

Longitudinal Growth in Children and Adolescents with Type 1 Diabetes

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Objective: To study longitudinal growth in children with type 1 diabetes mellitus.

Methods: Anthropometry, disease duration, insulin regimens and HbA1C recorded from patients with diabetes enrolled in a specialty clinic.

Results: 160 children (75 boys; mean (SD) age 9.4 (3.3) y) were enrolled. 35% children had low (<25th centile) height velocity. Disease duration and HbA1C affected height velocity (adjusted for puberty). Children on basal-bolus had higher height velocity Z scores than those on a split mix regimen [(0.5(1.6) vs. -0.3(1.4), $P<0.05$)]. Children diagnosed before 5 years of age had lowest height velocity. Of the children who reached final height, 53% remained below target height.

Conclusion: Children with type 1 diabetes mellitus have lower height velocity compared to healthy children; those diagnosed at younger age were at higher risk for growth failure.

Keywords: Diabetes mellitus, Growth Failure, Height, Short Stature.

Type 1 diabetes mellitus (T1DM) is known to adversely affect linear growth. Reduced growth and pubertal spurt in diabetic children could be due to abnormalities in physiological bone growth and perturbations in Growth hormone – Insulin-like growth factor – Insulin (GH-IGF-I) axis [1]. Studies suggest that abnormalities are common in subjects with poor metabolic control and longer disease duration [2-5]. We conducted this study with the objectives of (i) assessing height velocity of 4- to 16-year-old children with T1DM and identifying factors affecting it over a one-year period; and (ii) studying the effect of disease duration on growth during adolescent years and on final height.

METHODS

All children (age 4-16 y) visiting the type 1 diabetes clinic at a tertiary healthcare centre, in Western India were approached for the study (May 2012- June 2014). Patients on medication other than insulin for blood glucose control or with known co-morbidities (celiac disease, untreated hypothyroidism, and other chronic diseases) were excluded. Considering variability in velocity reported in studies [6], sample size of 160 (objective 1) and 91 (objective 2) had power of 0.9 at 5% level of significance and 5% margin of error. Ethical approval was granted by institutional ethics committee. Assent from children and consent from parents was obtained. Data on age at diagnosis, diabetes duration and insulin regimen were

collected. Tanner staging was performed.

Standing height (Leicester Height Meter, Child Growth Foundation, UK) and weight (electronic scale) was measured 3-monthly by the same observer, and converted to Z scores [7]. Yearly height velocity values were calculated by dividing difference between annual height measurements by age increment. Using LMS values (skewness (L), median (M), and coefficient of variation (S) of the measurement distribution) from the data on normal children ($n=1471$), height velocity Z-scores for diabetic children were calculated [8]. Parents' heights were recorded using the same stadiometer to calculate mid-parental height. Final height was defined when chronological age was >18 years or a growth rate <0.5 cm during the last 6 months, and was compared to target height [9].

Fasting blood sample was collected to measure HbA1C (HPLC). An average of readings taken 3-monthly was used to describe the metabolic control over one year.

Statistical analyses were carried out using SPSS (version 16). Differences in means were tested using Student's t test. Linear regression was used to identify factors affecting HV. Polynomial regression models were fitted for HV Z scores according to age at diagnosis.

RESULTS

We selected 160 children (75 boys) enrolled in the clinic

TABLE I BASELINE CHARACTERISTICS OF THE STUDY POPULATION

	Boys (n=75)	Girls (n=85)	Total (n=160)
Age (y)	9.3 (3.5)	9.5 (3.1)	9.4 (3.3)
Height (cm)	127.6 (20.4)	127.6 (17.3)	127.6 (18.9)
HFAZ score	-0.9 (1.3)	-0.9 (1.1)	-0.9 (1.2)
Weight (kg)	27 (11.2)	26.5 (10)	26.7 (10.6)
WFAZ Score	-0.8 (1.1)	-0.8 (1.0)	-0.8 (1.1)
BMI (kg/m ²)	15.8 (2.4)	15.7 (2.3)	15.7 (2.3)
BFAZ score	-0.5 (0.8)	-0.5 (0.9)	-0.5 (0.8)
HbA1C (%)	8.8 (1.8)	8.8 (1.9)	8.8 (1.8)
*Duration (y)	3.3 (2.7)	3.2 (2.7)	3.2 (2.7)

HFA: Height for age; WFA: Weight for Age; BFA: BMI for age; BMI: Body mass index; HbA1C: glycosylated hemoglobin.
 *Duration of diabetes.

for the study on height velocity. Mean (SD) HV at end of study was 5.5 (2) cm; mean (SD) HVZ score was -0.3 (1.5), and 35% had HV <25th centile [8] (**Table I**).

Children on basal-bolus regimen (n=72) had better mean (SD) HVZ score (0.5 (1.6) vs -0.3 (1.4), P<0.05) and significantly lower HbA1C (8.4 (1.7)% vs 9.0 (1.8)%) than those on split mix. Disease duration ($\beta = -0.091$, P=0.020) and HbA1C (1yr average, $\beta = -0.177$, P=0.001) were significant negative predictors of HVZ scores after adjusting for puberty.

We extracted retrospective data on 91 of these children for their height measurements during the past 2-11 years. Across adolescence, children who were diagnosed at <5 years of age (n=32) had the least and those diagnosed >10 years of age (n=25) had maximum HVZ scores (**Fig. 1**). HVZ scores peaked at 12 years for those diagnosed >10 years; at 14 years if diagnosed between 5-10 years (n=34), and at 15 years for <5 years. Amplitude of peak was highest in children diagnosed >10 years and smallest for those diagnosed < 5 years (**Fig. 1**).

Fifty percent (45/91) children achieved final heights, and 47% percent surpassed or equaled target height. According to age at diagnosis (<5, 5-10, >10 years), percentage of children who did not meet target height was 80%, 33%, and 50%, respectively. When compared to Indian references at 18 years, 18% children had HAZ scores below -2 SD.

DISCUSSION

Our study suggests that children with diabetes were shorter and had lower height velocity than healthy children. Longer disease duration and poor metabolic control were associated with low height velocity Z scores.

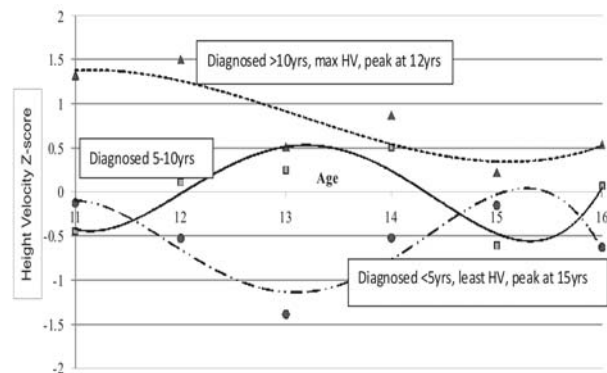
Height velocity of children diagnosed at younger years, was the least across adolescent years and majority of them fell short of target height.

Limitations of the study are data on height at diagnosis were not available as children were followed from the first time they visited the centre which was not necessarily at diagnosis. Moreover, we did not evaluate IGF1 concentrations which could have further helped in understanding the reason for lower height velocity and reduced final height. Some earlier studies [2,10-12] have also shown that children who had better metabolic control had higher HVZ scores, underlining the importance of improving metabolic control. Children on basal-bolus regime had better HVZ score and lower HbA1C; promoting the use of basal-bolus regime may help to optimize growth. Like others [1,2,13,14], our data also suggest that patients diagnosed before 5 years of age showed greatest height loss, and need more attention towards growth. In our study, half the children who had reached final height did not meet their target height, which is in contrast to other studies who have reported normal final height amongst diabetic children [1,2,3,5].

We conclude that children with T1DM are shorter, and have lower height velocity in comparison with healthy children. It is critical to monitor and improve metabolic control in children diagnosed at younger years as they seem to be at higher risk for long-term growth failure.

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Circle- diagnosed <5yrs; Square- diagnosed between 5-10 yrs; Triangle- diagnosed >10yrs.

FIG. 1 Height velocity Z scores during adolescence according to age at diagnosis (longitudinal follow up).

WHAT THIS STUDY ADDS?

- Children diagnosed with type 1 diabetes mellitus at younger years are at higher risk for long-term growth failure and reduced final height, which further worsens with poor metabolic control.

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