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Original Article

Clinical characteristics, types and complications of diabetics with young age at the onset (14–25 years)

Pranabananda Sahu*, Sidhartha Das

PG Department of General Medicine, SCBMCH, Cuttack, India

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ABSTRACT

Aims: To determine the distribution, clinical features and complications of the different types of diabetes in young age. Methods: The records of children and adolescents with age at the onset of DM (14–25 years) between January 2017 and August 2018, were reviewed. Clinical and laboratory characteristics of the patients at diagnosis and type of diabetes were recorded. Results: Out of 80 patients (48 males, 32 females), 53 had type 1 DM (66.2%) and 27 had type 2 DM (33.8%). Mean age at the onset of diabetes was 19.75 ± 4.01 years for type 1 DM and 21.37 ± 3.08 years for type 2 DM. Family history of DM was more common in type 2 DM (62.9% of parents, $p = 0.000389$). Mean BMI in type 2 DM (25.03 ± 5.88 kg/m2) was higher than in type 1 DM ($p = 0.009$). Osmotic symptoms were more common in type 1 DM (73.06%, $p = 0.00151$). Conclusion: Osmotic symptoms and ketosis were more common in young age type 1 DM. Family history of DM was more common in parents of type 2 DM.

1. Introduction

Diabetes mellitus (DM) is a heterogenous chronic metabolic disorder principally characterized by persistent hyperglycemia resulting from defects in Insulin secretion, action or both. DM comprises of a group of chronic metabolic abnormalities involving carbohydrate, protein and fats. The chronic hyperglycemia of diabetes is associated with long term damage, dysfunction and failure of different organs. According to ICMR INDIAB study, currently in India there are 62.5 million people living with diabetes [1]. Until recently, type 1 diabetes mellitus was not only the most common form of diabetes seen in youth, but also perhaps the only form of diabetes seen in children and adolescents. Type 2 diabetes mellitus (T2DM), earlier considered a disorder of middle age or elderly, is increasingly being reported among young adults and now also in adolescence and childhood, probably due to the burgeoning epidemic of childhood obesity. The most prevalent forms of diabetes among younger individuals are Type-1 Diabetes (Type-1 DM), followed by youth onset Type-2 Diabetes (Type-2DM). Other forms of diabetes such as latent autoimmune diabetes of adult (LADA), Maturity onset diabetes in young (MODY), Gestational diabetes, fibrocalculous pancreatic diabetes (FCPD) have also been observed in individuals less than 25 years of age. A wide spectrum of complications may develop in case of diabetes. These includes the acute metabolic complications, chronic complications and others. The acute metabolic complications are Diabetic ketoacidosis (DKA), Hyperosmolar Hyperglycemic state (HHS) and Hypoglycemia. Chronic complications can be broadly classified into two major categories: Vascular and Non-vascular. Vascular complications are further divided according to whether they are affecting Retina (Diabetic Retinopathy {DR}), Kidney (Diabetic nephropathy) and Peripheral nerves (Diabetic neuropathy) or macrovascular complications which includes coronary artery disease [CAD], peripheral arterial disease [PAD], and cerebrovascular disease (CVD). Conditions such as gastroparesis, infections, and skin changes constitute the non-vascular complications of diabetes. Although chronic hyperglycemia is an important etiologic factor leading to complications of DM, the mechanism(s) by which it leads to such diverse cellular and organ dysfunction is unknown but formation of advanced glycosylation end products (AGEs), glucose metabolism via sorbitol pathway, increased formation of diacylglycerols and hexosamine pathway are various theories to explain pathogenesis of complications of DM. Population-based estimates of T2DM in the young are lacking as screening for diabetes is not recommended in children and adolescents.

* Corresponding author.
E-mail address: s.sipua@gmail.com (P. Sahu).

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2. Materials and methods

Our study was hospital based observational study conducted in the post Graduate Department of Medicine, S·C·B Medical college, Cuttack between January 2017 to June 2018.80 patients with age at the onset of diabetes between 14 years and 25 years reported at OPD/admitted consecutively to Post Graduate Department of Medicine, S·C·B Medical college, Cuttack from January 2017 to June 2018 were enrolled for the study. DM was diagnosed according to WHO criteria. Blood glucose was done by glucose oxidase method in venous blood. Glycosylated hemoglobin estimation was done by ion exchange chromatography method. Height and weight of young diabetes patients were measured. BMI (kg/m2) were calculated within each annual age category. Family history of diabetes in grandparents, parents and siblings were taken.

Ketone bodies present in the urine samples were measured in urine dipstick method. All the selected patients were evaluated for the presence of microvascular complications (retinopathy, neuropathy and nephropathy) and macrovascular complications (coronary artery disease, cerebrovascular disease), acute metabolic complications, infections, fatty liver and hypertension. Direct/indirect fundoscopy was used to make the diagnosis and grading of retinopathy. Nephropathy was diagnosed based on 24 h urine collection for proteinuria. Neuropathy was diagnosed from history of numbness, parasthesia, tingling sensation and confirmed by touch sensation with 10 gm monofilament at distal plantar aspect of great toe, 128 Hz tuning fork for vibration perception and ankle reflex. CAD was diagnosed from history of myocardial infarction or angina documented by previous records or by ECG or Echocardiography. CVD diagnosed from the history of neurological deficit, clinical examination, and CT/MRI of brain whenever required. Hypertension was defined as a value $\geq$ 140/90 mmHg. A body mass index (BMI) cut-off of 25kg/m2 for men and 23kg/m2 for women was used for making a diagnosis of obesity. Patients with age less than 14 years and more than 25 years at the time of diagnosis are excluded from the study. The data was analysed by SPSS version 25. Quantitative data was analysed by Student's t-test and qualitative data was analysed by Chi-Square test.

3. Results

Total number of patients recruited for the study was 80 (48 males, 32 females). Out of 80 diabetic patients, 53 had type 1 DM (66.2%) and 27 had type 2 DM (33.8%). Mean age at the onset of diabetes was 19.75 ± 4.01 years for type 1 DM and 21.37 ± 3.08 years for type 2 DM. Positive family history of diabetes mellitus was more common in type 2 DM (62.9% in parents, 7.4% in siblings) than in type 1 DM. The correlation was statistically significant. Mean BMI in type 2 DM (25.03 ± 5.88 kg/m^2) was higher than in type 1 DM. The association was statistically significant. In type 1 DM patients, osmotic symptoms (73.5%), weight loss (58.49%) and ketosis (5.6%) were more common as compared to type 2 DM. Osmotic symptoms had significant correlation with type of diabetes. No significant microvascular or macrovascular complications were found.

4. Discussion

Diabetes mellitus (DM) is the most common metabolic disorder. The most prevalent forms of DM seen among younger individual is type 1 DM to be followed by youth-onset type 2 DM. Other forms of DM such as maturity-onset diabetes in youth (MODY), gestational diabetes (GDM), and fibrocalculous pancreatic diabetes (FCPD) have also been observed in individual less than 25 years of age. In the study by Amutha et al., among the total of 2,630 subjects with DM in the young, 1262 (48%)had T2DM, 1,135 (43.2%) had T1DM, 118 (4.5%) had GDM and 115 (4.4%) had other forms of DM including FCPD and genetic syndromes of diabetes [2].

Table 1
Clinical type of diabetes.

Type of Diabetes	Number	Percentage
Type 1	53	66.2%
Type 2	27	33.8%
Total	80	100%

In this study, out of 80 patients, the clinical types of diabetes revealed that 66.2% of patients had type 1 DM and 33.8% had type 2 DM (Table 1). Haliloglu et al. found that out of 835 patients with DM, 84% had type 1 DM and 5.7% had type 2 DM [3]. Constantino et al. found that in a series of 824 patients, 57.04% had young-onset type 1 DM and 42.96% had type 2 DM [4].

Gender distribution in our study showed 64.2% males & 35.8% females in type 1 DM and 51.8% males and 48.2% females in type 2 DM (p value = 0.288) (Table 2). Haliloglu et al. found that among type 1 diabetics, 51% were males and 49% females. Among type 2 DM, 29% were males and 71% were females [3] whereas Unnikrishnan AG et al. found that in young-onset type 2 DM, there was male preponderance (males = 58.3% and females = 41.7%) [5]. Female preponderance in type 2 DM in the Western countries while male preponderance in India is well documented. In a study by U·P.Gujral et al. the prevalence of type 2 diabetes by BMI category varied by ethnicity and sex. In underweight men, the prevalence of type 2 diabetes was 5.4% in Asian Indians. However, no White men who were underweight had type 2 diabetes. In normal weight men, the prevalence of type 2 diabetes was 23.5% and 6.1% in Asian Indians and Whites respectively. In underweight women, the prevalence of type 2 diabetes was 5.6% in Asian Indians and 2.3% in Whites. In normal weight women, the prevalence of type 2 diabetes was 13.6% and 2.8% in Asian Indians and Whites respectively. In both sexes, Asian Indians also had a greater prevalence of type 2diabetes in the overweight and obese categories compared to White individuals [6].

In this study, out of 80 patients, mean age at the onset of diabetes in type 1 DM was 19.75 ± 4.01 years and in type 2 DM was 21.37 ± 3.08 years (p value = 0.07) (Table 3). In a study by Song SH et al., out of 1287 patients with age at the onset below 40 years, the mean age at the onset was25.8 ± 6.9 in type 1 DM and 32.5 ± 5.9 years in type 2 DM ($p < 0.0005$). Overall, patients with T1D had a younger age at the onset [7]. Haliloglu et al., studied 835 children of age below 18 years and found that mean age at the onset in type 1 DM was 8.4 ± 4.2 years and in type 2 DM it was 13.2 ± 2.5 years [3]. Constantino et al. found that the age at the onset of diabetes was 25.6 ± 3.7 and 22.0 ± 4.3 years ($P = 0.01$)[4]. Our study was limited to

Table 2
Gender wise distribution among clinical type of Diabetes.

Clinical type	Male	Female
Type 1	34 (64.2%)	19 (35.8%)
Type 2	14 (51.8%)	13 (48.2%)
Total	48 (60%)	32 (40%)

Table 3
Mean Age at the Onset of diabetes.

Clinical Type	Mean Age at the onset (years)	P-VALUE*
Type 1	19.75 ± 4.01	0.07
Type 2	21.37 ± 3.08	
Total	20.30 ± 3.78	

Table 4
Correlation between family history and type of diabetes.

Family history: Parents			
	Present	Absent	P-VALUE*
Type 1	12 (22.6%)	41 (77.4%)	0.000389
Type 2	17 (62.9%)	10 (37.1%)	
Total	29 (36.25%)	51 (63.75%)	
Family history: Grand Parents			
	Present	Absent	–
Type 1	0	53 (100%)	
Type 2	0	27 (100%)	
Total	0	80 (100%)	
Family history: Siblings			
	Present	Absent	0.2190
Type 1	1 (1.9%)	52 (98.1%)	
Type 2	2 (7.4%)	25 (92.6%)	
Total	3 (3.75%)	77 (96.25%)	

Table 5
Correlation between BMI and type of diabetes.

Clinical Type	Mean BMI	SD	P value*
Type 1	21.01	6.55	0.009
Type 2	25.03	5.88	
Total	22.38	6.58	

Table 6
Correlation between clinical characteristics with type of diabetes.

Osmotic symptoms			
Clinical Type	Present	Absent	P-Value*
Type 1	39	14	0.00151
Type 2	10	17	
Total	49	31	
Weight Loss			
Clinical Type	**Present**	**Absent**	0.947
Type 1	31	22	
Type 2	16	11	
Total	47	33	
Ketosis			
Clinical Type	**Present**	**Absent**	0.547
Type 1	3	50	
Type 2	0	27	
Total	3	77	
Incidental			
Clinical Type	**Present**	**Absent**	-
Type 1	0	53	
Type 2	0	27	
Total	0	80	
Others			
Clinical Type	**Present**	**Absent**	-
Type 1	0	53	
Type 2	0	27	
Total	0	80	

Table 7
Long term Complication.

Complications	Number	Percentage
Retinopathy	0	0%
Nephropathy	1	1.8%
CAD	0	0%
CVA	0	0%
Peripheral vascular ds	0	0%

adults and didn't consider patients below 14 years of age at the onset as per the study design.

Family history of DM in the patients revealed that in type 1 DM 22.6% patients had history of DM in parents and 1.9% had history in siblings. In type 2 DM, 62.9% had history of DM in parents and 7.4% had history in siblings (p value = 0.00389). There was no history of diabetes in grandparents in any patient. History of diabetes in siblings was not significant (p = 0.2190) (Table 4). In a multi-centre study of young diabetes by Unnikrishnan AG et al. positive family history was more common in type 2 DM than in type 1 DM (64% vs 22%, p value = <0.0001)[5]. Martine Vaxillaire et al. found that T2DM shows a clear familial aggregation, with a risk for people with familial diabetes that is increased by a factor of 2–6 compared with those without familial diabetes; it does not segregate in a classical Mendelian fashion, and appears to result from several combined gene defects. T2DM is probably also multigenic, meaning that many different combinations of gene defects may exist among subgroups of people with diabetes [8].

In this study, the mean weight of patients in type 1 DM group was 50.68 ± 16.86 kg and in type 2 DM, it was 66.66 ± 17.13 kg (p = 0.002). Mean BMI was 21.01 ± 6.55 kg/m^2 in type 1 DM and it was 25.03 ± 5.88 kg/m^2 in type 2 DM (p = 0.009) (Table 5). Hannon, TS et al. showed that overweight or obesity is the most important risk factor for the development of T2DM in youth. Indeed, the increasing prevalence of overweight closely parallels the rise in the number of cases ofT2DM. Insulin resistance, which develops as a result of both genetic and environmental factors, is strongly associated with obesity. Moreover, insulin resistance is now widely believed to be the first step in the development of T2DM, cardiovascular disease, and other conditions [9]. In the study by Song et al., patients with type 1 DM had mean BMI of 26.6 ± 5.0 kg/m^2 and patients with type 2 DM had mean BMI of 34.7 ± 8.6 kg/m^2 [7]. Constantino et al., in a study on 354 type 2 DM and 470 type 1 DM found the mean BMI to be 25.6 ± 4.5 kg/m^2 in type 1 DM and 32.2 ± 7.6 kg/m^2 in type 2 DM [4]. Unnikrishnan et al. also found that in type 1 DM patients, mean BMI was 17.4 ± 4.3 and in type 2 DM, mean BMI was 25.5 ± 5.6 (p value < 0.001)[5].

In our study, osmotic symptoms were present in 73.06% of type 1 diabetics and 37% of type 2 diabetics. Ketosis was present in 5.6% of type 1 diabetics. Weight loss was present in 58.5% of type 1 diabetics and 59.3% of type 2 diabetics. Presence of osmotic symptoms had significant association with type of diabetes, being more common in type 1 DM than in type 2 DM (p value = 0.00151) (Table 6). Presence of weight loss and ketosis had no significant association with type of diabetes (p = 0.947, p = 0.547 respectively). In a study by Haliloglu et al., ketosis was found in 48.4% of type 1 DM patients and 6.5% of type 2 DM patients [3]. In a study by Suresh K et al., out of 130 patients before the age of 35 years, 26% of young diabetics presented with osmotic symptoms of polyphagia, polydipsia and polyuria [10].

In our study, 1 patient had developed nephropathy (Table 7). No other patient had any complications because of shorter duration of disease. In the series by Unnikrishnan et al., peripheral neuropathy was seen in 6% patients of type 1 DM and no patient of type 2 DM (p value = 0.12); retinopathy in 5% type 1 DM patients vs no patient of type 2 DM (p value = 0.16) and nephropathy in 5.4% of type 1 DM vs no patient of type 2 DM (p value = 0.14)[5].

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