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ORIGINAL ARTICLE

Profile of Diabetes Mellitus at presentation in children under 12 years of age

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Abstract:
Incidence of diabetes in children is on the rise due to both Type 1 and Type2 Diabetes Mellitus (DM). This retrospective study was conducted among 432 children diagnosed to have DM at less than 12 years of age . The profile of diabetes at presentation was studied in all these children. Type 1 DM was encountered in 81% of children. Two children were Type 2 DM. Age and gender did not show any statistical difference. BMI was less than 85 th percentile in all but two children. 58.6% of children presented with Diabetic keto acidosis. 93 % of the children presented with osmotic symptoms. Incidental diagnosis of DM was encountered in 45%. Missed diagnosis was encountered in 60% of children with DKA. 12.5 % were found to have autoimmune thyroid antibodies. Hypercholesterolemia was encountered in 16% and hyperlipidemia in 19%. Mortality at initial diagnosis was 2.7%. Type 1 DM is the commonest type encountered in children under 12 years of age from a lower socioeconomic strata and nearly 60% present with DKA at onset . 60% children with DKA have their diagnosis missed at first physician contact.

Keywords: Diabetes mellitus, children under 12 years age, onset, clinical features.
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Introduction

The incidence of diabetes mellitus (DM) in children is rapidly increasing. Prevalence of Diabetes in children less than 15 years is predicted to rise markedly with considerable health care implications especially countries with low incidence rates [1-3]. Data on childhood DM is mostly inclusive of adolescents with both Type1 and Type 2 diabetes. Existing literature from south India is predominantly on diabetes in the young adolescents and adults with Type 1 DM. Existing literature shows, the prevalence of DM to be 22.22/100,000 in the 5 to 16 years age group and 3.82/100,000 in the 0-5 year age group from hospital based registry [4]. The incidence of type 1 diabetes has been reported as 10.5/100,000 in a population based study carried out in 1996 in urban Chennai [5]. We do not have much literature from this part of the country with regard to DM in children less than twelve years of age especially from lower socio economic strata. Hence this study was conducted at the Diabetic clinic of Institute of Child Health and Hospital for Children, Chennai, TamilNadu (India), one of the biggest Pediatric tertiary care center which provides free health care for children predominantly from lower socio economic strata. This is a hospital run by the Government of TamilNadu, providing all treatment

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and medications free of cost to the children. This is an exclusive pediatric tertiary care Institute with all multispeciality departments. The clinical profile at presentation of these children was studied from the diabetic clinic records.

Material and methods

Retrospective data was collected from all the 432 children registered in the diabetic clinic from 1999 to 2010. The age at presentation, gender, mode of onset, mode of diagnosis, initial blood glucose, HBA1c at diagnosis, type of diabetes, BMI at presentation, clinical features, thyroid status, and the outcome at the initial presentation were analyzed. Diabetic Children less than 12 years at the time of first visit to the hospital were registered in the diabetic clinic of this Institute. The study parameters were analyzed from the hospital records. Statistical analysis was done using Epi Info 2008 software.

Age at presentation was taken as the day on which high blood glucose was documented. Diagnosis of DM was based on the random blood glucose more than 11 mmol/L or fasting blood glucose more than 7 mmol/L in the presence of osmotic symptoms of polyuria and polydipsia and weight loss. Mode of onset was classified as ketotic onset if presenting with Diabetic keto acidosis (DKA). The following criteria were adopted for DKA -blood glucose >11 mmol/L, Ph<7.3 and/or bicarbonate less than 15, with ketonuria. HBA1c at presentation was the value documented at the time of diagnosis. Diabetes was classified as Type I if they present without features of insulin resistance like acanthosis, obesity or hypertension. Onset less than one year of age was considered as infantile onset diabetes. Pancreatic diabetes was diagnosed in those with calcific pancreatitis, chronic pancreatitis, post pancreatectomy diabetes, pancreatic hypoplasia or aplasia. Drug induced diabetes was diagnosed when known agents like anticancer drugs related diabetes was encountered. Syndromic diabetes was entertained when there were clinical features of Downs's syndrome, deafness, optic atrophy, lipodystrophy. When their initial physician's diagnosis was anything other than diabetes leading on to a final diagnosis of diabetes in the same episode missed diagnosis was entertained. The Mode of diagnosis was incidental if diagnosed during routine investigation for intercurrent illness or by clinical features if diagnosed by clinical suspicion or as screening if diagnosed by parental insistence on work up for diabetes. Outcome at initial presentation was analyzed as death or survival to discharge from the hospital. Among the new onset DM who died at presentation persistent hyperglycemia more than 48 hours and/or documented HBA1c >6% or low c-peptide was adopted as a criteria in order to exclude stress hyperglycemia.

Results

432 children, less than 12 years were registered in the diabetic clinic from Jan 1999 to June 2010. Age at the time of diagnosis ranged from day two of life to 12 years, with a mean of 6.35 ± 3.52 years. Among the study group 42.6% (37.9-47.4) were boys and 57.4% (52.6-62.1%) were girls. Gender distribution revealed a male female ratio 1:1.35. Of all the registered children 58.6% presented with diabetic keto acidosis at the time of diagnosis. Family history of diabetes was present in 35% of children. 3.9% had diabetes in the sibling, 2.8% had one of the parents to be a diabetic (Type 2 DM) and 27.6% had diabetes in the other family members. Infantile onset diabetes was diagnosed in 9% (39), 14.8% (64) were toddlers (1-3 years), 27.5% (119) were preschool children (3-6 years) and 48.6% (210) were school children (6-12years). Children <5 years age at onset constituted 59%. Among all the diabetic children 71% were newly diagnosed to have diabetes and 29% were previously diagnosed and treated outside and referred to our center for further management.

The mean BMI of the study group at diagnosis was 13.43± 2.16, ranging from 8.18 – 22.5. Two children in the study group had a BMI more than 85th percentile at diagnosis. One of them was a female with Type 2 DM with acanthosis and obesity. The other was a male with Type 1 DM at risk for overweight, but no acanthosis, GAD antibodies were normal and C-peptide was low hence included under Type 1 DM. Type I diabetes was diagnosed in 81% (350). Two children had Type 2 DM, with incidental diagnosis of hyperglycemia, non ketotic onset , their c peptide levels were normal, and were started on oral antidiabetic drugs, one of them had acanthosis as discussed earlier. Among the five children with acanthosis at diagnosis one was type 2 DM, other four were lipodystrophic DM. The classification of types of DM encountered is listed in Table I. Among

Table I. The types of diabetes in children.

Type of diabetes	N / (%)
Type 1	350 (81%)
Infantile onset DM	39 (9%)
Diseases of exocrine pancreas	17 (3.94%)
Syndromic diabetes	13 (3%)
Type 2 Diabetes	2 (0.4%)
Others	11 (2.5%)

the 17 children with pancreatic diabetes 10 were calcific pancreatitis, three were post pancreatectomy and two were chronic pancreatitis and two had diabetes due to thallassemia induced hemo-chromatosis. Among the syndromic diabetes four were Downs syndrome, four with lipodystrophy, three with deafness and two were suspected DIDMOAD. Three children on chemotherapy for acute lymphoblastic leukemia developed transient diabetes, one of them succumbed at the time of diagnosis, one had transient diabetes and was on insulin for four months and weaned off insulin with normal c peptide values and the third child had diabetes lasting for three weeks and was later normoglycemic without insulin therapy. All the three children presented with DKA. 55% of diabetic children were diagnosed by clinical suspicion and 45% were diagnosed incidentally while investigated for some illness. Of those children presenting with DKA onset 60% had a missed diagnosis with multiple (1–3) physician consultations prior to the diagnosis of DM. Parental insistence for evaluation leading to the diagnosis was encountered in 15 children who had another sib with DM.

Initial blood glucose at diagnosis was available in 413 children and this ranged from 7.7 mmol/L to 55.5 mmol/L with a median of 22.5 mmol/L. HBA1c at presentation was available in 124 children. The mean HBA1c is 11.15% ± 3.2, ranging from 4.7– 20%. Thyroid evaluation revealed 10.4% to be hypothyroid. Of the 80 children who were evaluated for thyroid antibodies 12.5% (10) were positive for anti-microsomal antibodies and 6.25% (5) were positive for anti thyroglobulin antibodies. One of the study group had evidence of polyglandular autoimmune disease with diabetes, hypothyroid and Addison's and is on treatment. Fasting Lipid profile was available for 127 children in the study group 16.5 % of them had cholesterol more than 5.2 mmol/L and 19% had hypertriglyceridemia. Dietary modification was advised for these children. Two of the study group had very high levels suggestive of familial hypercholesterolemia with tendon xanthomas and arcus juvenalis at the time of diagnosis. But for these two children none of them were started on medications for hypercholesterolemia. Clinical features at presentation are given in the Table II.

Table II. The clinical features of diabetes mellitus.

Clinical feature	%
Polyuria	93
Polydipsia	92
Lethargy	61.1
Dehydration	43.3
Tachypnea	47
Fever	41.8
Weight loss	37
Pain abdomen	37.8
Vomiting	34.4
Nocturnal enuresis	26.4
Coma	10.4
Itching over the genitalia	10

The duration of illness ranged from 1 to 90 days with a mean of 5.34 ± 10.5 days. The mean duration of illness among DKA children was 3.93 ± 8.08 in comparison to 9.70 ± 15.3 among non DKA children. This was statistically significant ($p < 0.001$). Genital candidiasis at presentation was seen in 43 children (10%). Infections were found in 83 children (19%) at presentation. The common infections encountered at presentation were urinary tract infection, skin and soft tissue infections and pneumonia. Only 20% the children presenting with diabetic keto acidosis had a

blood glucose evaluated by the first treating physician. The mean insulin requirement after initial stabilisation was 1.27 ± 0.5 units/kg/day (ranged from 0.38 units to 3.75 units/kg/day). Mortality at presentation was 2.7%. Among the 12 children who died at presentation nine of them had missed their diagnosis at the first physician consultation and the cause of death were DKA with cerebral edema, ARDS, sepsis, shock, renal failure and acute CNS infection. Among those who died 41.6% (5 out of the 12) were less than one year of age at the time of diagnosis. Four of the five infants had their diagnosis missed at initial physician consultation and was subsequently diagnosed to have DKA.

Discussion

The predominant type of diabetes in children younger than 12 years is still Type 1 DM. Literature on diabetes in the young is much varied depending on the age group studied. Male preponderance of 1.6:1 was documented in childhood diabetes from hospital based studies in India [4,6]. The gender distribution in our study revealed a slight female preponderance. Age at presentation did not show any significant difference. Younger the age at onset of DM (<5 years), are more likely to present with DKA, as shown in literatüre [7]. This was statistically significant ($p<0.008$) in this study. Younger children will not be able to verbalize their complaints, it is likely that the diagnosis by clinical features is difficult and this delayed diagnosis may be a contributory factor for presentation with DKA. They are more likely to be diagnosed incidentaly ($p<0.04$) during intercurrent illness. Missed diagnosis is more common in younger children as they are likely to present with vague symptoms [8]. The mean duration of symptoms was less in children with ketotic presentation in comparison to those with non ketotic presentation. This may correlate to the severe illness at onset with rapid progression of symptoms. Lack of awareness by the parents in recognising the osmotic symptoms as abnormal could be a contributory factor.

The small number of Type 2 diabetes in this study population could be due to the fact that all children were < 12 years of age at the time of diagnosis and were all from lower socio economic strata where the incidence of obesity and hypertension is much lesser compared to children from the higher socioeconomic strata. Incidental diagnosis of diabetes and initial presentation as DKA constituted a higher percentage (45%, 58% respectively) for the same reason.

Among the pancreatic diabetes, children with calcific pancreatitis were much older, with short stature, were undernourished and had non DKA onset, with abdominal distension, abdominal pain and failure to thrive as the major clinical presentation in comparison to children with Type 1 DM. The incidence of calcific pancreatic DM is reported to be high, in the age group of young diabetics less than 30 years from India [9]. Since our study group was less than 12 years at the onset the incidence may be low. Apart from insulin therapy they need pancreatic supplements and dietary modification.

The association between type 1 diabetes and autoimmune thyroid disease has long been recognized and the prevalence of thyroid antibodies has been found to be 31 to 54% for thyroid peroxidase antibodies (TPO) and thyroglobulin antibodies (ATG) in Indian children [10]. Association of autoimmune antibodies and hypothyroidism was found to be statistically significant ($p<0.00$) from this study. Hashimoto's thyroiditis as defined by high titres of thyroid antibodies, elevated TSH in the absence of medications, was encountered in 8.75%. six of the 11 children with antibodies had visible goiter and one child had goiter but was negative for antibodies. For those diabetic children where the antibodies are positive but euthyroid on evaluation, they need to be followed up as they are likely to develop overt hypothyroidism. Prevalence of anti-bodies was not influenced by age, gender, presence of goiter or HBA1c levels, as shown in other studies [11].

Dyslipidemia at diagnosis in the study group is much lower compared to the studies showing much higher percentage from India [12]. Hypercholesterolemia in 35% versus 16.5% and hypertriglyceridemia in 55% versus 19% in our study. The incidence is much lower in our children and this would probably be due to the younger age group in our study and lower socioeconomic strata of the children which may be a major determinant with different life style habits.

Though 93% had polyuria and polydipsia the diagnosis by clinical suspicion of DM was made only

in 55%. Parental unawareness and failure to perform blood glucose by capillary method as a simple investigation in office practice are the major obstacles in the earlier diagnosis of DM and may be a contributory factor for majority of them (58%) presenting as DKA. Even in children presenting with Keto acidosis, at all levels of care (primary, secondary, and tertiary care) the blood sugar estimation as an investigation at presentation was done only in 20% overall. This missed opportunity for diagnosis could lead to unnecessary delay in the diagnosis and may be a contributory factor in the high mortality in DM at presentation. The common mistaken diagnosis was urinary tract infection and generalized weakness in non ketotic children. Of those who presented with DKA the diagnosis entertained were septic shock, acute abdomen, bronchopneumonia, bronchiolitis and acute CNS infections. Mortality at the time of diagnosis was encountered in 12 children who presented with DKA. Lack of awareness by the caregivers, lack of adequate health care access, delayed diagnosis , missed diagnosis and associated infections and presentation with severe decompensation may be the attributable factors. Children with missed diagnosis are more likely to present with DKA. (53.2% vs. 20.5%, $p<0.01$ based on literatüre [13,14]. This has been brought out in our study too. Most of the missed diagnosis could have been avoided if initial blood glucose estimation was done as a routine in all sick children at the first physician consult. Presence of osmotic symptoms or a candidal infection warrants an immediate blood glucose estimation in children [15]. Presence of candidal genital infection is a pointer to diagnosis of DM as this infection is uncommon in otherwise normal children. Ours being a tertiary care pediatric referral center offering free treatment including insulin, catering predominantly to children from lower socio- economic strata, the data may not be comparable with existing western literature or other hospital based studies.

The study emphasizes the definite need to create awareness among the parents and physicians to identify the features of DM and need to do blood glucose estimation as an initial investigation for any sick child at all levels of care. This paper has the following limitations. Being a retrospective study and the data for all children were not available with respect to some of the study parameters. Serum C Peptide levels and other antibodies for autoimmune diabetes could not be done for all these children for reasons of sosioeconomic constraints. Hence the classification of the types of types of DM was based on the clinical features.

Conclusions

Type 1 diabetes is still the commonest diabetes seen in 81% of children less than 12 years of age, from lower socioeconomic strata. 58% of the children present with DKA and only 55% are being diagnosed by clinical suspicion.

Missed diagnosis at first physician consult is a major factor in delayed diagnosis of DM.

Mortality in diabetic children from lower socio-economic strata at presentation in this study is 2.7%.

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