Original Article

Linear growth in children with type I diabetes mellitus – A one-year prospective study

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ABSTRACT

Introduction: Reduced growth velocity and delayed pubertal spurt are seen in Type1 diabetes mellitus and are influenced by a variety of factors. **Objective:** The objective of the study was to study various factors affecting linear growth in children with Type1 Diabetes. **Methods:** Age at diagnosis, auxological parameters, and hemoglobin A1c (HbA1c) were recorded from 116 children enrolled in the diabetic clinic. **Results:** Of 116 children, female to male ratio was 1:0.75. Mean age at diagnosis was 6.3±2.87 years. About 31.9% of children had early age of onset of diabetes (before 5 years). Majority (94.8%) had a normal height at diagnosis. At 1 year of follow-up 44% of children (38% males and 48.5% females) showed a decline in linear growth. About 48.3% of children presented initially with diabetic ketoacidosis (DKA). Only 10.7% of children with DKA at diagnosis had growth faltering. Mean age of diagnosis for those without and with growth faltering was 5.6±2.8 years and 7.3±2.6 years, respectively. Mean HbA1c for those with growth faltering and without growth faltering was 10.03±1.80 and 8.34±1.07, respectively. In 5–9.9 year age group, mean height velocity for children with better and poor glycemic control was 6.67±1.0 and 5.58±1.59, respectively; and in 10–14.9 year age group, it was 6.18±1.26 and 5.58±1.59, respectively. **Conclusion:** Majority of the children had normal height at diagnosis. Growth faltering was less common in children who presented with DKA at diagnosis. Children who were diagnosed at a younger age had less growth faltering. Good glycemic control was associated with better linear growth.

Key words: Linear growth, Type 1 diabetes, Velocity

Type 1 diabetes mellitus (T1DM) is characterized by deficient levels of endogenously produced insulin. Impaired growth is a well described complication of diabetes [1]. There is evidence to suggest that there are abnormalities in the hypothalamic-pituitary-growth hormone axis. These are common in children with poor glycemic control and a longer duration of diabetes. Impact of T1DM on growth is no longer a major concern in developed countries because of the more physiological insulin therapy and better self-monitoring of glycemic control [2]. However, in developing countries like India, there are various constraints including finances (cost of insulin and blood glucose monitoring) and knowledge, which make the management of diabetes a difficult task.

Linear growth velocity in children with insulin-dependent DM is related to metabolic control. Children, who are prepubertal or in the early stages of puberty, are the most vulnerable to growth suppression. Once puberty is well established, growth suppression does not occur unless marked hyperglycemia (hemoglobin A1c [HbA1c] >16%) exists [3]. Growth velocity is also affected by the age of the patient. Growth of children especially in pre-pubertal years has been reported to be affected by the disease process. It has been proposed that relatively poor growth is associated with younger age at onset [4]. In India, those diagnosed at a younger age, growth is likely to be affected. Objective of this study was to identify factors affecting linear growth in children with TIDM.

METHODS

Children with TIDM between 6 months and 18 years of age attending the pediatric diabetic clinic at SAT Hospital, Thiruvananthapuram, Kerala during the study period (August 2015–July 2016) were included in the study. Children with onset of diabetes before 6 months of age and those with other established chronic diseases and syndromes affecting growth were excluded

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from the study. Ethical approval was granted by the institutional ethics committee. Assent from children and consent from parents were obtained. Data regarding age at diagnosis of T1DM, auxological parameters (height, weight, and body mass index), and HbA1c at presentation were collected. A detailed clinical examination was performed at first contact with the patient.

The subjects were evaluated at 6 months interval during the study period. As per institution policy, all the children attending the clinic were undergoing insulin therapy under basal bolus regimen. At each visit height, weight, glycemic control as determined by HbA1c, dose of insulin used to achieve glycemic control were recorded. They were followed up for 1 year. Age and sex specific height standard deviation (SD) scores were calculated using software for SD score (SDS). The WHO growth charts were used for 0–5 years and Indian academy of pediatrics growth charts for 5–18 years. (A child is said to be short if height SDS is below −2). The patients were then divided into two groups: Group1: Whose height SDS did not change or showed an increase at the end of the year and Group 2: Whose height SDS showed a decline at the end of the year. The two groups were compared with respect to various clinical and lab variables. The height velocities were calculated for different age groups and compared.

Statistical analysis was carried out using the SPSS 20 software. Rates and ratios are expressed in percentages. Statistical significance of quantitative variables was assessed by t-test and that of qualitative variables using Chi-square test.

RESULTS

116 diagnosed cases of TIDM were included in the study and followed up for 1 year. Of the 116 cases, 43.1% (n=50) were males and 56.9% (n=66) were females. The mean age at diagnosis was 6.3±2.87 years (range: 1–12 years). About 31.9% of children had early age of onset of diabetes (before 5 years).

Only 12.1% had family history of DM. About 48.3% of children presented initially with diabetic ketoacidosis (DKA). About 94.8% had normal height at diagnosis. Among the children who were short at diagnosis, male: female ratio was 1:1.6% of the males were short at the time of diagnosis while 4.5% of the females were short at diagnosis; however, the difference was not statistically significant (p=0.726). The mean age at diagnosis for those without growth faltering was 5.6±2.8 years and for those with growth faltering was 7.3±2.6 years (p=0.001) (Table 1).

Only 10.7% of children with DKA at diagnosis had growth faltering, while 75% without DKA at diagnosis had growth faltering (p=0.001). At 1 year of follow-up, 44% of the study subjects had growth faltering. About 38% of males and 48.5% females had growth faltering. However, the association with sex was not statistically significant (p=0.260). The mean HbA1c was 10.03±1.80 for those with growth faltering at 1 year of follow-up and it was 8.34±1.07 for those without growth faltering (p<0.001) (Table 1).

The mean height velocity of age groups 0–4.9 years, 5–9.9 years, 10–14.9 years, and ≥15 years was 7.87±3.0, 5.87±1.52, 5.94±1.40, and 4.95±1.85 years, respectively. The mean height velocities of children with good and poor glycemic control in different age groups are given in Table 2 and the association of mean height velocity with glycemic control in all age groups was statistically significant.

DISCUSSION

Of the 116 cases, 43.1% were males and 56.9% were females. There was female preponderance in our study population. The female to male ratio was 1:0.75. Gale and Gillespie [5] have described that the sex ratio is almost equal in diabetic children under 15 years. Although data suggest a slight male preponderance in high incidence populations and a minor female excess in low-incidence populations, both genders carry almost equal risks. Male preponderance has been described in European population while slight female preponderance has been reported in African or Asian. Almost one-third (31.9%) of children were diagnosed to have Type I diabetes before the age of 5 years.

The mean age at diagnosis was 6.3±2.87 (range: 1–12 years). In a study by Gale *et al.* [6], the mean age at onset was 8.5±3.2 years in boys and 8.2±2.6 years in girls. About 12.1% had family history of DM. Steck and Rewers have described that children with genetically susceptible HLA genotypes and family history of type 1 diabetes have more than 1 in 5 risk of developing islet cell autoantibodies during childhood when compared to children without family history who have a risk of approximately 1 in 20 [7]. In our study, the majority (94.8%) of children had a normal height at diagnosis. Among the children who were short at diagnosis, male: female ratio was 1:1 and 6% of males and 4.5% of females were short at diagnosis (p=0.726). It was first noted in the 1920's that diabetic children have a tendency to be "over-height" on admission compared to normal children. In later years, conflicting results have been reported in over 30 studies on growth of children with T1DM.

Table 1: Height at 1 year of follow-up with respect to age at diagnosis and glycemic control

Variables	No faltering (n=65)		Faltering (n=51)	
	Mean	SD	Mean	SD
Age at diagnosis (years)	5.6	2.8	7.3	2.6
HbA1C	8.342	1.0673	10.033	1.8062

HbA1C: Hemoglobin A1c

Table 2: Glycemic control and mean height velocity in different age groups

Age groups	Better glycemic control			Poor glycemic control			p-value
	n	Mean height velocity	SD	n	Mean height velocity	SD	
≥15 years	5	4.5	2.0	15	5.1	1.86	0.007
10–14.9 years	16	6.18	1.26	39	5.83	1.46	0.000
5–9.9 years	9	6.67	1.0	24	5.58	1.59	0.000
0–4.9 years	1	7.5	–	7	7.9	3.27	0.001

Di Liberti [8] in 2002 assessed the relevant data in a meta-analysis and concluded that the diabetic children were taller at the time of diagnosis attributing this finding to the taller parental stature. In a study Demir *et al.* [9], it was revealed that diabetic children were taller when compared to their mid-parental height SDS. At 1 year of follow-up 44% of children showed a decline in linear growth, 38% of males and 48.5% females had growth faltering (p=0.260). In the present study, 48.3% of children presented initially with DKA. Only 10.7% of children with DKA at diagnosis had growth faltering while 75% without DKA at diagnosis had growth faltering (p=0.001).

Korcan *et al*. [10] found that DKA at the onset was significantly associated with maintaining or gaining height SDS. This might be because initial presentation with DKA might have caused the patient and his/her family to be more conscious and thereby better compliance and adherence to therapy and better glycemic control. In our study, 51% of the children with growth faltering were diagnosed between 5 and 9.9 years of age and the mean age at diagnosis of diabetes was significantly higher is children with growth faltering. However, in an Indian study by Khadilkar *et al.* [11] children who were diagnosed <3 years of age were shortest (HAZ − 1.6±1.1), while those diagnosed after 14 years were not different from controls.

In our study, the mean HbA1c was 10.03±1.80 and 8.34±1.07 for children with and without growth faltering at 1 year (p<0.001) which means children with better glycemic control had less growth faltering. In a study by Bonfig *et al.* [3], HbA1c levels <8% were associated with growth acceleration, and the most severe growth retardation occurred when HbA1c levels were >16%.

In this study, the mean height velocity of age groups 0–4.9 years, 5–9.9 years, 10–14.9 years, and 15 years was 7.87±3.03, 5.87±1.52, 5.94±1.40, and 4.95±1.85, respectively. We calculated that the mean height velocities were for broader age groups whereas Lavanya *et al.* [12] demonstrated the comparison of mean height velocities for narrower age groups with that of normal children and concluded that children with T1DM have lower height velocity than healthy children. In a study by Sunil *et al*. [1], it was demonstrated that the linear growth velocity in children with Type 1 diabetes was closely related to metabolic control.

CONCLUSION

Children who were diagnosed at a younger age had better linear growth and a better glycemic control was associated with better linear growth velocity. The factors significantly associated with growth faltering were diagnosis of diabetes at a later age and poor glycemic control while growth faltering was less common in those presenting with DKA at diagnosis.

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