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Original Article

Paediatrics Section

Clinical Profile of Type 1 Diabetes Mellitus in Children less than 18 years age, in a Tertiary Care Centre, Bhilai, Chhattisgarh, India: A Cross-sectional Study

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ABSTRACT

Introduction: Type 1 Diabetes Mellitus (T1DM) is a very common paediatric endocrine disorder and is increasing each year, particularly in younger children. The T1DM presents as Diabetic Ketoacidosis (DKA) in a significant number of patients. Race, ethnicity, age, and parent education plays an important role in the glycaemic control of the disease. Conflicting data are available about the age of onset, gender predominance, family history, and growth in various international and national studies.

Aim: To study the clinical presentation of T1DM in children aged less than 18 years.

Materials and Methods: The observational cross-sectional study was conducted from April 2011 to March 2013 at Jawaharlal Nehru Hospital and Research Centre, Bhilai, Chhattisgarh, India. Total 46 patients with T1DM, aged less than 18 years were included in the study. Socio-demographic data, clinical presentation, age, insulin dose, anthropometry, and laboratory investigations were collected using semi-structured performa. Statistical analysis was done by using Statistical Package for Social Sciences (SPSS) version 26.0.

Results: Total 46 patients with T1DM attended the hospital with 24 (52.8%) boys and 22 (47.2%) girls. A 28 (60.8%) of patients presented with DKA. 16 (34.8%) of patients were less than five years of age. The youngest patient was of 2.5 years of age. In the present study, stunting was noted in 12 (26.08%) patients. Polyuria (85%) was the most common presenting complaint in newly diagnosed diabetes patients and pain in the abdomen (50%), breathlessness (46.8%) were the most common presenting complaint in established diabetics. Patients with poor control (HbA1c- >8.5%) had significantly higher mean age (12.3±4.01) compared to the group with good control (HbA1c <8.5%) which has mean age (8.5±3.54 years). Availability of medical facilities, higher socio-economic status, and parents' education was found to be significantly associated with good glycaemic control.

Conclusion: Polyuria was the most common symptom in newly diagnosed diabetics. Higher age was a significant risk factor for poor control of diabetes. DKA may present with respiratory distress in a significant number of patients.

Keywords: Diabetic ketoacidosis, Glycaemic control, Polyuria, Short stature

INTRODUCTION

The T1DM is a common, chronic disease in children and adolescents. Approximately 5,00,000 children, less than 15 years of age are affected by T1DM [1]. Already 1,00,000 new children are detected to have T1DM each year. Every fifth T1DM infant on the globe is an Indian [1]. The incidence of T1DM, age of onset of disease, and gender varies in various international studies [2-6]. In India, the overall incidence of T1DM is 10.5/100,000/year and peaks at ages 10-12 years. Incidence also varies according to gender, 4.0/100,000 in girls and 3.7/100,000 in boys [7].

There is a wide variation in the range of children presenting with DKA as the initial manifestation of diabetes depending on the study population. A constellation of socio-demographic factors related to race, ethnicity, age, availability of access to health services, parent education, and socio-economic class plays role in the glycaemic control of disease [8]. In India, due to a lack of awareness about diabetes mellitus particularly parents in rural areas tend to ignore the symptoms and delayed treatment leading to serious complications like DKA. They are not well educated about the child's disease, leading them to search for alternative therapy. Primary care physicians may also miss these patients as symptoms overlap with other systemic diseases [8].

Knowledge among parents regarding symptoms of diabetes is important in early recognition of the disease. This responsibility lies with a paediatrician as most of the patients will attend paediatric Outpatient Department (OPD). Various similar studies have been carried out internationally and in India [1,3,7,9,10]. In India, most of these studies are carried out in South India, where parents are well-educated [1,2,11]. No study is published on T1DM in children in this region of central India. Hence, present study was carried out to study the clinical profile of children with T1DM in children, aged less than 18 years, so that the information generated can be used to maintain a hospital-based registry for T1DM and to educate the parents as well as ourselves.

MATERIALS AND METHODS

The observational cross-sectional study was done for 24 months, from April 2011 to March 2013 at Jawaharlal Nehru Hospital and Research Centre, Bhilai, Chhattisgarh, India. Written consent was taken before the interview from the parents or guardians, and patients who satisfied inclusion criteria after discussing the nature and goal of the work. No written Institutional Ethics Committee (IEC) approval is available as it was not mandatory at that time. But it is the paper of thesis which was accepted by NBE board (Ref NBE/ THESIS/131133/ 2013/2943).

Inclusion criteria: Consecutively all newly diagnosed patients with fasting plasma glucose 126 mg/dL, random plasma glucose >200 mg/dL, Glycosylated haemoglobin >6.5% [12], and patients previously diagnosed with T1DM attending the hospital within 24 months were included in the research.

Exclusion criteria: The patients who refused to give consent and those whose required medical records were inadequate, were excluded.

Sample size: The following formula was used for calculating the sample size:

$$n=Z^2 P(1-P)/d^2$$

Where n is the sample size, Z is the statistic corresponding to level of confidence, 'P' is expected prevalence and d is precision. 'Z' is considered as 95%, prevalence is 31.9/1000000 [5], precision 0.04. sample size calculated was 17 but all the 46 patients during the study period, who attended hospital were enrolled in the study.

Study Procedure

Information was gathered from patients, mothers, fathers, or guardian about the socio-demographic profile, age, treatment history, and symptoms at the interval of diagnosis in previously diagnosed patients, age and symptoms at the presentation. Socio-economic status was categorised according to Modified BG Prasad classification [6].

Detailed clinical examination and anthropometric examination were carried out on all patients. The precipitating factors for DKA such as, infection, missed insulin doses, intercurrent illnesses like trauma, burn, and viral infections were studied. Investigations were recorded from medical reports [13]. The Random Blood Sugar (RBS), HbA1c, urine sugar, urine ketone. Venous Blood Gas (VBG) was done in patients with DKA.

RBS was done by glucometer, and urine sugar and urine ketone were done by reagent strip. A total insulin dose in U/kg/day was calculated. The patient was considered moderately stunted if length/height-for-age ≤-2 SD and ≥-3 SD of the median, severely stunted if length/height-for-age <-3 SD of the median [14]. Weight for height was used for children less than five years age and Body Mass Index (BMI) is used for children 5-18 years of age as World Health Organisation (WHO) charts are not available for this age [14]. When HbA1c levels are categorised into two groups poor control (HbA1c >8.5%) and the good control group (HbA1c <8.5%) this categorisation is validated and previously used in Samanta D et al., study [8].

STATISTICAL ANALYSIS

Statistical analysis was done by ratio, percentage, mean and standard deviation. Data were statistically analysed by using the unpaired t-test, Fisher's test, and comparison of proportion. The SPSS version 26.0 was used for statistical analysis. A p-value of <0.05 was considered significant.

RESULTS

A total of 46 patients with T1DM attended the hospital. Out of 46 children, 24 (52.8%) were boys and 22 (47.2%) were girls. A total of 32 (69.6%) were previously diagnosed and attended hospitals. Out of 46, 28 (60.8%) patients presented to the hospital with DKA, and 18 (39.2%) presented with other than DKA. The youngest patient was of 2.5 years of age. In the present study, stunting was noted in 12 (26.08%) patients and wasting in 14 (30.43%) [Table/Fig-1].

Polyuria was the most common presenting complaint in newly diagnosed diabetes patients, followed by the recent weight loss, abdominal pain, nausea and vomiting [Table/Fig-2]. Pain in the abdomen and breathlessness were the most common presenting complaints in established diabetics [Table/Fig-3].

Mean HbA1c level was 9.45%. A 56.52% of patients were having poor control of the disease. In this study, stunting was found in diabetic patients with a period of less than one year in 3 (25%) and more than one year in 9 (75%) of patients which was statistically significant. The average random blood sugar in less than one year of diabetes was 423±136.9 mg/dL and 359.7±163 mg/dL in more than one year which is not statistically significant [Table/Fig-4].

Clinical parameters	n (%) (Total N=46)
Newly diagnosed/established	
Newly diagnosed	14 (30.4%)
Established diabetics	32 (69.6%)
Presented as DKA/Non DKA	
DKA	28 (60.8%)
Non DKA	18 (39.2%)
Age at diagnosis of disease (in years) (n=46)	
<5	16 (34.8%)
5-9	12 (26.1%)
≥10	18 (39.1%)
Wasting (n=14)	
Moderate wasting	9 (19.56%)
Severe wasting	5 (10.86%)
Stunting (n=12)	
Moderate stunting	6 (13%)
Severe stunting	6 (13%)
Insulin requirement (U/Kg/Day)	
Newly diagnosed	0.93±0.25
Established	1.26±0.34
Insulin regimen	
Premixed (NPH+R)	33 (71.7%)
NPH+Regular	11 (23.9%)
Regular (Insulin pump)	1 (2.2%)
Basal Bolus (Insulin analog+R)	1 (2.2%)
HbA1c levels in the study	
<8.5%	20 (43.48%)
>8.5%	26 (56.52%)
Family history	
Yes	7 (15.2%)
No	39 (84.8%)
Duration of T1DM	
<1 year	19 (41.3%)
>1 year	27 (58.7%)
Associated infections (n=8)	
Pneumonia	3 (6.52%)
Urinary tract infection	2 (4.34%)
Skin infection	1 (2.17%)
Oral candidiasis	1 (2.17%)
Chickenpox	1 (2.17%)

[Table/Fig-1]: Clinical characteristics of children presenting with T1DM.
DKA: Diabetic ketoacidosis; NPH: Neutral protamine hagedorn

Symptoms	No. of cases
Polyuria	12 (85.87%)
Recent weight loss	9 (64.28%)
Abdominal pain	8 (57.14%)
Nausea and vomiting	8 (57.14%)
Breathlessness	6 (42.85%)
Fever	5 (35.71%)
Altered sensorium	3 (21.4%)

[Table/Fig-2]: Symptoms in newly diagnosed T1DM (N=14).

Symptoms	No. of cases
Pain in abdomen	16 (50%)
Breathlessness	15 (46.87%)
Nausea and vomiting	14 (43.75%)
Polyuria	13 (40.62%)
Fever	8 (25%)
Altered sensorium	6 (18.75%)
Hypoglycaemic seizure	5 (15.6%)
Loose motions	5 (15.6%)
Dose adjustment	5 (15.6%)
Coma	3 (9.3%)
Lethargy and weakness	2 (6.25%)
Seizure disorder	1 (3.12%)
Neurological deficit	1 (3.12%)

[Table/Fig-3]: Symptoms in established T1DM (N=32).

Characteristic	<1 year	>1 year	p-value (Unpaired t-test)
Short stature	3 (25%)	9 (75%)	0.01
HbA1c (%)	9.53±1.71	9.35±1.51	0.07
RBS (mg/dl)	423±136.9	359.7±163.1	0.16
Wasting	10 (71.5%)	4 (28.5%)	0.07
DKA	14 (50%)	14 (50%)	0.5

[Table/Fig-4]: Association of short stature, HbA1c, and RBS with a duration of diabetes mellitus.
HbA1c: Glycated haemoglobin; RBS: Random blood sugar; DKA: Diabetic ketoacidosis

Patients with poor disease control had a substantially greater mean age (12.3±4.01) years than the group with good control (8.5±3.54) years. Availability of medical facilities, higher socio-economic status, and parents' education were observed to be strongly connected with good glycaemic control in present study [Table/Fig-5].

Parameters		Glycaemic control		(p-value) (Unpaired t-test and Fisher's test)
		Good control (HbA1c <8.5%)	Poor control (HbA1c >8.5%)	
Mean age (years)		8.5±3.54	12.3±4.01	**0.001** (Unpaired t-test)
Age (in years)	≤10 y	14	7	**0.006**
	>10 y	6	19	
Free medical facilities	Yes	7	2	**0.028**
	No	13	24	
Socio-economic status	I, II, III	19	17	**0.0277**
	IV, V	1	9	
Parents education	Illiterate, Primary	2	10	**0.043038**
	Secondary, Graduate	18	16	
Gender	Female	13	9	0.07318
	Male	7	17	

[Table/Fig-5]: Disease-related characterstics in relation to good control and poor control group.

The mean insulin demand for newly diagnosed DM was 0.93±0.25 unit/kg/day and in established diabetic patients mean was 1.26±0.34 unit/kg/day in the current research. A 71.7% of patients were on premixed intermediate-acting and regular insulin. All patients used an insulin syringe as injecting device except two patients one was using insulin pump and one used insulin pen for insulin administration.

DISCUSSION

Diabetes Mellitus is one of the most common chronic endocrine and metabolic disorder. It is characterised by insulin deficiency due to destruction of pancreatic β-cell leading to insulin deficiency. Only 10-15% of total diabetic population is of T1DM but it is most common form of diabetes in children.

In India, overall incidence of T1DM 10.5/100,000/year, and peaked at age 10-12 years. Incidence also varies according to gender, 4.0/100,000 in girls and 3.7/100,000 in boys [2]. The incidence of T1DM in Karnal, Haryana, is 26.6/100,000 in urban regions along with 4.27/100,000 in rural regions leading to a mean occurrence of 10.20/100,000 per population. The total age-adjusted prevalence of T1DM ranges from 0.7 per 100,000 annually in Karachi (Pakistan) to over 40 per 100,000 annually in Finland [9]. T1DM is increasing at a rate of 3-5% percent each year, particularly in younger children [10]. T1DM cases in children 1-4 year increased 84000 to 136000 from 2010 to 2015 [11]. This rise in incidence, along with improved insulin availability and survival rates, will soon result in a greater prevalence.

Age of onset of T1DM shows bimodal presentation one peak at 4-6 years age and another at puberty [12,15]. Genetic and environmental factors play role in aetiopathogenesis. There is 30% chance of affection of offspring if both parents had history of diabetes or monozygotic twin is affected [12]. Against most popular belief autoimmune diseases are common in female, various international studies shows male preponderance [15]. Significant number of patients presents with DKA at onset of diseases. Patients present with one of the following symptom polyuria, breathlessness, weight loss, pain in abdomen.

Despite the study's limited sample size and the fact that it was done at a teaching industrial hospital, this study gives a basic profile of T1DM in this part of the country where studies about T1DM are few. This study shows slight male preponderance which is against the consensus that autoimmune diseases are more common in females same finding is noted in various international studies [13,14,16]. A 61% of children were diagnosed before completion of the first decade of life out of this 35% was diagnosed in the first five years of life. This varies from most of the studies where the peak age for onset was 10-14 years [13,15]. European Diabetes: Aetiology Of Childhood Diabetes On An Epidemiological Basis (EURODIAB-ACE) suggests the age for onset was 10 to 14 years [17]. Family history of T1DM was found in 15.21% of patients nearly similar results are seen in other study [18]. Out of 46, 60.8% of patients presented with DKA whereas 39.2% of patients presented with non DKA symptoms. The same outcomes were reported in research from Nepal [19]. [Table/Fig-6] shows various studies showing different demographic data [12,20-23].

Study and characteristic	Passanisi S et al., [20]	Faisal KK and Chandani [12]	Prasad D et al., [21]	Ameyaw E et al., [22]	Rafique M et al., [23]	Present study
Place	Southern Italy	Kerala	Uttar Pradesh	Ghana	Saudi Arabia	Bhilai
Year	2012-17	2020	2010-12	2012-16	2011-15	2011-13
Sample size	106	52	40	106	141	46
Male:Female	1:1.26	1:1.6	1:1.2	1:2.5	1:0.96	1:0.9
Age (years)						
<5 yr	30%	9.6%	-	3.3%	25.5%	34.1%
5-10 yr	21.4%	40.8%	-	21.1%	44%	26.1%
>10 yr	38.6%	59.6%	40%	75.6%	30.5%	39.1%

DKA	46.1%	60%	92%	54%	39%	60.8%
Non DKA	53.9%	40%	8%	46%	61%	39.2%
Family h/o DM	-	20%	5%	21.4%	20.6%	15.2%
HbA1c	11.6%	-	-	12.7%	10.36%	9.45%

[Table/Fig-6]: Various studies showing basic demographic data [12,20-23].

In the current work, the patients who were newly diagnosed presented predominantly with signs of polyuria (85.71%), breathlessness (42.85%), and weight loss (64.28%). The findings are similar to several studies [19,23]. Stunting was noted in 12 of the total diabetics i.e., 26.1%. Out of 12 stunted, 25% had a duration of less than one year, and 75% had the duration of more than one year, which was statistically significant. This shows a subsequent slowing of development as the diabetes duration increases. None of the youngsters were higher than the projected age group. There is conflicting data available on growth in diabetes, stunting is present if the onset of the disease is less than three years of age and height is normal if the onset of the disease is in the pubertal age group [24]. A significant number of patients were stunted in the present study because almost 34% of patients were less than five years of age at the onset of the disease. When the disease duration was associated with other characteristics like HbA1c level, stunting, and mean RBS level it was found that only stunting was statistically significant with a duration of disease with a p-value <0.05.

Age was found to be a very important component in glycaemic control in this investigation. The mean age of the patients with poor control was substantially greater than that of the patients with excellent control. Several research provides evidence for this finding [21,22,25]. The average insulin demand was 0.75 units/kg/day of age group 0-5-year-old, 1 unit/kg/day for 5-12-year-old, and 1.4 units/kg/day for age 12 to 18-year-old. In newly diagnosed diabetics, the average insulin demand was 0.93 units/kg/day, but in older diabetics, the average insulin requirement was 1.26 units/kg/day. Many variables determine the daily insulin dose per kilogram of body weight. In pubertal children, the dosage is frequently greater. It is higher in patients with higher glycogen, protein, and fat store deficit and patients with high caloric needs. Most adolescents with new-onset diabetes, on the other hand, retain some residual β cell activity (the "honeymoon" phase), which lessens the requirement for exogenous insulin [17]. The average insulin needs in similar trials ranged from 0.7 to 1 units/kg/day in pre-pubertal age group and 1 to 2 units/kg/day during puberty [25].

Out of the total of 46 patients, 71.1% of patients used a premixed (NPH+R) regimen whereas 23.9% were on a separate NPH+R regimen and only one patient was on regular insulin and basal-bolus regimen. Basal-bolus dosage of "Insulin Glargine" and three injections of normal insulin had a considerably greater prevalence of adequate glycaemic control and fewer episodes of hypoglycaemia [24] than the premixed NPH+R regimen [26]. This could not be evaluated from the present study as very few patients were on other than a pre-mixed regimen. All patients were using insulin syringes for the administration of insulin except two one using an insulin pen and one insulin pump.

Limitation(s)

This study was of its first kind from this region but the observations of the study cannot be generalised.

CONCLUSION(S)

The DKA must be considered as a differential diagnosis for respiratory distress even in a patient less than five years of age. Polyuria was the most common symptom in newly diagnosed diabetics. Breathlessness and pain abdomen were predominant symptoms in established T1DM. Most of the children landed in DKA requiring hospital admission. The authors recommend there is a need for a study on T1DM in children less than five years of age. Also, longitudinal studies with larger sample size should be conducted for better results.

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