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Original Research Article

# A Single-Center Cross-Sectional Observational Study Determining the Prevalence and Predictors of Stunting in Children with Type-1 Diabetes

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**Abstract**

**Aim:** The aim of the present study was to determine the prevalence and predictors of stunting in children with Type-1 diabetes.

**Methods:** This was a single-center, cross-sectional, observational study. Children (1–18 years) with T1D along with their parents who attended the at department of pediatrics for 12 months. during the study period were approached. Parents were provided written informed consent and children gave assent for the study. 250 children were included in the study.

**Results:** Of the 250 children studied, 120 (48%) were boys and 130 (52%) were girls. Mean age of the children in the study group was 11.8±3.8 (1.2–18) years and the average duration of diabetes was 5.0±3.7 years. The children's mean HbA1c was 10.0±2.4%. We reported 20% prevalence of stunting in our cohort of children with T1D. Stunted children had higher cholesterol, lower hemoglobin, lower midparental height Z-scores, and higher urinary albumin creatinine ratio. Binary logistic regression revealed that pre-existing comorbidities, compromised renal function, longer disease duration, and short mid-parental height were significant predictors of stunting.

**Conclusion:** Our study suggested that a little under one-sixth of children with T1D had short stature. Monitoring growth in these patients, especially in subjects with short parents, prolonged duration of diabetes, existing comorbidities, and deteriorating renal function are critical.

**Keyword:** Children, Insulin-like growth factor 1, Midparental height, Stunting, Type-1 diabetes.



## Introduction

During childhood and adolescence, the longitudinal growth of bones represents one of the most relevant changes of the body composition. [1] Bone growth occurs at different rates and results from complex mechanisms involving a multitude of regulatory hormones. These events are directly influenced by the interaction between genetic and environmental factors. [1-4] Nutritional status represents one of the most relevant factors affecting these interactions. However, several other factors, and especially chronic diseases, might also strongly modulates these complex mechanisms. In fact, chronic diseases, by directly or indirectly modulating bone and hormonal status, may affect growth and final height of subjects with a disease onset during childhood or adolescence. Several lines of evidence have clearly shown that growth is often impaired in children and adolescents with type 1 diabetes (T1D).

Type-1 diabetes mellitus (T1DM) is a chronic disorder characterized by a deficiency in insulin production. It is the major form of diabetes diagnosed in children and is commonly referred to as "childhood-onset" diabetes. The worldwide prevalence of T1DM in children under the age of 20 years in 2021 was estimated to be 1.2 million cases (149,500 incident cases), with the highest prevalence in India. [5] Growth has previously been reported to be impaired in children with diabetes. [6-8] The Indian experience with paediatric diabetes is important to learn from, not only because of the high burden of diabetes (likely prevalence 5 million diabetic children and adolescents; of which 3–4 million face poverty along with diabetes) but also because of problems like death before diagnosis (due to missed diagnosis), poor management because of low awareness and high costs, limited availability of insulin and poor cold chains in rural areas, limited availability of blood glucose strips, yet greater

family support, as in many developing countries of Asia and Africa. In developing countries, medical training pays little attention to chronic disorders and long term care, since the focus is mainly on infections and other acute illnesses, vaccinations, reproductive issues, and nutrition. Other major limitations are poor infrastructure and low public expenditure on health, leading to significant out‐of‐pocket expenses by individuals. [9] Poor care and delayed or no prevention strategies lead to more complications. Due to these inadequacies in the medical care system, the patient and family are trapped in a vicious cycle of increased acute and chronic complications, thus further elevating costs, mortality, absenteeism from work and hence decrease in income, employability, and quality of life, further pushing the family into indebtedness and poverty.

The aim of the present study was to determine the prevalence and predictors of stunting in children with Type-1 diabetes.

## Materials and Methods

This was a single-center, cross-sectional, observational study. Children (1–18 years) with T1D along with their parents who attended the at department of pediatrics, Nalanda Medical College and Hospital, Patna, Bihar, India for 12 months. During the study period were approached. Since we wanted to assess the effect of complications and comorbidities on growth failure, all patients who attended the hospital during the study period and who agreed to take part in the study were included in the study. Parents were provided written informed consent and children gave assent for the study. 250 children were included in the study.

Clinical history and examination: Data on the age of patients, age at diagnosis of diabetes, duration of diabetes, current medications, number of admissions for ketoacidosis, birth weight, history of other illness, family history, type of insulin regimen, and total dose of insulin per day were collected using standardized questionnaires by a pediatrician. Medical history provided by parents was verified from hospital medical records. Tanner staging for sexual maturity was performed by a pediatric endocrinologist. Pubertal staging was classified as prepubertal, pubertal, and post-pubertal. [10,11] Physical activity was assessed using validated activity questionnaires adapted for Indian children. [12] Anthropometry: Standing height of patients and parents was measured using a portable stadiometer (Leicester Height Meter, Child Growth Foundation, and UK) to the nearest millimeter and weight was measured using an electronic scale to the nearest 100 g. Body mass index (BMI) was computed by dividing weight in kilograms by height in meter square. Subsequently, the height, weight, and BMI were converted to Z scores using Indian references. [13]

### Dietary Data

Dietary data were recorded using the 1day dietary recall method on 1 week day and a holiday and a mean were computed. Trained nutritionists interviewed the children along with their primary caregivers to get an accurate estimate of the foods consumed. Nutrient intakes were then computed using the cooked food database software, CDiet. [14] Adequacies of nutrient intakes were estimated by computing the percentage of the recommended dietary allowance (RDA) for Indian children for each nutrient consumed. [15]

Biochemical measurements: Glycemic control was evaluated by measuring glycosylated hemoglobin (HbA1c). A fasting blood sample (5 ml) was collected between 7 am and 9 am by a pediatric phlebotomist. HbA1c was measured by high-performance liquid chromatography (BIO-RAD, Germany). Hemoglobin was estimated by spectrophotometry at a wavelength of 555 nm using a Horiba Yumizen H500 hematology analyzer. The fasting blood samples were then assessed for lipid profile (total cholesterol, triglycerides, and HDL-C) using the enzymatic method and low-density lipoprotein-cholesterol concentrations were calculated by the Friedewald formula. The first voided urine sample was collected in a sterile container and urine was assessed for urine microalbumin, creatinine, and urine albumin: creatinine ratio (ACR) which were computed using a ratio of urine albumin to urine creatinine (urinary albumin and creatinine concentrations determined using radioimmunoassay and Jaffe's method, respectively). Samples were not taken during menstrual cycles, fever, after heavy exercise, or marked hyperglycemia. If ACR was in the range between 0 and 30 ug/mg, it was considered normal. Single high value of early morning urinary ACR (above 30 ug/mg) was considered as altered ACR. Serum IGF1 concentrations were analyzed by a solid-phase enzyme linked immunosorbent assay with an intraassay coefficient of variation (CV) of 4.7% and interassay CV of 7.2%. The IGF1 concentrations were then converted into Zscores using available reference data. [16]

### Statistical Analysis

All statistical analyses were carried out using the SPSS for Windows software program, version 26 (SPSS, Chicago, IL, USA). All outcome variables were tested for normality before performing statistical analyses. Differences in means were tested using Student's t-test for parametric data, Mann–Whitney U-test for non-parametric data, and Chi-square test for categorical variables. For testing

relationships between dichotomous dependent variables and continuous predictors, binary logistic regression analysis was carried out. The dependent variable in the model was stunting while the independent variables were midparental height Z-scores, tanner stage (classified into two groups as pre-pubertal and in puberty/post-pubertal), diabetes duration, glycemic control (HbA1c), and comorbidities/ complications such as hypothyroidism, altered ACR, and lipids. $p<0.05$ was considered statistically significant.

## Results

**Table 1: Clinical/laboratory findings of patients classified by stature**

| Parameter | Stunting (n=50) | No stunting (n=200) | p-value |
|---|---|---|---|
| Age (years) | 12±3.7 | 11.7±4 | 0.022 |
| Diabetes duration (years) | 7.3±4 | 4.6±3.2 | 0.000 |
| Height Z scores | –2.5±0.7 | –0.7±0.8 | 0.000 |
| (15.7% stunted) | | | |
| Weight Z scores | –1.6±0.7 | –0.7±0.8 | 0.124 |
| BMI Z scores | –0.5±0.8 | –0.5±0.7 | 0.000 |
| Midpaternal height Z scores | –1.5±0.7 | –0.7±0.7 | 0.000 |
| Physical activity (min/week) | 296.4±226.4 | 302.6±228.2 | 0.786 |
| PercentRDA energy (%) | 69.2±27.4 | 72.6±31.8 | 0.346 |
| PercentRDA protein (%) | 105.5±54.4 | 114.6±60.5 | 0.206 |
| PercentRDA zinc (%) | 67.3±52.4 | 68.2±47.3 | 0.889 |
| Insulin (unit/kg/day) | 1.2±0.4 | 1.1±0.3 | 0.162 |
| Creatinine (mmol/L) | 0.1±0.0 | 0.1±0.0 | 0.044 |
| HbA1c (mmol/L) | 13.7±0.8 | 13.6±0.8 | 0.314 |
| Vitamin D (ng/ml) | 19.4±9.1 | 18.4±9.1 | 0.540 |
| Hemoglobin (g/dl) | 12.8±1.4 | 13.7±1.4 | 0.022 |
| Total cholesterol (mmol/L) | 4.4±1.0 | 3.8±0.9 | 0.007 |
| LDL cholesterol (mmol/L) | 1.0±1.0 | 1.0±0.8 | 0.366 |
| Albumin Creatinine ratio (ug/mg) | 240.4±645.5 | 28.2±76.4 | 0.000 |

Of the 250 children studied, 120 (48%) were boys and 130 (52%) were girls. Mean age of the children in the study group was 11.8±3.8 (1.2–18) years and the average duration of diabetes was 5.0±3.7 years. The children's mean HbA1c was 10.0±2.4%. We reported 20% prevalence of stunting in our cohort of children with T1D. Stunted children had higher cholesterol, lower hemoglobin, lower midparental height Z-scores, and higher urinary albumin creatinine ratio.

**Table 2: Binary logistic regression to determine the predictors of stunting**

| Parameter | OR | Wald | Sig | 95% CI for EXP (B) | |
|---|---|---|---|---|---|
| | | | | Lower | Upper |
| Duration of diabetes | 1.424 | 20.80 | 0.000 | 1.232 | 1.710 |
| Midparental height Z-scores | 3.547 | 12.316 | 0.000 | 1.78 | 7.314 |
| Tanner stage | 0.160 | 8.188 | 0.005 | 0.047 | 0.560 |
| Children having comorbidities (hypothyroidism, vitiligo, and celiac disease) | 4.396 | 3.542 | 0.05 | 0.926 | 19.409 |
| Albumin: creatinine ratio | 5.760 | 8.232 | 0.005 | 1.745 | 19.028 |
| Cholesterol | 0.690 | 0.276 | 0.604 | 0.15 | 3.234 |
| Vitamin D | 0.744 | 0.445 | 0.508 | 0.24 | 1.867 |
| HbA1c | 1.64 | 0.882 | 0.342 | 0.548 | 4.325 |
| IGF1_zscores | 0.702 | 2.247 | 0.134 | 0.443 | 1.115 |
| Sports duration (weekly/min) | 1 | 0.01 | 0.924 | 0.949 | 1.002 |
| Percent RDA_energy | 0.997 | 0.036 | 0.867 | 0.96 | 1.018 |
| Constant | 0.004 | 14.4 | 0 | | |

While performing logistic regression analysis, we considered children with T1D with or without stunting as the dependent variable while diabetes duration, physical activity and dietary intake (energy percentage of as per recommended daily allowance), midparental height Z-scores, tanner stage, comorbidities, urinary ACR, serum cholesterol, HbA1c, and IGF-1 Z-scores as the independent variables. Binary logistic regression revealed that children with comorbidities (such as hypothyroidism, vitiligo, and celiac disease), children having compromised renal function,

longer disease duration, children who had achieved puberty, and children with short midparental height were significant predictors of stunting ($p<0.05$). Variables such as physical activity and dietary intake of energy, cholesterol concentrations, HbA1c, and IGF-1 concentrations were not significant predictors ($p>0.05$).

## Discussion

Type-1 diabetes mellitus (T1D) is one of the most common chronic pediatric endocrine disorders in which the ß-cells of the pancreas do not produce enough insulin to maintain normal glucose metabolism. [17] The International Diabetes Federation Atlas 10th edition estimates 1,211,900 children and adolescents younger than 20 years to have T1D globally. T1D age-standardized incidences are highest in populations of North European origin and in several countries in the Middle Eastern and North African Region. India and the United States of America have the highest numbers of estimated incident cases of T1D followed by various other populous countries. [18] T1D and its complications, including impaired childhood growth/short stature, thus remain a major concern. [19] A child with short stature or stunting is a child whose height/length is <–2SD (i.e., below the 2.3 percentile) for his/her age and gender. Stunting (low height-for-age) is considered to be a significant indicator of nutritional assessment of children and adolescents and is also an indicator of chronic under nutrition. [20]

Of the 250 children studied, 120 (48%) were boys and 130 (52%) were girls. Mean age of the children in the study group was 11.8±3.8 (1.2–18) years and the average duration of diabetes was 5.0±3.7 years. The children's mean HbA1c was 10.0±2.4%. We reported 20% prevalence of stunting in our cohort of children with T1D. Stunted children had higher cholesterol, lower hemoglobin, lower midparental height Z-scores, and higher urinary albumin creatinine ratio. While performing logistic regression analysis, we considered children with T1D with or without stunting as the dependent variable while diabetes duration, physical activity and dietary intake (energy percentage of as per recommended daily allowance), midparental height Z-scores, tanner stage, comorbidities, urinary ACR, serum cholesterol, HbA1c, and IGF-1 Z-scores as the independent variables. Binary logistic regression revealed that children with comorbidities (such as hypothyroidism, vitiligo, and celiac disease), children having compromised renal function, longer disease duration, children who had achieved puberty, and children with short midparental height were significant predictors of stunting ($p<0.05$). Variables such as physical activity and dietary intake of energy, cholesterol concentrations, HbA1c, and IGF-1 concentrations were not significant predictors ($p>0.05$). The pubertal peak in HbA1c is likely due not only to physiological changes, such as increased insulin resistance during puberty [21] but also to behavioral resistance to lifestyle change. [22] We also analyzed how individual differences in pubertal height growth relate to child specific physiological characteristics. The course of disease, in particular the age at diagnosis and the time since diagnosis, affected mean height and the timing of the growth spurt–later diagnosis and longer duration were independently associated with greater height and later puberty. However there was an important sex difference: girls were affected more in terms of size, particularly with mean HbA1c, where a 1 SD increase in HbA1c was associated with being 2 cm shorter. Boys were affected more in terms of timing and intensity, which was positively associated with age at diagnosis and the duration of the disease. Thus, broadly speaking, the impact of T1DM was to reduce height in girls, whereas in boys it slowed and delayed growth. The dependence of pubertal growth on growth hormone and testosterone in girls and boys, respectively, may be important for this observed difference as suggested by Dunger et al. [23] A recent study by Blasetti et al [24] also showed that shorter subjects had a higher HbA1c SDS, but they did not report any sex differences.

In our study, we did not find a role of glycemic control in causing stunting in children with T1D. Similar results have been reported in a study conducted in Royal Children's Hospital (RCH), Melbourne, Australia, which concluded no significant association between metabolic control and linear growth of children with T1D. [25] In contrast to our results, a study conducted in Jeddah Kingdom of Saudi Arabia from June to August 2017 showed that there was no association between the duration of diabetes and the height, weight, or BMI Z-scores. Besides, they also report a correlation between HbA1c levels and height Z-scores. This may be explained by exclusion of children with hypothyroidism, celiac disease, and familial short stature. [26,27]

## Conclusion

Our study suggested that a little under one-sixth of children with T1D had short stature. Monitoring growth in these patients, especially in subjects with short parents, prolonged duration of diabetes, existing comorbidities, and deteriorating renal function are critical.

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