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# Demographic and clinical profile of youth onset diabetes patients in India—Results from the baseline data of a clinic based registry of people with diabetes in India with young age at onset—[YDR-02]

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## Abstract

**Background:** We here report the demographic and clinical profile of the patients enrolled in the Indian Council of Medical Research funded Registry of people with diabetes in India with young age at onset (YDR) from 1 January 2000 to 31 July 2011.

**Methods:** The YDR registry recruits all diabetes cases (newly diagnosed or treated) reporting on or after 1 January 2000 with age of diagnosis ≤25 years, and residing within the assigned geographical area of the reporting centres. A baseline proforma was used to obtain information on demographic and clinical details at registration.

**Results:** The registry has enrolled 5546 patients (49.5% male; 50.5% female) with youth onset diabetes from 205 reporting centres linked to 8 regional collaborating centres (RCC) across India. T1DM (63.9%; n = 3545) and T2DM (25.3%; n = 1401) were the commonest variants of youth onset diabetes, though their relative proportion varied across RCCs. The mean (SD) age at diagnosis for T1DM was 12.9 (6.5) years, while that for T2DM was 21.7 (3.7) years. Nearly half the T1DM patients were registered within 6 months of the onset of disease. Most cases of T2DM (47.3%)

**Abbreviations:** RCC, regional collaborating centre; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus; YDR, registry of people with diabetes in India with young age at the onset.

were registered after 3 years from their date of diagnosis. 56.1% of patients had at least one episode of hospitalization at registration.

**Conclusion:** The observations from YDR registry indicate the need to establish a surveillance system in India to monitor diabetes in youth, not only to understand its complex etiology and natural history but also due to its detrimental socio economic impact.

**KEYWORDS**

clinical profile, diabetes registry, type 1 diabetes, type 2 diabetes, youth onset diabetes

## 1 | INTRODUCTION

The epidemic of diabetes has traversed all the age groups including children and adolescents. Studies in the past two decades have reported a consistent increase in the global burden of both youth onset type 1 (T1DM) and type 2 diabetes (T2DM).[1,2] Globally, TIDM is the predominant form of youth onset diabetes, accounting for most cases of diabetes diagnosed before 20 years of age.[3,4] While traditionally T2DM was a disease of middle and old age, it is now occurring frequently even among youth.[3,5,6] Youth onset T2DM occurs in all ethnic groups, but at a much higher prevalence in some migrant and minority populations such as those of black African descent, native North American, Hispanics, Asians, and South Asians.[2,3,7]

Published reports indicate a greater proportion of women in the reproductive age group are now affected with gestational diabetes.[8] Diabetes resulting from specific genetic conditions (maturity onset diabetes of youth), surgery, medications, infections, pancreatic disease, malnutrition, and other illnesses are also prevalent in the younger age groups.[9-14]

India, the home of world's second largest diabetes population, also has the second largest burden of T1DM patients.[15] According to the recent report from the International Diabetes Federation, an estimated 128 500 children and adolescents with T1DM are living in India, which may be an underestimate because this assessment is based on few clinic based studies.[15] It is also likely that the high background prevalence of diabetes along with increasing rates of obesity in youth would have altered the phenotypic landscape of T2DM in India. Moreover, studies conducted in Europe, America, and East Asia reported a high predilection for children and adolescents of Indian origin living in these regions to develop diabetes compared to their native counter parts.[16]

Current literature on youth onset diabetes is heavily skewed toward T1DM. There are limited data on other youth onset variants, even in the developed world. Apart from few isolated clinical reports, the data on distribution, clinical course, and prognosis of youth onset diabetes in India are largely unavailable. However, such information is pertinent to devise better strategies to curtail the health and economic impact of diabetes in youth. In an effort to address this gap, the Indian Council of Medical Research has established a national registry of youth onset diabetes-YDR. This study report the baseline demographic and clinical characteristics of youth onset diabetes patients recruited during phase-I (1 January 2000 to 31 July 2011) of the clinical Registry of people with Diabetes in India with Young age at onset (YDR).

## 2 | METHODS

Detailed methodology of the YDR registry is published elsewhere.[17] In brief, YDR is a multicentric clinic based registry of youth onset diabetes operating through Regional Collaborating Centres (RCC) and their interacting Reporting Centres (RC) across India. During phase-I of the YDR, 8 RCCs and 205 RCs participated in the data collection. The RCs ranged from single physician clinics to multi-speciality private hospitals to public funded tertiary care facilities. Patients reporting on or after 1 January 2000 at the RCs were enrolled in the registry if they satisfied the inclusion criteria, namely, age at diagnosis ≤25 years with fasting plasma glucose ≥126 mg/dL and/or 2 hours postload plasma glucose ≥200 mg/dL. All referred/non-referred, treated/untreated cases residing within the assigned geographical area of the RCs were included. Medical records available with the patients from the time of original diagnosis were used as source document to obtain information on clinical parameters. The date of first insulin injection was taken as the diagnosis date for T1DM. Diabetes classification was done by a trained physician at the respective RCs using symptom based clinical criteria (Supporting Information file S1), approved by the YDR expert group. A baseline proforma was used to obtain information on socio demographic details and clinical profile of the patients at registration. All results reported in this manuscript are derived from the baseline proforma of the YDR subjects. Privacy and confidentiality of the subjects were maintained during data collection and analysis. The registry obtained ethical clearance from the Institutional Ethics Committees of all the RCCs. There was no blood sampling as part of the YDR registry activities. In view of this, the registry steering committee and the ethics committees of the RCCs did not instruct for an individual consenting process.

### 2.1 | Statistical analysis

Descriptive statistics are presented as mean with 95% confidence intervals and frequencies with percentages. One way analysis of variance was used to compare continuous variables while $\chi^2$ test was used to compare proportions between the groups. Data have been described separately for T1DM and T2DM. Other diabetes types are clubbed together to form a category named as "others." However, data on all variants are reported wherever necessary. In all analyses, a

*P* value of <.05 was considered as statistically significant. Data analysis was done using SPSS 16.0 software for windows.

## 3 | RESULTS

Data of 5546 youth onset diabetes patients recruited between 1 January 2000 and 31 July 2011 were analyzed. Recruited cases were classified in to nine different categories of diabetes, which are common in clinical practice in India, based on pre-defined clinical criteria.[17] T1DM (63.9%) and T2DM (25.3%) contributed the majority of cases recruited. The other variants of diabetes in YDR were gestational diabetes (3.9%), maturity onset diabetes of the young (3.1%), chronic pancreatitis associated diabetes (1.3%), latent autoimmune diabetes in adults (1.0%), secondary diabetes (1.0%), drug induced diabetes (0.3%), and malnutrition mediated diabetes (0.1%). Subsequent analysis and presentation of results has been restricted to T1DM and T2DM, given that these two disease categories contributed to 89.2% of all cases in the Registry.

Out of total patients enrolled, 50.5% were females. There was a significant gender difference in the proportional distribution of diabetes categories (Figure 1). Among males, the proportion of individuals with T1DM and T2DM was 66.9% and 26.0%, respectively, while that in females was 61.1% and 24.5%, respectively.

The distribution of diabetes types based on age at diagnosis is depicted in Figure 2. In the childhood onset group (age at diagnosis ≤ 10 years), 96% of the cases were T1DM, while 1.4% were categorized as T2DM. Among adolescents (age at diagnosis: 11-19 years), the proportion of TIDM and T2DM cases were 77.3% and 14.6%, respectively. However, in the adult onset group (age at onset ≥ 20 years), majority of the cases (49.5%) were youth onset T2DM.

The YDR registry noticed a significant regional variation in the distribution of T1DM and T2DM cases (Figure 3). Centres, RCC03 (Chennai) and RCC05 (Dibrugarh) have recruited equal proportion of T1DM and T2DM cases. In all other centres, T1DM contributed most of the cases and the proportion varied from 71.4% to 94.4%.

### 3.1 | Demographic profile

Table 1 shows the demographic profile of youth onset diabetes patients at registration according to the diabetes type. T2DM patients were older and had longer duration of diabetes since diagnosis compared with those with T1DM. While 49.3% T1DM patients registered within 6 months of onset of disease, 47.3% of the T2DM cases were registered more than 3 years after their date of diagnosis. In both T1DM and T2DM categories; number of males with disease was more compared to females (51.7% vs 48.3% in T1DM and 51.3% vs 48.7% in T2DM).

The mean age at diagnosis varied significantly between the diabetes types. Most of the T1DM patients (42.5%) developed diabetes during their adolescent period (11-19 years). On the contrary, 78.2% of the T2DM subjects were diagnosed with diabetes after 20 years of age. The mean age at diagnosis of the diabetes categories did not show much variation across the RCCs, except the centre -RCC05 (Dibrugarh), which reported a later age at diagnosis for both T1DM [Mean age at diagnosis: 17.5 (16.8, 18.2) years] and T2DM [Mean age at diagnosis: 23.0 (22.6, 23.4) years] compared to other centres.

### 3.2 | Clinical profile

#### 3.2.1 | Mode of presentation at diagnosis

The most common modes of presentation reported by T1DM patients were a combination of osmotic symptoms (polyuria, poydypsia) and weight loss (28.8%). Ketosis was reported by 25.2% of the T1DM patients (Table 1). Mode of presentation at diagnosis for T2DM

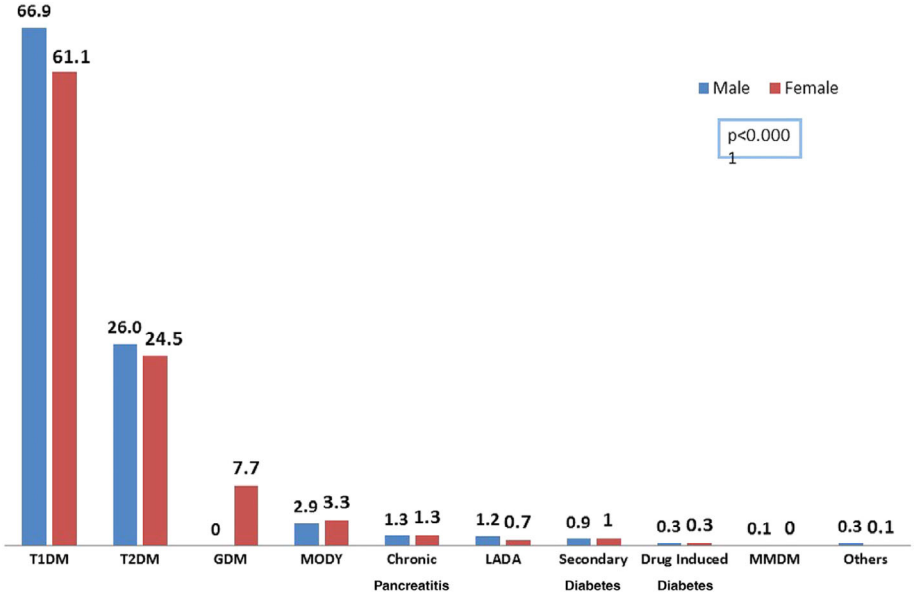


**FIGURE 1** Gender wise distribution (%) of diabetes categories in YDR registry. GDM, gestational diabetes mellitus; LADA, latent autoimmune diabetes in adults; MMDM, malnutrition mediated diabetes mellitus; MODY, maturity onset diabetes of young; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus; YDR, young age at onset

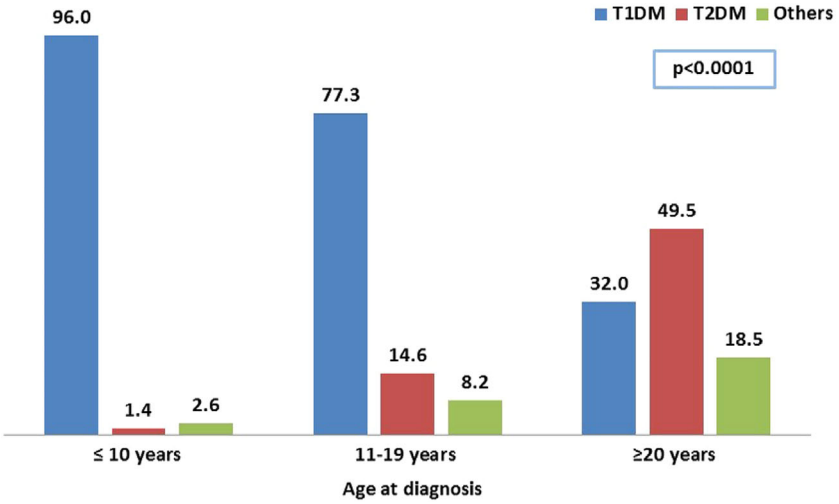


**FIGURE 2** Age at diagnosis wise distribution (%) of diabetes categories in YDR registry. YDR, young age at onset

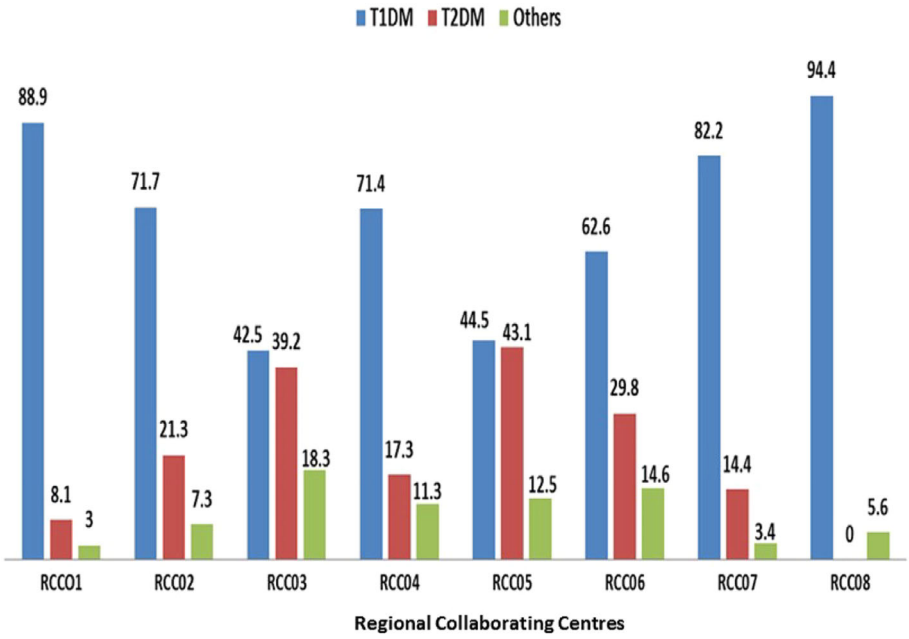


**FIGURE 3** Regional variation in the distribution (%) of diabetes cases in YDR registry. RCC01—All India Institute of Medical Sciences (AIIMS), New Delhi; RCC02—University College of Medical Sciences (UCMS), New Delhi; RCC03—Madras Diabetes Research Foundation (MDRF), Chennai; RCC04—SCB Medical College, Cuttack; RCC05—Assam Medical College (AMC), Dibrugarh; RCC06—KEM hospital, Mumbai; RCC07—P.D Hinduja hospital, Mumbai; RCC08—Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh. YDR, young age at onset

ranged from osmotic symptoms (27.1%) to ketosis (3.7%). Unlike T1DM, 33.6% of the T2DM cases were identified incidentally during routine medical examination. In T2DM patients, 13.3% presented with a combination of osmotic symptoms and weight loss, while 22.6% presented with weight loss alone at diagnosis.

### 3.2.2 | Family history of diabetes

Family history of any type of diabetes was significantly higher among youth onset T2DM compared to T1DM (Table 1). The prevalence of family history in at least one parent was four times higher among T2DM patients compared to their T1DM counterparts. In both diabetes categories, paternal history of diabetes was more common than maternal history of diabetes. Both paternal and maternal history of diabetes was reported by 66.2% of the T2DM patients. However in T1DM, only 16.8% had both their parents diagnosed with diabetes.

### 3.2.3 | Markers of insulin resistance and urine ketones

YDR patients were examined for the presence of markers of insulin resistance such as acanthosis nigricans or skin tags on the nape of neck, axilla, cubital fossa, and back. 16.0% of subjects with youth onset T2DM and 3.8% of the T1DM patients presented with cutaneous manifestations of insulin resistance (Table 1). History of urine ketones was significantly higher among T1DM (32.6%) than T2DM (6.0%) and other categories (8.5%) of youth onset diabetes.

### 3.2.4 | Comorbidities

The distribution of comorbidities did not differ significantly between the diabetes categories (Table 1). Among T1DM patients, the most common comorbid conditions were hypothyroidism (2.9%), tuberculosis

**TABLE 1** Demographic and clinical profile of youth onset diabetes

| | T1DM | | T2DM | | Others | | *P* value |
|---|---|---|---|---|---|---|---|
| | N | | N | | N | | |
| Age at registration (years) [Mean (95% C.I.)] | 3545 | 16.1 (15.9, 16.4) | 1401 | 27.2 (26.7, 27.6) | 600 | 23.0 (22.4, 23.5) | <.0001 |
| Gender *Female n (%)* | 3545 | 1713 (48.3) | 1401 | 678 (48.7) | 600 | 408 (67.7) | <.0001 |
| Age at diagnosis (years) [Mean (95% C.I.)] | 3545 | 12.9 (12.7, 13.1) | 1401 | 21.7 (21.5, 21.9) | 600 | 20.2 (19.8, 20.6) | <.0001 |
| Duration of diabetes since diagnosis (years) [Mean (95% C.I.)] | 3545 | 3.2 (3.0, 3.4) | 1401 | 5.5 (5.1, 5.9) | 600 | 2.8 (2.3, 3.2) | <.001 |
| Mode of presentation at diagnosis n (%) | | | | | | | |
| Osmotic symptoms alone | 2907 | 771 (26.5) | 697 | 186 (27.1) | 327 | 58 (17.7) | <.0001 |
| Weight loss alone | 2907 | 384 (13.2) | 697 | 159 (22.6) | 327 | 5 (17.4) | <.0001 |
| Osmotic symptoms and weight loss | 2907 | 836 (28.8) | 697 | 93 (13.3) | 327 | 40 (12.2) | <.0001 |
| Ketosis alone or with other symptoms | 2907 | 734 (25.2) | 697 | 26 (3.7) | 327 | 17 (5.1) | <.0001 |
| Osmotic symptoms or weight loss or ketosis | 2907 | 2725 (93.7) | 697 | 46 (66.5) | 327 | 172 (52.6) | <.0001 |
| Incidental | 2907 | 182 (6.3) | 697 | 234 (33.6) | 327 | 155 (47.4) | <.0001 |
| Family history of diabetes n (%) | | | | | | | |
| Maternal history of diabetes | 3207 | 257 (8.0) | 1303 | 596 (45.7) | 539 | 185 (34.3) | <.0001 |
| Paternal history of diabetes | 3217 | 374 (11.6) | 1300 | 670 (51.5) | 530 | 211 (39.8) | <.0001 |
| Both parents with diabetes | 3235 | 543 (16.8) | 1354 | 896 (66.2) | 563 | 324 (57.5) | <.0001 |
| Acanthosis nigricans n (%) | 3152 | 121 (3.8) | 1204 | 193 (16.0) | 521 | 52 (10.0) | <.0001 |
| Urine ketones n (%) | 3093 | 1007 (32.6) | 1150 | 69 (6.0) | 508 | 43 (8.5) | <.0001 |
| History of comorbidities | | | | | | | |
| Hypothyroidism | 3545 | 103 (2.9) | 1401 | 30 (2.1) | 600 | 21 (3.5) | .2 |
| Hypertension | 3545 | 59 (1.7) | 1401 | 101 (7.2) | 600 | 14 (2.3) | <.0001 |
| Dyslipidemia | 3545 | 26 (0.7) | 1401 | 159 (11.3) | 600 | 23 (3.8) | <.0001 |
| Coeliac disease | 3545 | 22 (0.6) | 1401 | 0 | 600 | 1 (2.2) | .7 |
| Tuberculosis | 3545 | 100 (2.8) | 1401 | 15 (1.1) | 600 | 8 (1.3) | .6 |
| Sepsis | 3545 | 100 (2.8) | 1401 | 21 (1.5) | 600 | 10 (1.7) | .6 |
| History of hospitalization[a] n (%) | 3545 | 2103 (59.3) | 1401 | 626 (44.7) | 600 | 334 (55.4) | .1 |
| Reasons for hospitalization | | | | | | | |
| Hypoglycemia | 2016 | 480 (23.8) | 574 | 60 (10.5) | 314 | 24 (7.6) | .07 |
| Diabetic ketoacidosis/uncontrolled hyperglycemia | 2016 | 1155 (57.3) | 574 | 313 (54.5) | 314 | 194 (61.8) | |
| Others | 2016 | 381 (18.9) | 574 | 201 (35.0) | 314 | 96 (30.6) | |

Abbreviations: T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.
[a]Within 1 year preceding registration; N-Denominator.

(2.8%), and sepsis (2.8%). The prevalence of self-reported dyslipidemia (11.3%) and hypertension (7.2%) were significantly higher among T2DM compared to T1DM. The prevalence of tuberculosis in T1DM and T2DM were 2.8% and 1.5%, respectively.

### 3.2.5 | History of hospitalization

In YDR, more than 50% of the registered patients had at least one episode of hospitalization due to acute medical conditions related to diabetes. The prevalence of hospitalization was higher among T1DM with 59.3% having at least one episode of hospitalization in the year preceding registration (Table 1). In all diabetes categories, the most common reason for hospitalization was diabetic ketoacidosis or uncontrolled hyperglycemia. Approximately one fourth of the T1DM patients had a history of hospitalization due to severe hypoglycemia.

## 4 | DISCUSSION

To the best of our knowledge, this is the largest multicentric registry based study of youth onset diabetes from India. According to the

study, T1DM and youth onset T2DM accounted for nearly 90% of the cases in India. There was significant variation in the distribution of diabetes categories with respect to gender, age at diagnosis, and the geographic locations across the country. The maternal or paternal history of diabetes was significantly associated with youth onset T2DM.

Available literature suggests a definite global variation in the distribution of diabetes type in the younger age groups. In YDR, more than 96% of the diabetes population diagnosed below 10 years was T1DM. This was consistent with the findings of the Swedish diabetes registry and the SEARCH for Diabetes in Youth Study.[3,18] Children and adolescents belonging to African, Hispanic, and Asian ethnic group are at higher risk for developing T2DM compared to their Caucasian peers. In Japan, 80% of all new cases of diabetes in children and adolescents were T2DM.[2]

Our analysis showed a definite regional variation in the overall distribution of diabetes type with two RCCs recruiting a significantly high proportion of T2DM cases compared to others. The variation was much higher in the adult onset (20-25 years) group. In adolescents, the proportion of T2DM cases varied between the RCCs (7.3%-26.2%). In the SEARCH registry, the proportion of T2DM out of the total sample of adolescents with diabetes ranged from 6% (in non-Hispanic whites) to 76% (in American Indians).[6] However, the observed regional variation in YDR should be interpreted with caution as the distribution of cases might be due to nature of the reporting centres (eg, referral centres, speciality clinics, pediatric clinics, etc.) and patient's health care seeking behavior. Reporting bias due to death prior to reaching reporting centres also should be considered. Our findings underline the need for future studies to examine the trends as well as regional variation in the incidence of youth onset diabetes from India.

The incidence of T1DM generally peaks between 10 and 14 years of age.[3,4,19,20] Our data were consistent with this notion and suggested a pubertal peaking of incidence of T1DM in Asian Indian population. In the current literature, the mean age of adolescents with T2DM has ranged from 12 to 14 years.[7,21] In YDR, adolescents with T2DM had a slightly later age at diagnosis (14.9 years).

In general, youth onset T2DM is more prevalent among females.[22] Unlike other autoimmune diseases, which disproportionately affect females, there is no gender difference in T1DM.[23] On the contrary, our study reported a male excess in both diabetes categories. According to the current literature, 60% to 80% of T2DM patients have a family history of diabetes in their first-degree relatives.[2,24,25] The present study had similar findings with strong parental history of diabetes. However, data on type of diabetes in the family members was not available with our registry.

T2DM patients often present with signs of chronic hyperglycemia, while T1DM patients are more likely to have acute metabolic decompensation. In the EURODIAB study on T1DM, polyuria was the most common presenting symptom (96%), followed by weight loss (61%) and fatigue (52%). In our study the prevalence of osmotic symptoms and weight loss in T1DM were 60% and 43%, respectively. The pattern of clinical presentation reported by T2DM patients in our study was consistent with the existing literature and ranged from mild osmotic symptoms to ketosis.

This study reported a high burden of hospitalization among both T1DM and T2DM patients, primarily due to diabetic ketoacidosis or uncontrolled hyperglycemia prior to registration at the reporting centres. This suggests the need for early diagnosis of diabetes in youth to reduce the metabolic derangement at presentation.[26,27]

It is pertinent to discuss the limitations of our study. The study population was selected from hospitals and may not be representative of the general population. Hence, estimates may not reflect the actual characteristics of youth onset diabetes population in India. This registry followed symptom based clinical criteria for classifying diabetes, which may leave some chance for misclassification. The data on family history of diabetes is incomplete as there was no pedigree chart in the baseline proforma. However, the study has certain strengths as well. With a large sample size, it was sufficiently powered to detect the difference between the diabetes categories. Uniform guidelines and standardized instruments have reduced the potential bias in data collection. YDR collected data from a large network of reporting centres, including private and government hospitals, which ensured heterogeneity in sample selection.

## 5 | CONCLUSION

This study identified significant variation in the distribution of youth onset diabetes in India with respect to their gender, age at diagnosis, and the geographic location. Further, there is a notable overlap in the clinical profile of youth onset T1DM and T2DM, which in a proportion of cases interferes with disease classification, and planning appropriate therapy in routine clinical practice. From the YDR, it is clear that the youth onset T2DM is not a rare entity in India. YDR data emphasize the need to target children, adolescents, and youth with strong family history of diabetes for future diabetes prevention programs. Despite several limitations, the findings of the YDR registry support the need for establishing a diabetes surveillance system to continuously monitor the burden of youth onset diabetes in India.

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### CONFLICT OF INTEREST

None of the authors have any potential conflicts of interest relevant to the manuscript.

### AUTHOR CONTRIBUTIONS

Authors N.T., T.K, R.D., A.D., and C.Y. conceptualized and designed the study. P.P. prepared the first draft of the manuscript, N.T. and V.M. revised it. Authors N.T., S.M., V.M., S.D., S.K., N.S., M.C., and S.B. involved in the execution of registry in the field. All authors have contributed to manuscript revisions and read and approved the final manuscript.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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