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Impact Of Type 1 Diabetes Mellitus On Growth Velocity Among Children And Adolescents

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Abstract
Objectives:
The study aimed to assess the growth parameters and the effect of age at diagnosis, duration of diabetes, hemoglobin A1C (HbA1c), and insulin regimens on the growth of children with T1D.
Material and Methods:
The study included subjects with T1D between the ages of 1 and 18 years, with a duration of diabetes for at least one year. Height for age Z-scores (HAZ), weight for age Z-scores (WAZ), and body mass index for age Z-scores (BAZ) were calculated using standard Indian Academy of Pediatrics 2015 growth charts for Indian children. The study design was an observational cross-sectional study.
Results:
The number of subjects was 18(F: M 10:8). The median age (interquartile range) was 13.8 (9–17.1) years, the age at diagnosis was 8 (4–11.5) years, and the mean duration of T1D was 5 (3–7) years. The mean HbA1c was 10.33 ± 1.88%. The growth parameters as assessed by HAZ −0.83 (−1.98–−0.16), WAZ −0.98 (−1.72–−0.11), and BAZ −0.55 (−1.41–0.1) were low in comparison to the population medians. The age at diagnosis, duration of diabetes, and the type of insulin regimen did not significantly impact HAZ and WAZ. Children with HbA1c <8.5% had better HAZ −0.21 (−0.94–0.35) versus −1.07 (−2.07–−0.25), (P = 0.069), and WAZ −0.33 (−0.73–0.23) versus –1.07 (−1.77–−0.29), (P =
0.041) compared to those with HbA1c >8.5%.
Conclusion:
Children with T1D were shorter and leaner than age- and sex-matched controls. Age at diagnosis, duration of diabetes, and insulin regimens did not significantly impact growth, whereas children with lower HbA1c had better HAZ and WAZ.

Keywords: *Type 1 diabetes, Growth monitoring, Height for age Z-scores, Weight for age Z- scores*

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I. Introduction

The Indian experience with type 1 diabetes mellitus (T1D) is of great importance due to the high burden of the disease. Poor management resulting from the lack of awareness and low public expenditure on health contributes to more complications.[1] Monitoring the growth of children with T1D is crucial for their overall well-being, as youth with suboptimal control may have poor growth while those with adequate control maintain normal growth, as highlighted by the ISPAD Clinical Practice Consensus Guidelines 2022.[2,3] Despite often being tall at diagnosis, children with T1D may experience growth retardation and pubertal delay later, potentially linked to poor glycemic control, hypothyroidism, celiac disease, and complications. Therefore, assessing growth and its relation with age at diagnosis, disease duration, glycemic status, and comorbid autoimmune diseases is essential.

Unfortunately, data on growth parameters for Indian children, are limited. The current study aims to fill this gap by examining height-for-age Z- scores (HAZ), weight-for-age Z-scores (WAZ), and body mass index (BMI)-for-age Z-scores (BAZ) in children with T1D, using the standard World Health Organization (WHO) 2006 and Indian Academy of Pediatrics (IAP) 2015 combined growth charts for Indian children as reference.[4] The study also explores the impact of age at diagnosis, duration of diabetes, glycemic status, and insulin regimens on the growth of children with T1D. By understanding these aspects, we can enhance the care and management of children and adolescents with T1D in India and work toward improving their quality of life.

The significance of the Indian experience with type 1 diabetes mellitus (T1D) stems from the disease's high prevalence. More issues arise from poor management brought on by a lack of knowledge and little governmental investment in health.[1]As the ISPAD Clinical Practice Consensus Guidelines 2022 emphasise, tracking a child's development is essential to their general health since children with inadequate management may grow poorly, while those with appropriate control continue to grow normally.[2,3]Children with T1D may have growth retardation and pubertal delay later in life, despite frequently being tall

hypothyroidism, celiac disease, and other problems. Thus, evaluating growth in connection to

concomitant autoimmune disorders, age upon diagnosis, length of disease, and glycemic status is essential.

Using the standard World Health Organisation (WHO) 2006 and Indian Academy of Paediatrics (IAP) 2015 combined growth charts for Indian children as reference, the current study aims to close this gap by examining height-for-age Z-scores (HAZ), weight-for-age Z-scores (WAZ), and body mass index (BMI)-for-age Z-scores (BAZ) in children with T1D.In [4]The effects of glycemic status, length of diabetes, age of diagnosis, and insulin regimens on the growth of children with T1D are also examined in this study. By being aware of these factors, we can improve the treatment and care given to children and teenagers in India who have type 1 diabetes and try to raise their standard of living.

II. Objective

The study aimed to assess the growth parameters and the effect of age at diagnosis, duration of diabetes, hemoglobin A1C (HbA1c), and insulin regimens on the growth of children with T1D.

III. Material And Methods

This observational cross-sectional study was conducted on subjects with T1D attending the Department of pediatrics, NC medical college and hospital. The study included subjects with T1D diagnosed between the ages of 1 and 18 years with a duration of diabetes for at least one year.A total of 11 children were recruited for the study after excluding children with new-onset T1D, children with the onset of T1D after 18 years of age, and children using non-insulin therapies as treatment. The growth parameters of the children were compared with standard IAP/WHO growth standards/ references. The diagnosis of T1D was established by the need for insulin for blood glucose control, started at or shortly after diagnosis, and used continuously after that, the presence of florid osmotic symptoms and diabetic ketoacidosis at diagnosis. A detailed history, physical examination with anthropometric data, and treatment details were collected. Standing height was measured to the nearest millimeter using a portable stadiometer. Weight was measured using an electronic scale to the nearest 100 g. HAZ, WAZ, and BMI-for-age Z-scores (BAZ) were calculated using standard WHO 2006 and IAP 2015 growth charts for Indian children. The same individual performed Tanner staging for sexual maturity in all the patients. The insulin regimens used were either basal-bolus (BB) or pre-mixed. Laboratory tests were done in all subjects, including hemoglobin A1C (HbA1c), serum thyroid-stimulating hormone (TSH), thyroxine (T4), tri-iodothyronine (T3). HbA1c was measured by high-performance liquid chromatography Informed consent from parents and assent from children were taken at enrollment into the study. Institutional ethics committee clearance was obtained.

Statistical methods

Data entry was done in Microsoft Excel Worksheet, and the statistical analysis was performed using latest available software. Categorical variables were represented as proportions or percentages; quantitative variables were represented as the mean ± standard deviation (SD) of the mean and median with interquartile range. The Chi-square test/Fisher Exact test, Mann–Whitney U test, and Kruskal– Wallis tests were applied to the data to find a significant association. $P < 0.05$ was considered statistically significant.

IV. Results

Of the 18 subjects with T1D who were included (M:8, F:10). The baseline characteristics of the subjects are shown in [Table 1]. The growth parameters at the time of diagnosis and HbA1c were comparable between boys and girls. The growth parameters, including HAZ, WAZ, and BAZ were low compared to the population medians. The percentage of children with HAZ, WAZ, and BAZ scores <−2 SD was 24.5%, 15.7%, and 8.77% respectively.

Table 1: Baseline characteristics of the study population

Parameters	Total(n=18) (Median,IQR)	Boys(n=8) (Median,IQR)	Girls(n=10) (Median,IQR)
Age	13.8 (9 to 17.1)	13.6 (9.0 to 16.0)	15.0(11.4 to 18.0)
HbA1c	10.3±1.9%	10.3±1.9%	10.28±1.8%
HAZ	-0.83(-1.98 to -0.16)	-1.36(-2.18 to -0.09)	-0.21(-0.70 to 0.55)
WAZ	-0.98(-1.72 to -0.11)	-1.17(-1.88 to 0.23)	-0.88(-1.16 to 0.327)
BAZ	-0.55(-1.41 to 0.1)	-0.522(-1.47 to 0.05)	-0.568(-1.31 to 0.91)

HAZ: Height for age Z-score, WAZ: Weight for age Z-score, BAZ: BMI for age Z-score, IQR: Interquartile range

Table 2: Comparison of growth parameters by the age at diagnosis and duration of diabetes.

Criteria	Number	HAZ	WAZ	BAZ
Age at diagnosis (years)	>10 (*n*=7)	–0.83 (−1.4 to −0.36)	−1.1 (−1.77 to −0.61)	−1.12 (−1.5 to −0.31)
	5–10 (*n*=5)	−1.37 (−2.09 to −0.13)	−1.08 (−1.71 to 0.16)	−0.4 (−1.37 to 0.1)
	<5 (*n*=6)	−0.61 (−1.97 to 0.22)	−0.53 (−1.04 to 0.36)	−0.51 (−1.38 to 0.39)
Duration of diabetes (years)	<5 (*n*=12)	−0.76 (−1.75 to −0.04)	−0.81 (−1.7 to 0.24)	−0.45 (−1.27 to 0.24)
	>5 (*n*=6)	−1.19 (−2.12 to −0.27)	−1.08 (−2.46 to −0.61)	−1.06 (−1.87 to −0.31)

[Table 2] shows the growth parameters as per the age at onset and duration of diabetes. Age at diagnosis of T1D has been divided into three groups, i.e., <5 years, between 5 and 10 years, and >10 years of age. Children were divided into two groups based on the duration of diabetes (>5 years and <5 years).

Table 3: Comparison of growth parameters by insulin regimens and HbA1c categories

Criteria	HAZ	WAZ	BAZ
Insulin regimen			
Basal bolus (n=12)	-0.77(-1.75 to -0.17)	-1.01(-1.7 to -0.13)	-0.51(-1.45 to 0.19)
Pre-mixed (n=6)	-0.92(-2.15 to -0.08)	-0.88(-1.75 to 0.23)	-0.71(-1.46 to 0.01)
Hba1c			
<8.5%(n=4)	-0.21(-0.94 0.35)	-0.33(-0.73 to 0.23)	-0.31(-0.71 to 0.19)
>8.5%(n=14)	-1.07(-2.07 to -0.25)	-1.07(-1.77 to 0.29)	-0.62(-1.51 to 0.06)

[Table 3] compares growth parameters across various insulin regimens and HbA1c. About 6 (33%) children were on a Pre-mixed insulin regimen, and 12 (67%) were on a BB regimen. The HAZ, WAZ, and BAZ were higher in those children on BB regimen compared to pre-mixed insulin, although not statistically significant. Children with an HbA1c of <8.5% had significantly higher WAZ and a higher HAZ that trended toward significance.

V. Discussion

The standard WHO 2006 and IAP 2015 growth charts for Indian children were used in this study to compare the anthropometric measures of children with T1D to a control group. The NC Medical College and Hospital in Panipat served as the study's site. Due to a lack of knowledge about insulin therapy, ideal glycemic control, and problems associated with diabetes, the research participants' poor glycemic control was observed. Further factors contributing to the research individuals' high HbA1c levels (10.3 ± 1.9%) were poor nutrition, financial barriers to a balanced diet, injection anxiety that resulted in missing doses, and restricted access to insulin during school hours. With a HAZ of −0.83 (−1.98–−0.16), the study found that children with T1D were shorter than age- and sex-matched controls. In our study, the majority of individuals were in the pubertal age range, going through a growth spurt, which may have contributed to the significantly superior HAZ despite the longer duration of diabetes and higher HbA1c levels. HAZ was similar for boys and girls when comparing genders, which is in line with a research by Bonfig et al.[5]Nonetheless, Khadilkar et al. discovered a larger height disadvantage in girls in another investigation.[6]While Khadilkar et al. had younger individuals with shorter diabetes duration and lower HbA1c levels, our research participants had a median age of 13.8 years, a median duration of diabetes of 5 years, and a mean HbA1c of 10.3 ± 1.9%. Our investigation did not reveal any tendencies similar to those described by a previous study from Chandigarh, India, which suggested slight variations in the development of boys and girls with T1D.(7)Brown et al. (UK) also noted a reduced peak height velocity and a blunted development spurt in children with T1D.(8)A median WAZ of −0.98 was also seen in our study for children with T1D, which was lower than that of controls; in contrast, Khadilkar et al. reported a WAZ of −1.2 ± 1.3.

These results highlight the significance of taking into account anthropometric measurements and growth trends in children with T1D, since their development might be impacted by things like glycemic management. Younger children with T1D were found to have higher HAZ and WAZ than older children, according to our research [Table 2]. In contrast to Khadilkar et al.'s findings, this one shows that a lower WAZ was linked to a younger age at diagnosis. The "accelerator hypothesis," which postulates that children's HAZ and

WAZ were higher and decreased later before T1D onset, may be best illustrated by our findings.Among our patients, we did not discover any appreciable differences between boys and girls. The causes of T1D's shorter stature are still up for discussion. Taller prepubertal children at diagnosis are shown in some research, while others indicate that stature is most affected when a diagnosis is made prior to puberty.The increased HAZ and WAZ in our study may be related to the younger children's shorter history of diabetes. Prior research suggests that the length of diabetes and glycemic management have a significant impact on T1D children's stature, especially when the diabetes has been present for four to seven years.Nevertheless, there was no discernible effect of diabetes duration on HAZ and WAZ in either our investigation or the study of Khadilkar et al. All things considered, the connection between T1D, age at diagnosis, and stature is complicated and needs more research to fully comprehend the underlying mechanisms and potential long-term implications on growth.

Pre-mixed regimens are thought to be less physiological than the BB regimen, which has been demonstrated to be superior in terms of glucose control in multiple trials. It has been demonstrated that starting rigorous therapy early can avoid growth deficit in children with diabetes.Khadilkar et al.'s study revealed that children on varying insulin regimens had significantly different HbA1c levels (intensive 8.6 ± 1.8% vs. conventional 9.6 ± 2.2%, P = 0.040), however our research indicated that both BB and pre-mixed regimens had higher HbA1c levels. Insulin regimens, however, had no discernible effect on growth measures in either research. Dayal et al.'s recent study, which focused on parents with lower educational levels and poorer compliance to enhance glycemic control, reaffirmed the need of diabetes education. According to the results of our study, children with T1D typically have smaller statures and weigh less than their age-matched peers. It's interesting to note that children's height and weight did not significantly change with the age at which T1D was diagnosed, but younger children tended to exhibit superior growth metrics. Nonetheless, the length of diabetes had a significant impact; higher diabetes duration was linked to more severe weight and height deficiencies. Children with T1D require close observation of their growth at regular intervals, and sustaining appropriate glycemic control—ideally with the BB regimen—is critical to promoting their development.

VI. Conclusion

It is important to acknowledge the limitations of our study, such as its cross-sectional design and small sample size, which may impact the generalizability of the results. Future research with larger and more diverse samples and longitudinal studies would be valuable in validating and expanding upon these findings. Despite these limitations, our study provides valuable insights into the growth patterns of children with T1D and sheds light on potential factors that may influence their growth trajectories. Understanding how growth parameters evolve, particularly considering various socioeconomic factors, will be critical in offering better support and care for children with T1D.

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