3]</sup> A similar trend has also been observed in South Asian T2DM patients.<sup>[4]</sup>

Several studies have demonstrated a stronger association with CVD of early-onset T2DM than late-onset T2DM. In a large study from Sweden, T2DM patients with age at diagnosis of  $<40$  years had the highest risk for coronary artery disease (hazard ratio, HR: 4.33), heart failure (HR: 4.77), and CV mortality (HR: 2.72), whereas another study from China

reported a higher rate of nonfatal CVD in T2DM with an early age of onset ( $<40$  years).<sup>[5,6]</sup>

Importantly, a large Danish study has demonstrated a higher rate of sudden cardiac death in young ( $<50$  years of age) patients with T2DM than those with type 1 DM (T1DM) or without diabetes.<sup>[7]</sup> Due to these unique characteristics, it has been proposed to make young-onset T2DM a high-CV risk group. However, the American Diabetes Association (ADA) recommends considering statin therapy in T2DM patients younger than 40 years, only if one additional CV risk

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factor (obesity/overweight, hypertension, dyslipidaemia, smoking, a family history of premature coronary disease, chronic kidney disease, and the presence of albuminuria) is present.<sup>[8]</sup> Despite having higher LDL-cholesterol levels, early-onset Asian T2DM patients less frequently receive statin therapy than those with late-onset T2DM.<sup>[9]</sup> The need for more intensive management of CV risk factors among young T2DM adults has been emphasized in recent years.<sup>[10]</sup>

The frequent association of young T2DM patients with CV risk factors has been reported.<sup>[11]</sup> Recent data from the UK has demonstrated an increase in cardiovascular multimorbidity (two or more CV risk factors) by 14–17% in young adults with newly diagnosed T2DM during 2005–2016.<sup>[10]</sup> However, the data on the CVD and CV risk factors in young Indian adults with T2DM is limited. A higher rate of CV mortality, especially of stroke, among eastern states than in the rest of India has been reported.<sup>[12]</sup> The only Indian study that evaluated the CV risk factors among young adult T2DM patients did not include participants from eastern India.<sup>[13]</sup> Therefore, the present study is designed to assess the prevalence of CV risk factors in young adults with T2DM from eastern India.

## MATERIALS AND METHODS

This retrospective study was conducted at a tertiary care centre, Vydehi Institute of Medical Sciences, Bengaluru. The study was approved by the institutional ethics committee, and a waiver for consent was granted in view of its retrospective nature. The diabetic medical health check records performed between March 2018 and January 2019 were reviewed. The data of T2DM patients with their residing address registered from eastern India (West Bengal, Bihar, Assam, Nagaland, Mizoram, and Arunachal Pradesh), aged between 18 and 40 years, for whom history and physical examination, including anthropometric data, investigations for evaluation of the type of diabetes, and diabetes-related complications which were available, were collected as per the standard protocol prepared. Patients with T1DM, gestational diabetes mellitus, those confirmed or suspected to have latent autoimmune diabetes, pancreatic DM, Cushing's syndrome, acromegaly, and drug-induced hyperglycaemia were excluded. The prevalence of atherosclerotic CV risk factors such as serum LDL-cholesterol of  $\geq 100$  mg/dL,<sup>[14]</sup> hypertension ( $>140/90$  mmHg), smoking, chronic kidney disease (eGFR of  $<60$  ml/min), and a urinary microalbumin to creatinine ratio of  $\geq 30$   $\mu\text{g}/\text{mg}$ . Patients on statins with unavailable baseline (pre-statin) lipid parameter data were excluded from the initial analysis.

The diagnosis of diabetes mellitus was based on the ADA criteria. Blood pressure (BP) was measured in the sitting position according to the method described by the Seventh Report of the Joint National Committee. Patients with known hypertension on antihypertensive agents as well as newly diagnosed hypertension (systolic BP:  $\geq 140$  mmHg and/or diastolic BP:  $\geq 90$  mmHg on two separate occasions) were considered to have hypertension. The diagnosis of dyslipidaemia

was made when the LDL-cholesterol was  $\geq 100$  mg/dl either before the initiation of statins or other hypolipidemic agents or at the visit for a diabetic medical health check (DMHC). The presence of albuminuria was considered if the microalbumin to creatinine ratio was  $\geq 30$   $\mu\text{g}/\text{mg}$  on two separate occasions. The body mass index (BMI) was defined as the ratio of body weight in kilograms to body height in meter squares; obesity and overweight were defined with a BMI of  $\geq 25$   $\text{kg}/\text{m}^2$  and 23–24.9  $\text{kg}/\text{m}^2$ , respectively.

## Statistical analysis

The collected data were entered into a Microsoft Excel sheet and analysed using SPSS (Statistical Package for Social Sciences) version 26.0 software. The results were presented in tabular and graphical format. For quantitative data, mean  $\pm$  SD was calculated, whereas qualitative data were expressed as absolute numbers or percentages.

## RESULTS

A total of 3280 patients from eastern India underwent DMHC, of whom 679 (20.7%) were  $\leq 40$  years of age. Of the 679 young eastern-Indian adult T2DM patients, 67 patients were on statins, for whom the baseline (pre-statin) lipid parameter data were not available, and the other eight with incomplete data on CV risk factors were excluded from the analysis.

Of the 604 study participants, 383 (63.4%) were males. The mean age of the study population was  $34.94 \pm 4.23$  years. The mean duration of diabetes was  $3.26 \pm 3.55$  years. The mean glycated haemoglobin (HbA1c) was  $8.29 \pm 2.36\%$  and the BMI was  $25.59 \pm 3.87$ . Nine (1.46%) patients had established atherosclerotic CVD (ASCVD).

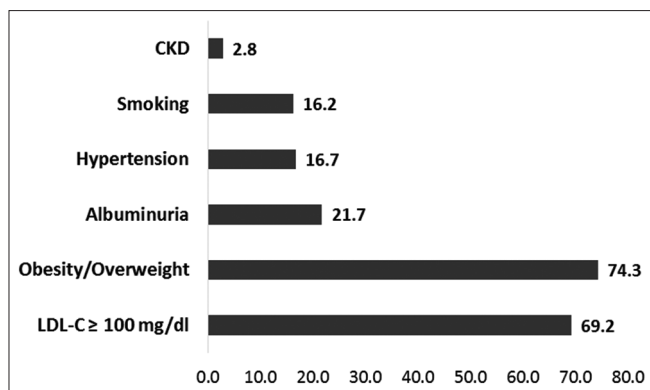
The prevalence rates of various CV risk factors are shown in Figure 1. Obesity/overweight and elevated serum LDL-cholesterol were the most common additional CV risk factors.

When obesity/overweight was considered a CV risk factor, at least one CV risk factor was present in 576 (95.36%) patients, whereas at least two additional CV risk factors were present in 409 (67.7%) [Figure 2a].

When obesity/overweight was not considered a CV risk factor, at least one CV risk factor was present in 472 (78.1%) patients, whereas at least two additional CV risk factors were present in 169 (28%) [Figure 2b].

## DISCUSSION

This is the first study that estimates the prevalence of CV risk factors in young adults with T2DM from eastern India. The study finds almost universal (95.4%) presence of additional CV risk factors among them. The most common additional CV risk factors were obesity/overweight and elevated serum LDL-cholesterol  $\geq 100$  mg/dl. Even when obesity/overweight was not considered as an additional CV risk factor, at least one CV risk factor was present in more than three-fourths of patients.

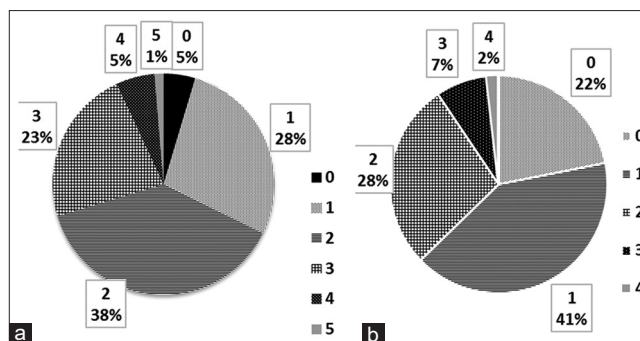


**Figure 1:** Prevalence of cardiovascular risk factors in young adult type 2 diabetes mellitus patients from eastern India. CKD: chronic kidney disease; LDL-C: low-density lipoprotein cholesterol

A previous multicentre study that evaluated the CV risk factors in young Indian T2DM adults included patients from southern and western parts of India.<sup>[13]</sup> The study had found similarly high rates of additional CV risk factors. The prevalence rates of obesity/overweight (74.3% vs 83.2%), LDL-cholesterol  $\geq 100$  mg/dl (69.2% vs 62.4%), and smoking (16.2% vs 24.3%) in the present study are comparable to those of Sosale *et al.*<sup>[13]</sup> These factors suggest uniformly high obesity/overweight and elevated serum LDL-cholesterol in Asian Indian young adults with T2DM. However, the prevalence of hypertension (16.7% vs 27.6%) was relatively lower in our cohort. This is in contrast to the higher rates of hypertension in the eastern-Indian general population and warrants further studies to understand the differential observation.<sup>[15]</sup> The discrepancy in the prevalence of nephropathy (21.7% vs 0.9%) is due to differences in the definition of nephropathy (spot urinary microalbumin to creatinine ratio:  $\geq 30$   $\mu\text{g}/\text{mg}$  vs  $>300$   $\mu\text{g}/\text{mg}$ ) and differences in the duration of T2DM ( $3.26 \pm 3.55$  years vs  $<3$  months).<sup>[13]</sup> The latter difference also explains a higher prevalence of CKD (2.8%) in our study.

As discussed earlier, young-onset T2DM itself is a high-risk group for CVD. Although the established ASCVD was not pronounced in our cohort, the role of additional CV risk factors in the pathogenesis of CVD and their contribution to increased CV mortality in the subsequent years/decades is well known. Almost universal occurrence of additional CV risk factors in the young Asian Indian T2DM adults is likely to contribute to greater CV risk in them. Notably, all observed additional CV risk factors were modifiable. Hence, there is a need for intensive screening and management of these modifiable CV risk factors in young Indian adults with T2DM.

Most of the patients in this study fulfilled the criteria to receive statin therapy according to the ADA guidelines.<sup>[14]</sup> However, only a small proportion of patients received statin therapy despite the majority of them being previously diagnosed with T2DM at other healthcare facilities. Currently, the ADA recommends statin therapy to all T2DM patients



**Figure 2:** The frequency of the number of evaluated cardiovascular (CV) risk factors when obesity/overweight was considered (a) and not considered (b) as a CV risk factor

aged  $\geq 40$  years irrespective of the presence of additional CV risk factors. Our study findings may suggest considering the reduction of the age cutoff among Asian Indian T2DM patients to initiate statins. However, there is a paucity of studies that evaluate the efficacy of statins in reducing CVD and CV mortality in young T2DM adults, and further studies are warranted to address this question.

This is the first study to report the prevalence of CV risk factors among a large number of young T2DM patients from the eastern part of India. However, the study had a few limitations. This was a retrospective study with its inherent limitations. Importantly, the data regarding family history of premature ASCVD, one of the important CV risk factors, was not available, which might have underestimated the CV risk. Also, there was no data on the novel CV risk factors such as elevated high sensitivity to C-reactive protein, coronary calcium score, etc. In addition, around 67 patients on statin therapy were excluded due to the lack of the pre-statin LDL-cholesterol level. As such patients are likely to have a high CV risk, their exclusion might have underestimated the prevalence of CV risk factors in the study population. Notably, as all of the participants in this study were from the eastern part of India and travelled to the southern part of India (Bangalore) for health care, there may be a potential selection bias. Nevertheless, the inclusion of patients only from out-patient services but not from in-patient services and a low prevalence of established ASCVD suggest the lack of significant selection bias. However, further community-level studies from eastern India are warranted to validate the study findings.

To conclude, the study demonstrates a high prevalence of additional CV risk factors among eastern-Indian young adults with T2DM. The study emphasizes the need for an intensive approach to managing the CV risk factors in this population.

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#### Conflicts of interest

There are no conflicts of interest.

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