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Study of growth parameters in children and adolescents with type 1 diabetes mellitus

Manasa Mynepally[1], Borra Rajesh Yadav[1], Ayyagari Mythili[1], Bongi Vivekananda[1], Kandregula A. V. Subrahmanyam[1]

[1]Department of Endocrinology, Andhra Medical College, Visakhapatnam, Andhra Pradesh, India.

***Corresponding author:**
Ayyagari Mythili,
Department of Endocrinology,
Andhra Medical
College, Visakhapatnam,
Andhra Pradesh, India.

mythili.endo@gmail.com

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ABSTRACT

Objectives: Data on anthropometry in children with type 1 diabetes mellitus (T1D) are sparse in India. 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 57 (F: M 30:27). 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

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, especially in South India, 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.

MATERIAL AND METHODS

This observational cross-sectional study was conducted on subjects with T1D attending the Department of Endocrinology, King George Hospital, Visakhapatnam, between April 2018 and December 2019. 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 71 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. Out of these, 14 children with hypothyroidism and celiac disease were excluded, making the sample size 57. 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. Other diagnostic criteria, namely, a low-fasting C-peptide and positive anti-insulin and GAD antibodies, were considered when there was a diagnostic dilemma. Patients with monogenic causes of diabetes (syndromic or otherwise) were excluded, and likewise, those who had signs of insulin resistance and did not require insulin for glycemic control were also excluded from the study. 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. Heights were measured in triplicate, with variation not more than 0.3 cm by the same individual in all the patients, and mean height was recorded as corrected to the nearest millimeter. 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.[4] 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), anti-thyroperoxidase (TPO) antibodies, total immunoglobulin A (IgA), and IgA tissue transglutaminase (tTg) antibodies. HbA1c was measured by high-performance liquid chromatography (BIO-RAD, Germany). Serum T3, T4, free T4, TSH, and anti-TPO antibodies were analyzed in the Beckman Coulter machine using chemiluminescence immunoassay. Serum Total IgA and IgA tTg were done using fluorescence enzyme immunoassay (enhanced enzyme-linked immunosorbent assay) method.

Informed consent from parents and assent from children were taken at enrollment into the study. Institutional ethics committee clearance was obtained.

Statistical analysis

Data entry was done in Microsoft Excel Worksheet 2016, and the statistical analysis was performed using SPSS software (version 19). 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.

RESULTS

Of the 71 subjects with T1D who were recruited, 14 with hypothyroidism and celiac disease were excluded, and finally, 57 (F: M, 30:27) were included. 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 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).

At enrollment, 64.9% of the children had entered puberty. The median WAZ was significantly higher in the pre-pubertal children compared to the pubertal group (−0.04 [−1.39–0.42] vs. −1.05 [−1.77–−0.48], $P = 0.039$). The median HAZ and BAZ were also higher in the pre-pubertal age group and had a trend toward significance.

Table 1: Baseline characteristics of the study population.

Parameters	Total (*n*=57) (Median, IQR)	Boys (*n*=27) (Median, IQR)	Girls (*n*=30) (Median, IQR)	*P*-value
Age	13.8 (9 to 17.1)	13.6 (9.0 to 16.0)	15.0 (11.4 to 18.0)	0.491
HbA1c	10.3±1.9%	10.39±1.9%	10.28±1.8%	0.962
HAZ	−0.83 (−1.98 to −0.16)	−1.36 (−2.18 to −0.09)	−0.21 (−0.70 to 0.55)	0.414
WAZ	−0.98 (−1.72 to −0.11)	−1.17(−1.88 to 0.23)	−0.88 (−1.16 to 0.327)	0.543
BAZ	−0.55 (−1.41 to 0.1)	−0.522 (−1.47 to 0.05)	−0.568 (−1.31 to 0.19)	0.923

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*=21)	−0.83 (−1.4 to −0.36)	−1.1 (−1.77 to −0.61)	−1.12 (−1.5 to −0.31)
	5–10 (*n*=17)	−1.37 (−2.09 to −0.13)	−1.08 (−1.71 to 0.16)	−0.4 (−1.37 to 0.1)
	<5 (*n*=19)	−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*=38)	−0.76 (−1.75 to −0.04)	−0.81 (−1.7 to 0.24)	−0.45 (−1.27 to 0.24)
	>5 (*n*=19)	−1.19 (−2.12 to −0.27)	−1.08 (−2.46 to −0.61)	−1.06 (−1.87 to −0.31)

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

[Table 3] compares growth parameters across various insulin regimens and HbA1c. About 19 (33%) children were on a Pre-mixed insulin regimen, and 38 (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.

DISCUSSION

In this study, we compared the anthropometric measurements of children with T1D to a control group using the standard WHO 2006 and IAP 2015 growth charts for Indian children.[4] It is worth noting that this is the first study conducted in South India focusing on the anthropometry of children with T1D. The study took place in a government hospital primarily serving patients from lower to middle socioeconomic backgrounds. The study subjects exhibited poor glycemic control, which can be attributed to a lack of awareness regarding optimal glycemic control, insulin therapy, and diabetes-related complications. In addition, inadequate nutrition, financial constraints in accessing a healthy diet, fear of injections leading to skipped insulin doses, and limited insulin availability during school hours contributed to the observed high HbA1c levels (10.3 ± 1.9%) in the study subjects.

The study revealed that children with T1D had a lower height than age- and sex-matched controls, with a HAZ of −0.83 (−1.98–−0.16). This aligns with similar studies from North India and German/Austrian children with T1D, which also reported a height deficit.[5] Despite the longer duration of diabetes and higher HbA1c levels in our study, most participants were in the pubertal age group, undergoing a growth spurt, potentially explaining the relatively better HAZ.

Comparing genders, HAZ was comparable between girls and boys, consistent with a study by Bonfig *et al*.[5] However, another study by Khadilkar *et al*., found a greater height deficit in girls.[6] The median age of our study participants was 13.8 years, with a median diabetes duration of 5 years and a mean HbA1c of 10.3 ± 1.9%, whereas Khadilkar *et al*. had younger participants with shorter diabetes duration and lower HbA1c levels. Although a recent study from Chandigarh, India, reported subtle differences in the growth between boys and girls with T1D, we did not find such trends in our study.[7]

In addition, Brown *et al*., from the UK, observed a blunted growth spurt and decreased peak height velocity in children with T1D.[8] Our study also found that children with T1D tended to be leaner than controls, with a median WAZ of −0.98, whereas Khadilkar *et al*. reported a WAZ of −1.2 ± 1.3.

These findings underscore the importance of considering anthropometric parameters and growth patterns in children with T1D, as factors such as glycemic control can influence their growth and development.

Our study observed that children diagnosed with T1D at a younger age tended to have higher HAZ and WAZ than older children [Table 2]. This finding contrasts with Khadilkar *et al*., where younger age at diagnosis was associated with lower WAZ. Our study might exemplify the "accelerator hypothesis" suggesting that HAZ and WAZ of children before T1D onset were higher and declined later.[9,10] We did not find any significant difference between boys and girls among our patients.

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

Criteria	HAZ	*P*-value	WAZ	*P*-value	BAZ	*P*-value
Insulin regimen						
Basal bolus (*n*=38)	−0.77 (−1.75 to −0.17)	0.925	−1.01 (−1.7 to −0.13)	0.925	−0.51 (−1.45 to 0.19)	0.640
Pre-mixed (*n*=19)	−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*=11)	−0.21 (−0.94 to 0.35)	0.069	−0.33 (−0.73 to 0.23)	0.041*	−0.31 (−0.71 to 0.19)	0.11
>8.5% (*n*=46)	−1.07 (−2.07 to −0.25)		−1.07 (−1.77 to −0.29)		−0.62 (−1.51 to 0.06)	

HAZ: Height for age Z-score, WAZ: Weight for age Z-score, BAZ: BMI for age Z-score, HbA1c: Hemoglobin A1C ; *indicates statistical significance.

The reasons for reduced stature in T1D are still debated. Some studies suggest that stature is most affected when diagnosed before puberty, whereas others show taller pre-pubertal children at diagnosis.[11-14] In our study, the higher HAZ and WAZ in younger children may reflect their shorter duration of diabetes.

Previous studies indicate that the duration of diabetes and glycemic control strongly influence the stature of T1D children, particularly when diabetes duration ranges from 4 to 7 years.[15-17] However, our study and the one by Khadilkar *et al*. did not find a significant impact of diabetes duration on HAZ and WAZ.

Overall, the relationship between T1D, age at diagnosis, and stature is complex and requires further investigation to understand the underlying mechanisms and potential long-term effects on growth.

The BB regimen is considered more physiological than pre-mixed regimens, and several studies have shown its superiority in terms of glycemic control. Early initiation of intensive therapy has been shown to prevent growth impairment in children with diabetes.[18] In the study by Khadilkar *et al*., children on different insulin regimens had significantly different HbA1c levels (intensive 8.6 ± 1.8% vs. conventional 9.6 ± 2.2%, $P = 0.040$), whereas our study found higher HbA1c levels in both BB and pre-mixed regimens. However, insulin regimens did not significantly impact growth parameters in either study. A recent study by Dayal *et al*. reiterated the importance of diabetes education, focusing on parents with lower education strata and poor compliance to improve glycemic control. Perhaps it is a more impactful measure that merits more time and resources for appropriate diabetes care in children.[19]

Our study findings suggest that children with T1D generally exhibit shorter stature and lower weight than their age-matched peers. Interestingly, the age at which T1D was diagnosed did not significantly impact their height and weight, but younger children tended to show better growth parameters. However, the duration of diabetes had a notable effect, with longer diabetes duration associated with greater deficits in height and weight.

Regular monitoring of the growth of children with T1D is crucial, and maintaining good glycemic control, preferably through the BB regimen, is essential for supporting their growth.

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 in South India 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.

CONCLUSION

Children with T1D tend to have shorter stature and lower weight than their peers. While not statistically significant, factors such as younger age at diagnosis, the use of the BB regimen, and lower HbA1c levels are associated with slightly better growth parameters. Regular monitoring, good glycemic control, and managing associated autoimmune conditions are essential for supporting the growth and well-being of children with T1D. Further research, especially longitudinal studies with larger and diverse populations, will help us better understand the evolving growth patterns of these children and develop targeted interventions to improve their overall outcomes.

Ethical approval

The author(s) declare that they have taken the ethical approval from IRB/IEC.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript, and no images were manipulated using AI.

REFERENCES

1. Virmani A. Growth disorders in Type 1 diabetes: An Indian experience. Indian J Endocrinol Metab 2015;19:S64-7.
2. Adolfsson P, Taplin CE, Zaharieva DP, Pemberton J, Davis EA, Riddell MC, *et al.* ISPAD Clinical Practice Consensus Guidelines 2022: Exercise in children and adolescents with diabetes. Pediatr Diabetes 2022;23:1341-72.
3. ElSayed NA, Aleppo G, Aroda VR, Bannuru RR, Brown FM, Bruemmer D, *et al*. 14. Children and adolescents: Standards of care in diabetes-2023. Diabetes Care 2023;46 Suppl 1:S230-53.
4. Khadilkar VV, Khadilkar AV. Revised Indian Academy of Pediatrics 2015 growth charts for height, weight, and body mass index for 5-18-year-old Indian children. Indian J Endocrinol Metab 2015;19:470-6.
5. Bonfig W, Kapellen T, Dost A, Fritsch M, Rohrer T, Wolf J, *et al.* Growth in children and adolescents with Type 1 diabetes. J Pediatr 2012;160:900-3.e2.
6. Khadilkar VV, Parthasarathy LS, Mallade BB, Khadilkar AV, Chiplonkar SA, Borade AB. Growth status of children and adolescents with Type 1 diabetes mellitus. Indian J Endocrinol Metab 2013;17:1057-60.
7. Ganvir RH, Bhalla AK, Dayal D. Growth attainments of Indian children with Type 1 diabetes: A mixed longitudinal study. Indian J Pediatr 2015;82:245-52.
8. Brown M, Ahmed ML, Clayton KL, Dunger DB. Growth during childhood and final height in Type 1 diabetes. Diabet Med 1994;11:182-7.
9. Wilkin TJ. The accelerator hypothesis: Weight gain as the missing link between Type I and Type II diabetes. Diabetologia 2001;44:914-22.
10. Price DE, Burden AC. Growth of children before the onset of diabetes. Diabetes Care 1992;15:1393-5.
11. Knip M, Tapanainen P, Pekonen F, Blum WF. Insulin-like growth factor binding proteins in pre-pubertal children with insulin-dependent diabetes mellitus. Eur J Endocrinol 1995;133:440-4.
12. Tapanainen P, Käär ML, Leppäluoto J, Huttunen NP, Knip M. Normal stimulated growth hormone secretion but low peripheral levels of insulin-like growth factor I in pre-pubertal children with insulin-dependent diabetes mellitus. Acta Paediatr 1995;84:646-50.
13. Drayer NM. Height of diabetic children at the onset of symptoms. Arch Dis Child 1974;49:616-20.
14. Blom L, Persson LA, Dahlquist G. A high linear growth is associated with an increased risk of childhood diabetes mellitus. Diabetologia 1992;35:528-33.
15. Penfold J, Chase HP, Marshall G, Walravens CF, Walravens PA, Garg SK. Final adult height and its relationship to blood glucose control and microvascular complications in sIDDM. Diabet Med 1995;12:129-33.
16. Du Caju MV, Rooman RP, op de Beeck L. Longitudinal data on growth and final height in diabetic children. Pediatr Res 1995;38:607-11.
17. Malone JI, Lowitt S, Duncan JA, Shah SC, Vargas A, Root AW. Hypercalciuria, hyperphosphaturia, and growth retardation in children with diabetes mellitus. Pediatrics 1986;78:298-304.
18. Chiarelli F, Giannini C, Mohn A. Growth, growth factors and diabetes. Eur J Endocrinol 2004;151 Suppl 3:U109-17.
19. Dayal D, Yadav J, Kumar R, Gupta S, Yadav A, Nanda P. Glycaemic control and factors affecting it in Type 1 diabetes in children: Experience from a tertiary care centre in India. Pediatr Endocrinol Diabetes Metab 2022;28:281-6.

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