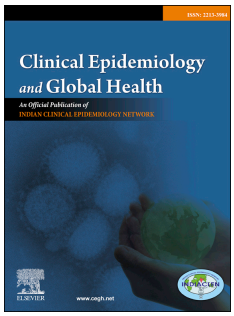
Journal Pre-proof



Childhood and adolescent onset type 2 diabetes mellitus (CAT2DM): The yoke of the young diabetics

Cynthia Amrutha Sukumar, Nandakrishna Bhat, Ajit Singh, Sudha Vidyasagar, Avinash Holla

PII: S2213-3984(22)00143-9

DOI: https://doi.org/10.1016/j.cegh.2022.101101

Reference: CEGH 101101

To appear in: *Clinical Epidemiology and Global Health*

Received Date: 20 October 2021

Revised Date: 7 June 2022

Accepted Date: 20 June 2022

Please cite this article as: Sukumar CA, Bhat N, Singh A, Vidyasagar S, Holla A, Childhood and adolescent onset type 2 diabetes mellitus (CAT2DM): The yoke of the young diabetics, *Clinical Epidemiology and Global Health* (2022), doi: https://doi.org/10.1016/j.cegh.2022.101101.

Childhood and adolescent onset type 2 diabetes mellitus (CAT2DM): The yoke of the young diabetics

Cynthia Amrutha Sukumar[1], Nandakrishna Bhat[1], Ajit Singh[1], Sudha Vidyasagar[1], Avinash Holla[1]

Running Title – Young type 2 diabetes in South Indian population

Affiliations –

1. Dr. Cynthia Amrutha Sukumar, MD
   Assistant Professor, Department of Medicine, Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Manipal, India – 576104
   cynthiaamrutha@gmail.com
2. Dr. Nandakrishna Bhat, MD
   Assistant Professor, Department of Medicine, Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Manipal, India – 576104
   nandaksb@gmail.com
3. Dr. Ajit Singh, Ph.D.
   Research Associate III, Department of Medicine, Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Manipal, India – 576104
   ajitjsingh.mcops@gmail.com
4. Dr. Sudha Vidyasagar, MD
   Professor, Department of Medicine, Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Manipal, India – 576104
   vsagar33@gmail.com
5. Dr. Avinash Holla, Ph.D.
   Research Scholar, Department of Medicine, Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Manipal, India – 576104
   holla.avinash@gmail.com

Correspondence to –

Dr. Sudha Vidyasagar, MD
Professor, Department of Medicine, Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Manipal, India – 576104
vsagar33@gmail.com
+91 9880083580

Childhood and adolescent onset type 2 diabetes mellitus (CAT2DM): The yoke of the young diabetics

Highlights of the study

1. CAT2DM has emerged among young adults as a major subgroup, in the last decade.
2. One-third of the patients are incidentally detected, which emphasizes the need for screening.
3. Blood sugars were uncontrolled in 41% of CAT2DM, emphasizing the need for early detection and prompt treatment.

Childhood and adolescent-onset type 2 diabetes mellitus (CAT2DM): The yoke of the young diabetics

Abstract

Aims: To study the prevalence, clinical characteristics, complications, and treatment pattern of childhood – and adolescent-onset type 2 diabetes among young diabetes patients (<25 years at diagnosis).

Methods: We conducted an observational retro-prospective study among young diabetics at a tertiary care hospital between January 2012 and December 2020. A detailed medical assessment, laboratory evaluation, and screening for complications were done in all patients.

Results: We analyzed a total of 130 patients, with a mean age of 23 years. Forty-seven (36.2%) had a family history. Osmotic symptoms and weight loss were the predominant features, 4 had ketosis, but 34.65% were detected incidentally. Seventy-two (55.2%) were overweight and obese. Most of the patients were uncontrolled, with a mean HbA1c of 9.4 ± 2.8 %. There were 1.5%, 1.5%, and 2.3% of retinopathy, nephropathy, and neuropathy cases detected at evaluation. Seventy-nine (60.8%) patients were controlled on oral hypoglycemic agents (OHAs) alone, and 45 (34.5%) needed insulin at onset for control.

Conclusion: This study on CAT2DM emphasizes the fact that diabetes has emerged over the past decade among young adults. Screening may be needed in high-risk groups, and prompt, effective treatment may change prognosis significantly.

Keywords: CAT2DM, Early-onset type 2 diabetes mellitus, Type 2 diabetes mellitus, Young diabetes

Childhood and adolescent-onset type 2 diabetes mellitus (CAT2DM): The yoke of the young diabetics

INTRODUCTION

Three decades ago, type 2 diabetes mellitus (T2DM) was almost unheard of in the pediatric and adolescent population. However, the past few years have witnessed a gradual increase in T2DM among children, adolescents, and young adults worldwide [1]. The wave of increasing cases of T2DM among this age group paralleled the rampant increase in obesity among children and adolescents [2]. Despite this climb in cases, screening for T2DM among children and adolescents is not recommended.

However, though we have recently recognized this problem, many children and adolescents are wrongly diagnosed with type 1 diabetes mellitus (T1DM), and over-weight children and adolescents with auto-immune diabetes are misdiagnosed as T2DM. Childhood and adolescent-onset type 2 diabetes mellitus (CAT2DM) is usually associated with complications that may be present at the time of diagnosis itself, identifying this condition and management of associated dyslipidemia and hypertension important.

METHODOLOGY

We studied the prevalence, clinical characteristics, clinical and biochemical profile, complications, and treatment pattern of CAT2DM (with age equal to or less than 25 years at the time of diagnosis) among young diabetics who visited our tertiary care hospital in South India between January 2010 to December 2019.

Operational definitions

Type 2 diabetes mellitus (T2DM): defined as fasting plasma glucose ≥126 mg/dl and/or 2hr postprandial plasma glucose ≥200mg/dl and/or glycated haemoglobin (HbA1c) >6.4% (according to ADA guidelines).

Childhood and adolescent onset type 2 diabetes mellitus (CAT2DM): Diagnosed based on the absence of ketosis, good b-cell reserve evidenced by non-requirement of insulin, absence of pancreatic calculi on abdominal X-ray and response to oral hypoglycaemic agents.

Childhood- and adolescent-onset type 1 diabetes mellitus (CAT1DM): Patients with a history of diabetic ketoacidosis and, low fasting C-peptide values (< 0.6 pmol/mL) and requirement of insulin from the time of diagnosis.

Inclusion and exclusion

This observational retro-prospective study included all cases of diabetes reporting on/after 1st January 2012, with age equal to or less than 25 years at the time of diagnosis of diabetes attending Kasturba Hospital as an outpatient or admitted in the medicine department.

Our exclusion criteria screened out:

-Patients on corticosteroids or other drugs causing short-term hyperglycemia.

-Stress hyperglycemia due to any other cause.

-Childhood- and adolescent-onset type 1 diabetes mellitus (CAT1DM)

-Gestational diabetes mellitus was diagnosed according to the American Diabetes Association13 (O'Sullivan and Mahan criteria revised by the National Diabetes Data Group).

At our hospital, national young diabetes registry as part of the Indian Council of Medical Research (ICMR) has been in existence since June 2015, and for all patients in the registry, a standardized protocol was used. All the participants who satisfied the inclusion and exclusion criteria were included in the study. After the registration procedure, all patients were evaluated by the research staff.

CAT2DM was diagnosed based on the absence of ketosis, non-requirement of insulin, good b-cell reserve as shown by fasting C-peptide assay (‡ 0.6 pmol/mL), absence of pancreatic calculi on abdominal X-ray (if indicated clinically), and response to oral hypoglycaemic agents.

A detailed medical history including demographics (age, sex, place of residence, socio-economic status) was taken along with a family history of diabetes. Also, details of, age of onset of diabetes, duration of diabetes, history of insulin resistance (acanthosis nigricans) were collected. Details of presenting history such as the presence of osmotic symptoms at onset, presence of infections other complications were also taken. Details of past and current medications, hospitalization, and previous investigations done for glycaemic control like HbA1c were also documented.

Anthropometric measurements, including height, and weight were documented using standardized techniques. Body mass index (BMI) was calculated as per standard criteria. Blood pressure was recorded in the sitting position in the right arm with a mercury sphygmomanometer using appropriate cuffs and rounded off to the nearest 2 mmHg. A detailed physical examination was carried out by physicians, specifically looking for signs of insulin resistance like acanthosis nigricans.

Investigations for CAT2DM were done for all participants. This included a fasting venous blood sample (obtained after an overnight fast of at least 8 h). Fasting plasma glucose (FPG) and, post-prandial plasma glucose (PPPG) was measured estimated on a COBAS 502 Chemistry analyzer. Postprandial blood glucose was obtained 2 hours after a standard meal, and Glycosylated hemoglobin (HbA1c) was estimated by the COBAS 502 Chemistry analyzer as well. Fasting C-peptide levels were estimated by the electrochemiluminescence (COBAS 8000 e801 Immuno module analyzer).

All patients were evaluated for complications of T2DM. The cardiac evaluation was done for all patients with an electrocardiogram and a 2D-ECHO. To detect retinopathy, the ocular fundi were photographed using four-field stereo colour retinal photography (model FF 450 Plus camera, Carl Zeiss, Jena, Switzerland) and graded by an ophthalmologist according to the Early Treatment Diabetic Retinopathy Study criteria. The minimum criterion for diagnosis of diabetic retinopathy was the presence of at least one definite microaneurysm. Microalbuminuria was defined as urinary albumin excretion of 30–299 mcg/mg of creatinine. Nephropathy was diagnosed in those with macroalbuminuria (i.e., urinary albumin excretion of more than 300 mcg/mg) or microalbuminuria. Nerve conduction studies were done to evaluate for evaluation and classification of diabetic neuropathy.

Statistical analysis:

Means and the standard deviation were used to present continuous data like age, glycosylated hemoglobin, FBS and BMI, etc. Proportions were calculated for categorical data, including gender, family history, diabetic complications, and drug utilization, etc. Categorical variables were compared using the Chi-square test, and continuous variables were compared through independent sample t-tests. Statistical significance was considered at a P value less than 0.05. SPSS for Windows version 22.0 (SPSS, Inc., Chicago, IL) was used for data analysis.

RESULTS

Prevalence of CAT2DM

One hundred and thirty (13.2%) patients were categorized into CAT2DM among 986 young diabetic patients between 2012 and 2019 of the on-going 'Young Diabetic Registry (YDR)' of ICMR. **Table 1** shows the year-wise distribution of the CAT2DM cases in our study.

Socio-demographical, clinical and biochemical profile, and complications

The mean age of the study population was 23.3±5.7 years at presentation and 20.9±4.6 years at onset. The majority of the patients, 97 (74.6%), were in the older age group (21-25 years) of the population, followed by 27 (20.8%) in the middle age group (16-20 years) and only 6 (4.6%) were equal to or younger than 15 years. Seventy-one (54.6%) patients were male. The majority, 81 (62.3%) of the CAT2DM subjects, were studying graduation, and only 14 (10.7%) were lesser than high school, and 3 (2.3%) did not go to school.

Among the total, 47 (36.2%) have had a family history of diabetes; maternal, paternal, and sibling's diabetic history was in 26 (20%), 17 (13.1%), and 4 (3.0%), respectively. **Table 2** shows the study patients' demographic profiles, including their age, gender, education status, and family history.

On the first presentation to registry study, 45 (34.6%) patients presented with osmotic symptoms, followed by 36 (27.7%) with weight loss. Ketosis was presented in 4 (3.1%) patients who were treated successfully during the hospitalization: approximately one-third, 45 (34.6%) patients evaluated with nonspecific symptoms of fatigue. Acanthosis was present in 11 (8.5%) patients.

Eleven (8.5%) patients presented with diabetes-related infectious and non-infectious complications, i.e., 2 (1.5%) had diabetic nephropathy, and 3 (2.3%), 2 (1.5%), and 2 (1.5%) have had neuropathy, retinopathy, and sepsis, respectively. Other diabetic complications like stroke, coronary artery disease/ischemia, and tuberculosis were not developed in any patient. The clinical and biochemical profile of the patients is shown in **Table 3**.

As per the BMI, more than half, 72 (55.4%) of the patients were overweight and obese, and 33 (25.4%) were underweight, where only 25 (19.2%) were normal. This trend is shown in **Figure 1**. There was a significant difference in the mean BMI between males (24.8±4.7) and females (27.0±5.8) with a p-value of 0.041.

We noted the uncontrolled FBS, PPBS, RBS, and HbA1c in recruited population. For the clinical significance, we categorized the glycated hemoglobin (HbA1c) into three categories, and it was found that the glycated hemoglobin was <7 (well-controlled) in 47 (36.2%) patients, 7-9 (poorly-controlled) in 29 patients (22.3%) and >9 (uncontrolled) in 54 (41.5%) patients. C-peptide was measured only for 41 (31.5%) patients, and the median value was 2.00 (Q1, 1.40; Q2, 2.00; Q3 3.23)**. Table 3** shows the laboratory investigations done in our recruited population.

Drug utilization review in CAT2DM patients

The majority of the patients, 124 (95.4%), continued or started on pharmacological therapy for further management after confirmed diagnosis; 6 (4.6%) were told to follow only lifestyle modifications. Seventy-nine (60.8%) patients were on oral hypoglycemic agents (OHAs) alone, where 45 (34.5%) were on both insulin and OHA.

Regular insulin was used in 45 (34.5%) patients, and biguanide (metformin) was the most used OHA in 107 (82.7%) patients, followed by sulfonylureas, glucosidase inhibitors, DPP IV inhibitors, and glitazones in 26 (20.0%), 5 (3.8%), 4 (3.1%) and 3 (2.3%) patients respectively. Along with pharmacological therapy, 127 (97.7%) patients were counseled to follow a restricted diet and to start exercising and yoga. **Table 4** shows the drug utilization review in CAT2DM patients.

DISCUSSION

The start of the 21st century saw several gaps in our understanding of CAT2DM. Though we recognized CAT2DM, we did not know much regarding its clinical profile, complications, and treatment. Almost all young diabetics were considered T1DM unless proved otherwise. India is the diabetic capital of the world and accounts for over 60 million diabetics. Asian Indians have also proven to be more susceptible to T2DM. Keeping this in mind, when our young diabetic population was screened for CAT2DM, we found an initial incidence of 8.8% that escalated over the years to reach 25% in 2019.

The SEARCH study done in the United States was one of the largest multi-center studies on young diabetics [3]. It noted an increase in the prevalence of all types of diabetes in youth (< 20 years of age) from 1.8/1000 youth in 2001 to 2.2/1000 youth in 2009. The prevalence of CAT2DM increased during this period by 30.5% (95% CI 17.3–45.1). Our study spanned the years between 2012 and 2019 and similarly mirrored an increasing trend in the number of CAT2DM cases from 6.9% to 17.7% over the years. The prevalence of CAT2DM was 13.2% among our pool of 986 young diabetics who visited our hospital over the study period and gradually increased over the time period of our study.

An Indian registry for young diabetics made during 1992-2009 indicated an astonishing prevalence of 48% CAT2DM patients in their registry of 2630 young diabetics [4]. This could be due to the selective diabetic population in the diabetes care center where this study was conducted. As our study was done in the years following the study mentioned above, we can estimate an increase of two-fold (0.16-0.32%) in the first decade in the study mentioned above and a further increase of two-fold (8%-16%) in the following decade of the 21st century.

The mean age of the CAT2DM patients in our study was 23.3±5.7 years at presentation and 20.9±4.6 years at onset. Almost 75% of the patients were in the older age group between 21-25 years. This corroborates with data from the MEDI study (Multicenter Survey of Early Onset Diabetes in India), which noted that among early-onset diabetics, type 2 diabetics are older than type 1 [5]. The Indian young diabetes registry also noted the mean age of CAT2DM patients to be 28.2±10.2 years [4]. This could be attributed to the fact that screening for diabetes is still not routinely recommended among the children and adolescent population. As CAT2DM is also a relatively unknown entity, there could be delays in the patient presenting to a tertiary care hospital unless the patient had symptoms.

There was also a female preponderance among our CAT2DM subjects. There were only 59 males compared to 71 females**.** In the age group between 21-25 years, there were 57 women and 40 men, in the 15 to 20 years age group, there were 11 women and 16 men, while less than 15 years had 3 men and 3 women. This could be due to the early puberty spurt among girls, leading to insulin resistance [6]. This hormonal change could be an important triggering factor for the development of CAT2DM among girls. This female predominance has a significant bearing on women's health as these young CAT2DM women, if undetected, will progress on towards pregnancy and encounter the complications of gestational diabetes. Hence, early

detection of CAT2DM becomes important in these women to ensure healthy pregnancies with good maternal and fetal outcomes.

It was also noted that a majority of the patients were studying graduation, and only a mere 10% were educated less than in high school. This indicates that literacy among patients could be playing an important role in encouraging them to seek medical help for their glycaemic control. A population-based study in South India also showed better literacy among diabetic patients contributes to seeking early care and thereby has better outcomes [7].

Among the 130 CAT2DM patients, 47(36%) had a family history of diabetes. It is common knowledge that genetic predisposition plays an important risk factor in the development of early-onset T2DM. In a study in the United Kingdom, it was noted that 84% of the adolescents with T2DM had family history [8]. While this contrasts the numbers obtained in our study, our lower percentage of family history could be due to a paucity of information in our study. Many of the parents were not aware of their current diabetic status, and some were prejudiced to allow us to test them for T2DM. A North Indian study also mirrored the U.K. study findings, with over 80% of their subjects having a family history of diabetes [9]. Though a lot of attention is given to genetic predisposition, it should be remembered that families often share their environment and not just their genes.

On their first presentation, a majority of our CAT2DM patients presented with osmotic symptoms (such as polyuria, polydipsia, and polyphagia), while weight loss was also noted among in 36 patients. A huge cohort of patients (42) were detected to have CAT2DM with only nonspecific clinical symptoms such as generalized weakness and fatigue. It was interesting to note that 4 patients presented with ketosis. These patients were admitted with diabetic ketosis. However, on follow up they achieved glycaemic control with oral hypoglycaemic drugs alone. This shows that they may belong to the category of ketosis-prone type 2 D.M. and not type 1 diabetes.

On examination, more than half of the patients (72) were overweight and obese (as shown in Figure 1), according to their BMI. Though it is a common understanding that obesity is associated with T2DM, it is interesting to note that 45% of our study population was normal or underweight despite having T2DM. This was also noted in a pilot study done in India, where a sizeable proportion of patients from all ethnic groups who were normal or lean (as per the Asian cut-offs for BMI) had a higher prevalence of T2DM compared to the white population [10]. This was explained by a varying pathophysiological pathway in normal/lean diabetics in

comparison to obese diabetics. They also noted lower fasting insulin levels and poor insulin secretion among normal/lean diabetics.

A majority of the patients who presented to us had uncontrolled sugars (shown in Table 3) as noted by high mean values of FBS, PPBS, and HbA1C. On evaluation, glycated hemoglobin (HbA1c) was used, and patients were categorized into normal (<7), well-controlled (7-9) or poorly controlled (>9). A majority of our CAT2DM patients had uncontrolled diabetes at presentation. A large cross-sectional study done in Denmark showed the HbA1c >9 (i.e. poorly controlled diabetes) among early-onset diabetics to be 12% [11]. This is low compared to the 54% poorly controlled diabetics in our population. Our study also showed that over 52% of the patients were diagnosed at their first point of contact with us, i.e., at presentation, and 48% have had diagnosed with type 2 diabetes before the presentation, but control of diabetes was the same in both the groups. CAT2DM has significantly worse outcomes later on in life than late-onset diabetes, as the duration of diabetes is longer in CAT2DM. Thereby it is associated with a higher BMI and HbA1c in addition to complications in lipid metabolism, microvascular and macrovascular complications [12].

C-peptide was done in 41 patients in our study population. Five of them (3.8%) were noted to have low C-peptide levels of <1.1. C-peptide was especially important in patients who were discharged on insulin and OHAs. They were managed later only on OHAs showing good beta-cell reserve. A low C-peptide level may indicate only a transient need for insulin, thereby reiterating that the patient was CAT2DM, who probably needed adjunct insulin for a short period.

Among the complications associated with diabetes, only 2 patients presented with sepsis. The microvascular complications were noted in nine patients wherein 4 (3.0%) had diabetic nephropathy, and 3 (2.3%) and 2 (1.5%), have had neuropathy and retinopathy respectively. T2DM by itself is a harbinger of cardiovascular complications. CAT2DM only underscores these complications with severity and early occurrence. However, it should be noted that we identified the complications in our patients at the time of diagnosis. As we did not follow up these patients for their complications, the reported data for complications may be lower than expected.

Rates of retinopathy in CAT2DM were found to be lower than in adult onset T2DM in a longitudinal study in the United States [13]. Our study showed 1.5% of the CAT2DM population having diabetic retinopathy. Our patients were evaluated for diabetic retinopathy at

the first point of contact during their diagnosis, 2 patients had evidence of retinopathy on fundoscopy. Even this is important as it was detected during the index visit.

Though retinopathy occurred less commonly than nephropathy in CAT2DM, the opposite was found in the adults with T2DM. Renal involvement is usually more commonly described in CAT2DM than the other microvascular complications. Nephropathy was diagnosed in those with macroalbuminuria (i.e., urinary albumin excretion of more than 300 mcg/mg) or microalbuminuria (urinary albumin excretion of 30–299 mcg/mg of creatinine). We had 2 patients of diabetic nephropathy in our study, one of them had chronic kidney disease while the other had proteinuria. A dataset from Canada showed a 4-fold increase in the risk of renal failure among CAT2DM when compared to youth onset T1DM and a 23-fold increase compared to controls [14]. Surprisingly, hypertension had no bearing on youth onset T2DM according to the Canadian study.

As the method of testing for diabetic neuropathy in different studies vary, neuropathy has been noted in up to 57% patients with early onset diabetes. A population-based cohort was studied and peripheral neuropathy was found in 7.6% of CAT2DM patients compared to 5% of CAT1DM [15]. Our study shows 2.3% with peripheral neuropathy. Despite the varying numbers, it is now clear that neuropathy develops earlier in T2Dm than T1DM, and this rampant course can lead to early foot ulceration (in 2 years' time) and amputation (in 10 years' time). Macrovascular complications of diabetes like stroke and coronary artery disease/ischemia were not noted in any patient.

Treatment of CAT2DM hinges on oral hypoglycaemic agents (OHAs) alone or in combination with insulin. Our study noted that 95% of our patients received OHAs with or without insulin, while 60% received OHAs alone. Though insulin is freely approved for use in the pediatric and adolescent age group, the OHAs do not enjoy the same unrestricted use in this population. Drug licensing restrictions create significant hurdles in the management of CAT2DM.

Almost 82% of our CAT2DM population receive metformin as OHA, while 20% were on glimepiride. Among the 45 patients who were on OHAs and insulin, eighteen patients could be maintained on OHAs alone on follow-up. Nine patients on follow-up did not require any drug therapy and were able to achieve glycaemic control on diet and lifestyle modifications alone. Three of them had normal C-peptide levels, thereby confirming that they were CAT2DM patients in the first place.

Fifteen of the forty-five patients (on OHAs and insulin) could not be followed up as they did not visit the hospital following discharge. However, even among these 15 patients (who could not be followed up), 12 were obese and 3 were overweight. None of these 15 patients had ketosis on presentation. Thus, we can concur that all of these patients are probably CAT2DM.

In the early 21st century, a multi-center trial concluded that metformin was safe to use in children above 10 years of age. A reduction in the HbA1c by 1.2% was noted over the 16-week period of treatment with metformin alone when compared to the placebo limb [16]. A few years later another study indicated that glimepiride (sulfonylurea) reduced the HbA1c like metformin [17]. The TODAY trial is a randomized control trial where those recently diagnosed with T2DM were randomly assigned to either metformin alone, metformin and lifestyle intervention, or metformin plus rosiglitazone. The metformin with rosiglitazone limb was found to be superior to metformin alone [18].

It was noted that two-thirds of our population were well controlled with OHAs alone, while one-third of the population required insulin in addition to OHAS. This trend is similar in all age groups (<15years, 16-20 and >21 years). Among the OHAs, biguanides were the most common prescription, followed by sulfonylureas in the 15-20 years and >21 years population. The younger than 15 years population received only metformin in our study. Among the insulin therapy, almost all patients required only short-acting and pre-mix insulin. This indicates that the study population, being CAT2DM, required insulin only initially to achieve glycaemic control as most of them presented with uncontrolled sugars (mean FBS, 198.7 ± 89.6 and mean PPBS, 278.7 ± 133.3). This also confirms the adequate b-cell activity as most of the patients requiring insulin were easily managed on OHAs alone on follow-up. Thus, we can concur that CAT2DM is a diagnosis worth making as its early detection paves the way for an easy management with only OHAs or even diet and lifestyle modifications.

CONCLUSION

This study on CAT2DM gives us a perspective on this category of diabetes that has emerged over the past decade among the young diabetes community. Recognition of this subgroup early in the course of the disease is important, for protecting them from unnecessary insulin use by being mislabelled as type 1 diabetes. Screening for diabetes when this group presents even with nonspecific symptoms, emphasizing the need for lifestyle changes, control of sugars, ensuring compliance and emotional support and reassurance to patients and their families are essential

aspects of management. This study may have implications for preventing complications in this group and may impact national policy in young diabetes patients.

CONFLICT OF INTEREST

The authors do not declare any conflict of interest.

ACKNOWLEDGEMENT

The team wants to thank the Indian Council of Medical Research (ICMR) for the support through the 'Young Diabetic Registry.'

TABLE AND FIGURE LEGENDS

Table 1. Year-wise Data Distribution

Table 2. Socio-demographic profile of the CAT2DM patients

Table 3: Clinical and biochemical profile of CAT2DM patients

Table 4. Treatment pattern and drug utilization in CAT2DM patients

Figure 1: Patient distribution based on the body-mass index

REFERENCES

1. Rosenbloom AL, Silverstein JH, Amemiya S et al. ISPAD Clinical Practice Consensus Guidelines 2006-2007. Type 2 diabetes mellitus in the child and adolescent. *Pediatr Diabetes* 2008; 9: 512-526.
2. Lobstein T, Frelut ML. Prevalence of overweight among children in Europe. *Obes Rev.* 2003; 4: 195-200.
3. Liu LL, Yi JP, Beyer J, Mayer-Davis EJ et al.; SEARCH for Diabetes in Youth Study Group: Type 1 and type 2 diabetes in Asian and Pacific Islander U.S. youth: the SEARCH for Diabetes in Youth Study. Diabetes Care 2009;32(Suppl 2):S133–S140.
4. Amutha A, Datta M, Unnikrishnan I.R. et al. Clinical profile of diabetes in the young seen between 1992 and 2009 at a specialist diabetes centre in south India. Prim. care diabetes. 2011;5(4):223-9.
5. Unnikrishnan AG, Bhatia E, Bhatia V et al. Type 1 diabetes versus type 2 diabetes with onset in persons younger than 20 years of age. Ann NY Acad Sci 2008;1150:239–244.
6. Kaufman FR: Insulin resistance syndrome: a pediatric perspective. Endocr Pract 2003;9(Suppl 2):78–80.
7. Hussain R, Rajesh B, Giridhar A et al. Knowledge and awareness about diabetes mellitus and diabetic retinopathy in suburban population of a South Indian state and its practice among the patients with diabetes mellitus: A population-based study. Indian J Ophthalmol. 2016;64(4):272-6.
8. Haines L, Wan KC, Lynn R et al. Rising incidence of type 2 diabetes in children in the U.K. Diabetes Care. 2007; 30(5):1097-101.
9. Vikram NK, Tandon N, Misra A et al: Correlates of Type 2 diabetes mellitus in children, adolescents and young adults in north India: a multisite collaborative case-control study. Diabet Med. 2006;23:293–298.
10. Das S, Samal KC, Baliarsinha AK et al. Lean (underweight) NIDDM—peculiarities and differences in metabolic and hormonal status—a pilot study. J Assoc Physicians India. 1995;43:339–342.
11. Bo A, Thomsen RW, Nielsen JS et al. Early-onset type 2 diabetes: Age gradient in clinical and behavioural risk factors in 5115 persons with newly diagnosed type 2 diabetes-Results from the DD2 study. Diabetes Metab Res Rev. 2018;34(3).
12. Huang Jx., Liao Yf, Li Ym. Clinical Features and Microvascular Complications Risk Factors of Early-onset Type 2 Diabetes Mellitus. *CURR MED SCI.* 2019;39, 754–758.

13. Krakoff J., Lindsay R., Looker H. et al. Incidence of retinopathy and nephropathy in youth onset compared with adult-onset type 2 diabetes. Diabetes Care. 2003;26: 76–81
14. Dart AB, Sellers EA, Martens PJ et al. High burden of kidney disease in youth-onset type 2 diabetes. Diabetes Care. 2012;35(6):1265-71.
15. Dart AB, Martens PJ, Rigatto C et al. Earlier onset of complications in youth with type 2 diabetes. Diabetes Care. 2014;37(2):436-43.
16. Jones KL, Arslanian S, Peterokova VA et al. Effect of metformin in pediatric patients with type 2 diabetes: a randomized controlled trial. Diabetes Care. 2002; 25(1):89-94.
17. Gottschalk M, Danne T, Vlajnic A et al. Glimepiride versus metformin as monotherapy in pediatric patients with type 2 diabetes: a randomized, single-blind comparative study. Diabetes Care. 2007; 30(4):790-4.
18. Zeitler P, Hirst K, Pyle L et al; TODAY Study Group. Clinical trial to maintain glycemic control in youth with type 2 diabetes. N Engl J Med. 2012 Jun 14; 366(24):2247-56.

Table 1. Year-wise Data Distribution

Year	**N (%)/130**
2012	11 (8.5)
2013	9 (6.9)
2014	14 (10.8)
2015	22 (16.9)
2016	23 (17.7)
2017	16 (12.3)
2018	23 (17.7)
2019	12 (9.2)

Table 2. Socio-demographic profile of the CAT2DM patients

Socio-demographic Characteristics	
Mean Age at presentation (Years)	23.3±5.7
Mean Age of Onset (Years)	20.9±4.6
Age Category	
≤15 Years	6 (4.6)
16-20 Years	27 (20.8)
21-25 Years	97 (74.6)
Gender	
Male	59 (45.4)
Female	71 (54.6)
Education	
Literate	3 (2.3)
Primary	5 (3.8)
Middle	9 (6.9)
Secondary	27 (20.8)
Technical	5 (3.8)
College & Above	81 (62.3)
Family History	47 (36.2)
Mother	26 (20.0)
Father	17 (13.1)
Siblings	4 (3.1)

Table 3: Clinical and biochemical profile of CAT2DM patients

Presentation	
Osmotic	45 (34.6)
Ketosis	4 (3.1)
Weight Loss	36 (27.7)
Non-specific symptoms	45 (34.6)
BMI Category	
<18 kg/m^2	33 (25.4)
18-22.9 kg/m^2	25 (19.2)
23-27.4 kg/m^2	33 (25.4)
>27.5 kg/m^2	39 (30.0)
Comorbid conditions	
Hypertension	7 (5.4)
Acanthosis nigricans	11 (8.5)
Diabetes complications	
Retinopathy	2 (1.5)
Nephropathy	2 (1.5)
Neuropathy	3 (2.3)
Sepsis	2 (1.5)
Biochemical profile	
Fasting blood sugar	198.7 ± 89.6
2 hours post-prandial blood sugar	278.7 ± 133.3
Random blood sugar	330.8 ± 134.3
Glycated Hemoglobin	9.4 ± 2.8
C-Peptide	2.00 (median) 1.40, 2.00, 3.23

Table 4. Treatment pattern and drug utilization in CAT2DM patients

Drugs	**N (%)/130**
OHA Alone	79 (60.8)
Combination (OHA and Insulin)	45 (34.6)
No medication	6 (4.6)
Regular and pre-mix Insulin	45 (34.5)
Long Acting	5 (3.8)
Biguanides	107 (82.3)
Sulfonylureas	26 (20.0)
Glitazones	3 2(2.3)
Glucosidase Inhibitors	5 (3.8)
DPP IV Inhibitor	4 (3.1)

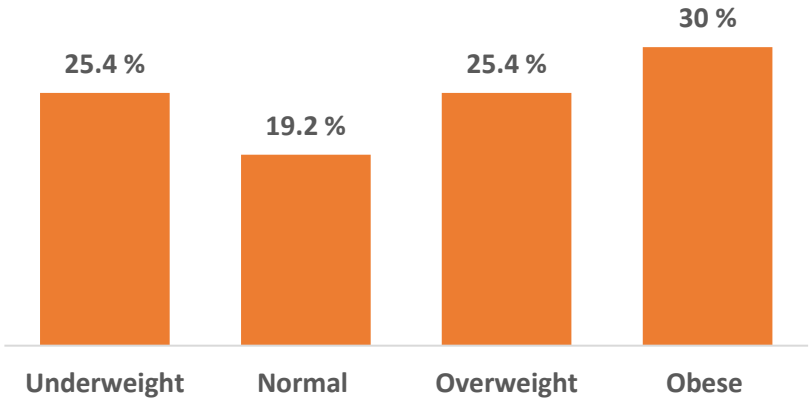


Figure 1: Patient distribution based on the body-mass index