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Original Article

Differential Impact of Type 1 Diabetes on Bone Outcomes in Children

Poon SW et al. Impact of Diabetes on Bone in Children

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Abstract
Objectives: Type 1 diabetes (T1D) is a recognized risk factor for skeletal fragility in adults, but its impact on bone microstructure in children remains incompletely characterized. In particular, data on trabecular bone quality remain scarce. This study aimed to evaluate skeletal parameters in this group of children and examine their associations with clinical variables.
Methods: This retrospective cross-sectional study evaluated children with T1D at the Hong Kong Children's Hospital from June 2023 to December 2024. Skeletal parameters, including trabecular bone score (TBS), bone health index (BHI), bone mineral density (BMD) by dual-energy x-ray absorptiometry, and serum vitamin D and HbA1c levels, were evaluated alongside fracture history. A parent-reported questionnaire measured participation in physical activity. Correlations between bone parameters and clinical variables were analyzed.
Results: Sixty-eight children with T1D (male 42.6%, mean 12.7 ± 3.7 years, 44.1% prepubertal, mean HbA1c 7.3%) were included. A substantial proportion of children (19.6%) had low cortical bone density as reflected by BHI Z-score ≤ -2, whereas deficits in trabecular bone (TBS Z-score ≤ -2) were less common (4.8 %). Regression analysis confirmed that higher lean mass was associated with higher total body less head (TBLH), lumbar spine (LS) and TBS Z-scores (β=0.0001, $p < 0.05$), while disease duration had a negative association with these measurements (β=-0.1413; β =-0.1335, β=-0.2270, $p < 0.05$).
Conclusion: In this cohort of children with T1D, a pattern of skeletal involvement was observed, characterized by a high prevalence of low BHI Z-scores and a relatively low prevalence of low TBS Z-scores. This may suggest differential involvement of cortical bone with relative preservation of trabecular microarchitecture. Whether these structural differences translate into fracture risk remains unknown. Longitudinal studies are needed to elucidate the evolution of bone alterations over time and to identify determinants underlying skeletal vulnerability in childhood-onset diabetes. Higher lean mass was associated with higher bone mass and microarchitectural indices, whereas longer disease duration may have a negative association with these parameters. These findings highlight modifiable and disease-related factors that may influence bone health, warranting confirmation in larger controlled studies.
Keywords: Type 1 diabetes; children; trabecular bone; cortical bone

What is already known on this topic?
Existing evidence links T1D to skeletal fragility in adult populations. Data in children are limited. Conventional DXA fails to capture microstructural changes, and although new tools including Trabecular Bone Score (TBS) and Bone Health Index (BHI) show promise for bone health assessment, application in paediatric T1D remains scarcely explored.

What this study adds?
It provides new evidence that early skeletal alterations in children with well-controlled T1D primarily involve cortical rather than trabecular bone, contrasting with patterns observed in adults. TBS and BHI could serve as a useful complementary tool for bone health assessment for this group of children.

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Introduction
Globally, more than 200,000 children and youth are diagnosed with type 1 diabetes (T1D) annually (1). T1D is an autoimmune condition characterized by insulin deficiency and chronic hyperglycaemia. Beyond the well-recognized metabolic complications, it has emerged as a significant risk factor for skeletal fragility. While substantial evidence links T1D to skeletal fragility and increased fracture risk in adult populations, its impact on children remains less well-understood. The impact of hyperglycaemia on bone health is likely multifactorial, involving reduced bone turnover, osteocyte senescence, accumulation of advanced glycation end products, and increased sclerostin production (2–4). In addition, dysregulation of the growth hormone(GH)/ insulin-like growth factor-1 (IGF-1) axis may further disrupt bone remodelling and hinder peak bone mass attainment in children with T1D (5). Prior studies using peripheral quantitative computed tomography (pQCT) showed conflicting effects of T1D on trabecular and cortical compartments (6,7). Importantly, bone quality in T1D is influenced not only by changes in bone mineral density (BMD), but also by alterations in bone microarchitecture. Experimental mouse models and clinical studies in white youth have demonstrated decreased trabecular number and thickness, impaired trabecular homogeneity, and increased trabecular separation in individuals with T1D. These microarchitectural deficits collectively contribute to diminished bone strength and elevated fracture risk, often disproportionate to changes in BMD alone (8,9). Conventional assessment of skeletal health with dual-energy X-ray absorptiometry (DXA) is limited by its inability to assess alterations in trabecular bone microarchitecture. Trabecular bone score (TBS), on the other hand, provides an indirect measure of trabecular integrity independent of BMD (10). While widely used in adult subjects, application of TBS in the pediatric diabetes population remains scarce (11). To date, only one pediatric study has explored the application of TBS in children with diabetes. However, interpretation of its findings was limited by the absence of age- and sex-adjusted Z-score normalization, constraining meaningful clinical interpretation (12).
Complementary to TBS and DXA measurements, Bone Health Index (BHI), derived from the automated software BoneXpert (BX), has emerged as a practical alternative modality in bone health assessment in children. Various studies have demonstrated the sensitivity of BHI in detecting changes in bone density in children at risk of skeletal fragility, including those with inflammatory bowel disease, juvenile idiopathic arthritis and renal conditions (13–15). While two prior paediatric studies reported decreased BHI in children with T1D, both cohorts had poor glycaemic control with mean HbA1c 9.7%-9.8% – substantially higher than levels typically observed in high-income countries (16,17). Whether similar deficits occur in children with better glycaemic control remains unknown. This study thus aimed to evaluate the bone health status in children with T1D, by assessing TBS using the recently established paediatric reference, alongside BHI, to elucidate the early effects of T1D on trabecular versus cortical bone during critical periods of skeletal maturation. We also sought to examine correlations between conventional BMD measurements with TBS and BHI. Furthermore, associations between glycaemic control and disease characteristics and bone parameters within this population were examined.

Materials and Methods
This retrospective study was conducted at the Hong Kong Children's Hospital from June 2023 to December 2024. The study cohort comprised all children aged </= 18 years with T1D, in whom both a DXA scan and a bone age assessment were performed within a 3-month window as part of routine clinical care during the study period. T1D was diagnosed according to the ISPAD 2022 guideline (18). Exclusion criteria included medical conditions other than diabetes that may affect skeletal metabolism, including celiac disease, hypogonadism, untreated thyroid dysfunction, chronic renal diseases, a history of malignancy, immobility or use of long-term systemic steroids. Children with microvascular complications were also excluded from the analysis.
Anthropometric measurements were collected on the day of the DXA scan and converted to age and gender-specific body mass index (BMI) Z-scores derived using the Hong Kong 2020 Growth reference. Pubertal assessment was performed with Tanner staging during follow-up in the 3-month period by an

endocrinologist. Demographic data and clinical information were retrieved from the electronic medical records. Glycaemic outcome was assessed by the average glycosylated haemoglobin (HbA1c) in the year preceding bone health assessment. Serum 25(OH) vitamin D levels were measured by liquid chromatography-mass spectrometry, with concentrations ≥ 50 nmol/L considered sufficient according to the Global Consensus Recommendations on Prevention and Management of Nutritional Rickets (19). As previous data demonstrated no significant seasonal variation in vitamin D status locally, the season in which serum vitamin D was measured was not specified in this study (20).

Physical activity data were recorded using standardized questionnaires completed by parents during the study period. Information on duration and intensity of physical activity was recorded, with regular participation defined as at least 60 minutes of physical activity daily.

Bone densitometry (DXA measurements) of the whole body was carried out with Hologic Horizon A densitometer. Areal bone mineral density (BMD in g/cm2) for total body less head (TBLH) and lumbar spine (LS L1-L4) were measured, with respective Z-scores calculated using gender-and age-specific reference data from The Bone Mineral Density in Childhood Study(21) . "Low BMD" was diagnosed when the BMD Z-score was ≤ -2.0. Height-adjusted BMD Z-scores were computed for children with short stature whose body height was less than the 2nd centile on the local growth chart. TBS, a two-dimensional textural analysis of lumbar spine DXA images reflecting trabecular bone microarchitecture, was performed using TBS iNsight software on LS DXA images, and TBS Z-scores were calculated using reference ranges previously determined in a paediatric cohort (22). Lean mass (g) was also measured in the whole body DXA scan.

Standardized radiographs of the left hand were performed within a 3-month window in all children and the BoneXpert software program (BoneXpert Version 3.2.2) was used for analysis. The method of analysis was previously described by Thodberg et al. Standard anteroposterior radiographs of the left hand were obtained. The Bone Health Index (BHI) was calculated based on cortical thickness measurements of the second to fourth metacarpal bones, quantified via density gradient analysis to delineate the inner and outer cortical boundaries. To account for inter-individual variation in skeletal size among growing children, metacarpal width and length were integrated into the BHI computation. (23). BHI Standard Deviation Score (BHI SDS) calculation is performed based on the bone age derived from the same x-ray, with reference curves previously determined from a paediatric Dutch cohort (23,24).

The study protocol was conducted in accordance with the Declaration of Helsinki and was approved by the Hong Kong Children's Hospital Research Ethics Committee (PAED-2025-013).

Statistical analysis

All statistical analyses were carried out using IBM SPSS Statistics version 27. Descriptive statistics were reported in absolute numbers and percentages. All variables were assessed for normality before analysis and expressed as mean ± SD for parametric and median [interquartile range (IQR)] for nonparametric distributions. Differences in means were tested using Student's t-test for parametric data and Mann-Whitney U test for non-parametric data. Pearson correlation coefficient was used to determine the correlation between TBS Z-score, BHI SDS and bone densitometry Z-score. Multiple regression analyses with a backward stepwise selection method were used to investigate the relationship between bone indexes (TBLH Z-score, LS Z-score, TBS Z-score and BHI SDS) and variables of interest such as age, pubertal status, lean mass, HbA1c, treatment modality and physical activity participation. Results were expressed as unstandardized regression coefficients (B) and standard errors (SE). Statistical significance was defined by a two-sided *P* value <0.05 for all analyses.

Results

Sixty-eight children (42.6% male, 86.7 % Chinese) with T1D were included. The mean age was 12.7 ± 3.7 years and 76.2% were pubertal. The median duration of diabetes was 3.5 years (IQR 2.1 - 7.0 years). Most of the children (77.9%) were on multiple daily insulin injections, while the remaining were on insulin pump therapy. The mean HbA1c level in the preceding year was 7.3 ± 1.0 %, with 38.2 % achieving the optimal glycaemic target with a mean HbA1c ≤ 7%. Mean 25(OH)vitamin D level was 50.9 ± 19.5 nmol/L and 44.6 % of children had vitamin D deficiency with 25(OH)vitamin D < 50nmol/L. A history of long bone fracture was reported in 3 children (4.4%), each experiencing a single fracture episode, with 2 cases occurring prior to their diagnosis of T1D. Therefore, none of them fulfilled the International Society Of Clinical Densitometry (ISCD) criteria of clinically significant fracture history (25).

Regarding their bone health status, the median BMD Z-score at TBLH and LS were -1.2 (IQR -2.0 to -0.4) and -0.3 (IQR -0.9 to 0.6) respectively. Among them, 25.8 % had TBLH Z-scores ≤ -2 whereas only 2.9 % had LS Z-score ≤ -2. The median TBS Z-score was 0.3 (IQR -0.2 to 0.9), with 4.8% having TBS Z-score ≤ -2. The median BHI SDS was -0.8 (IQR -1.7 to -0.3) and 19.6 % had BHI SDS ≤ -2. Clinical characteristics and bone health measurements of children are presented in Table 1.

Correlations for densitometry Z-score and BHI SDS were shown in Figure 1 and Figure 2. Positive but weak correlations were found between BHI SDS with both TBLH and LS Z-score, with a stronger correlation with TBLH Z-score. ($r = 0.51$ vs $r = 0.36$, $p < 0.05$). Similarly, TBS Z-score also had a weak but significant correlation with BHI SDS ($r = 0.29$, $p < 0.05$), TBLH Z-score ($r=0.46$, $p < 0.05$) and LS Z-score ($r=0.47$, $p < 0.05$).

No significant differences were observed in any bone parameters between those with HbA1c ≤ 7% and those with HbA1c >7% (Table 2). Pubertal children had lower TBS Z-scores, while other bone measurements did not differ between the prepubertal vs pubertal groups (Table 3). In contrast, children who participated in regular physical activity exhibited significantly higher TBLH, LS, TBS Z-score and BHI SDS compared to those who were sedentary (Table 4). In multivariate regression analyses, lean mass was a significant factor associated with higher TBLH, LS, and TBS Z-scores, while longer disease duration was associated with lower TBLH, LS, and TBS Z-scores (Table 5). Age, pubertal stage, insulin delivery modality, vitamin D status, or physical activity were not associated with low DXA measurements or BHI values.

Discussion

We observed a high prevalence of low BHI Z-scores and a relatively low prevalence of low TBS Z-scores in our cohort of children with T1D. This pattern may suggest a greater involvement of cortical bone with relative preservation of trabecular microarchitecture. However, in the absence of an age- and sex-matched healthy cohort, these findings remain tentative. Longer disease duration and lower lean mass were associated with poorer bone parameters.

The mechanisms underlying the adverse effects of chronic hyperglycaemia on bone health in children are complex. Studies involving youth with T1D have consistently demonstrated lower serum levels of osteocalcin and procollagen type I N-propeptide compared with healthy controls, with a possible link to increased markers of oxidative stress in T1D (26)(27). Both insulin deficiency and reduced circulating IGF-1 levels in children with T1D have been demonstrated to result in diminished osteoblastic activity (28)(29). In addition, hyperglycaemia, and the consequent accumulation of advanced glycation end products promote increased sclerostin secretion by osteocytes, thereby inhibiting the Wnt-pathway critical for osteoblastogenesis (30). Collectively, these contribute to a state of low bone turnover status characteristic of diabetic bone disease in paediatric T1D. An inverse association between disease duration and bone parameters was observed in our cohort. However, given the cross-sectional design, this finding should be interpretated with caution. The observed association may also be influenced by residual confounding, including age, pubertal status, body composition, physical activity and other unmeasured factors. As such, no temporal or causal relationship could be established with this finding, and further longitudinal studies are warranted to determine whether longer disease duration contributes to worsening bone health.

Studies in adults with diabetes have documented more profound impairment in trabecular microarchitecture and quality in individuals with T1D, which contrasts with what is observed in our cohort. Indeed, similar observations have been reported in other pediatric studies. Bechtold et al used peripheral quantitative computed tomography (pQCT) in 41 children and adolescents with T1D, showing significant reductions in cortical thickness and cortical BMD at the tibia and radius compared to healthy controls, while trabecular BMD was even higher in the group with T1D (6). Similar computer tomography study also found lower cortical but preserved trabecular BMD in 48 children with T1D (31). This differential pattern in children may reflect the heightened modeling and remodeling dynamics of cortical bone during growth, rendering it more susceptible to hyperglycaemia-induced insults. Another possible explanation relates to the differential growth patterns of the axial and appendicular skeleton, whereby axial growth mainly occurs during the pubertal years while appendicular growth takes place mainly in the prepubertal years. As the majority of the children in the study cohort developed T1D before puberty, any effects of the disease may have a greater impact on the appendicular skeleton, which is primarily composed of cortical bones, than on the axial skeleton, which consists predominantly of trabecular bone (32). Alternatively, preservation of trabecular microarchitecture could relate to the low prevalence of microvascular complications in our cohort, aligning with adult data showing trabecular deficits only in individuals with diabetic microangiopathy (33). Components of the metabolic syndrome, including diastolic blood pressure, obesity, triglycerides and insulin resistance, have been associated with reduced TBS in T1D, potentially via systemic inflammation promoting trabecular bone resorption (34,35). The relatively low prevalence of obesity and microvascular complications in the present cohort likely explains the preserved trabecular quality in most.

Notably, pubertal subjects in our cohort demonstrated lower TBS Z-score, despite puberty being a period of accelerated bone accrual. One possible explanation is the longer disease duration (6.1years vs 2.9 years, $p < 0.05$) in this group of children, which may be associated with greater cumulative exposure to the detrimental effect of hyperglycaemia. Dynamic changes in bone remodeling during puberty may also influence trabecular microarchitecture. Furthermore, residual confounding factors such as body composition, physical activity and glycaemic control may also contribute to the observed association, and that a chance observation is plausible given the modest sample size. Therefore, further studies are required to clarify the relationship between pubertal status and trabecular bone health in children with T1D. Nevertheless, monitoring TBS in youth with T1D remains important, as emerging evidence demonstrates its value in fracture prediction independent of BMD (36). The clinical significance of TBS is further highlighted by its incorporation into the FRAX model in adults, which has been shown to enhance fracture risk prediction compared to the use of FRAX alone (37). As deterioration in trabecular microarchitecture may precede

BMD changes, which may also explain why pubertal subjects had comparable LS BMD Z-scores to prepubertal counterparts despite lower TBS Z-scores, longitudinal TBS assessment could enhance risk stratification in this vulnerable population.

A positive yet weak correlation between BHI SDS with DXA BMD Z-score indicates that these indices reflect complementary but distinct aspects of bone properties. BHI offers several advantages particularly in the paediatric population. Compared to DXA scan, BHI is less expensive, involves lower radiation and is easier to perform in routine clinical settings. A notable benefit of BHI also lies in its adjustment of cortical BMD for metacarpal width and length. This size correction enhances the accuracy and representativeness of BHI in evaluating bone health in growing children with widely variable skeletal dimensions (38). In the context of T1D, given the pattern of cortical bone involvement observed in this study, BHI may serve as a complementary tool to DXA for detecting compromised bone health.

Our results revealed early cortical bone impairment in children with short disease duration. This is of particular clinical concern, as fractures tend to occur at cortical-rich sites e.g. long bones in the paediatric population. In fact, Weber et al reported reduced TBLH bone mineral content, femoral neck and tibia cortical volumetric BMD at the time of T1D diagnosis compared to reference values in children (39). Additionally, a decrease in bone formation markers was already documented among newly diagnosed paediatric T1D subjects (40). Collectively, these findings, together with our results, highlight the need for early bone health surveillance in children with T1D to enable timely detection of early alterations in bone integrity.

There is scarce data on bone health in Asian children with T1D, all of which involve youth with poor metabolic control (41–44). In contrast, we did not observe any influence of glycaemic outcome on bone health parameters. Although impaired bone accrual has been hypothesized to relate to chronic hyperglycaemia through deficit in osteogenesis and accumulation of advanced glycation end products, the cross-sectional nature of our study precludes conclusions on the impact of glycaemic exposure on these pathways (45–47). Nonetheless, lifelong surveillance of skeletal health in this vulnerable population is necessary.

Higher lean mass was identified as a protective factor associated with better bone outcomes in our study. This observation is consistent with findings in meta-analyses and population-based studies, which have demonstrated a strong positive relationship between lean mass and BMD across different skeletal sites, in both genders and across paediatric and adult populations (48)(49)(50). Bone mass is primarily influenced by dynamic mechanical loading generated through muscular contraction, which triggers bone remodelling, rather than by the static mechanical load by body weight alone (51). As lean mass serves as a surrogate for skeletal muscle mass, greater lean mass is likely to exert a beneficial influence on BMD. To this end, a large population-based cohort study in children from the United Kingdom reported that physical activity promotes periosteal apposition, partly mediated through increase in lean mass (52). Although participation in physical activity was not significantly associated with better bone outcomes in our regression analysis - likely due to limited sample size – the established role of physical activity in enhancing lean mass underscores the importance of promoting regular exercise and preventing underweight as key strategies to optimize bone health in children with T1D.

The present study did not identify any association between serum vitamin D levels and bone parameters, including BHI, DXA-derived BMD, or TBS measurements. However, the detrimental effects of vitamin D deficiency on bone health in this population is well established, with supplementation resulting in significant improvements in BMD and cortical thickness (53,54). Therefore, ensuring age-appropriate intake of calcium and vitamin D is essential for all children with T1D. Additionally, promoting physical activity, along with providing guidance on diet and insulin dosage adjustments, should be integrated into routine diabetes care from the time of diagnosis. Given the evidence of early skeletal impact demonstrated in our results, proactive bone health assessment for children with T1D prior to transition to adult care is recommended.

This study is one of the few to employ both TBS and BHI in a paediatric population. As pQCT is not readily available in clinical practice, TBS could serve as useful complementary index in bone health evaluation in children by offering additional insights into trabecular integrity. Our cohort also represents a population with relatively satisfactory glycaemic control compared to prior studies, illustrating the early impact of T1D on skeletal measurements in the real-world setting with modern diabetes care.

Study limitations

Several limitations merit consideration in this study. The retrospective cross-sectional design precludes any inference of causality. The absence of an age and sex-matched healthy control cohort also limits our ability to make direct inferences about the magnitude of bone deficits attributable to T1D. In fact, local children have an alarmingly low rate of physical activity participation, which may itself be associated with suboptimal bone health (55). Importantly, the relatively modest sample size may be insufficient for multivariable analysis, leading to reduced statistical power. Variables, such as age, pubertal status, lean mass, physical activity and disease duration, are biologically related and are likely intercorrelated. Given the potential impact of collinearity among these variables, collinearity diagnostics were assessed via variance inflation factors (VIF) and tolerance values. No evidence of problematic multicollinearity was noted in the final models, with all VIF values <5 and all tolerance values >0.2.

In addition, BMD references used for Z-score calculation were derived from a predominantly white population due to a lack of data among the Asian population, which may introduce bias and affect the interpretability of the derived Z-scores. Ethnic differences in bone density have been well documented. Accordingly, our findings should be interpreted with caution as the use of non-population-specific reference standards may lead to misclassification of bone health status. Prospective longitudinal studies examining the natural history of bone deficits in children with T1D, as well as the predictive values of TBS and BHI for future fractures, are warranted.

Conclusion

In summary, our study identified a higher prevalence of low BHI SDS alongside largely preserved TBS Z-score in a predominantly Chinese paediatric cohort with relatively well-controlled T1D. While the absence of a healthy control group represents a significant limitation in the interpretation of these findings, our observations may nonetheless suggest differential involvement of cortical and trabecular compartments in the growing skeleton. This pattern appears to contrast with that typically seen in adults with T1D, who frequently demonstrate compromised trabecular microarchitecture. This observed difference may reflect the shorter disease duration, ongoing skeletal growth, and fewer metabolic and vascular complications in paediatric patients. Although the clinical impact of these findings on long-term fracture risk remains uncertain, this study provides valuable insights into early skeletal alterations in youth with type 1 diabetes—a population in whom data remain limited. Prospective longitudinal studies are needed to clarify the trajectory of bone changes and identify key determinants for skeletal health outcomes across the disease course. Greater lean mass was associated with higher bone mass and microarchitectural indices, while disease duration showed a negative association with these parameters. These findings highlight modifiable and disease-related factors that may influence bone health, warranting confirmation in larger controlled studies.

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Table 1: Demographics and bone health measurements of children included in the study

	Type 1 diabetes (n=68)
Demographics	
Gender, n (%)	29, (42.6% male)
Ethnicity, n (%)	59, (86.7% Chinese)
Age (years), (mean, S.D.)	12.7 ± 3.7, 76.2% pubertal
Age of diagnosis (years), (mean, S.D.)	7.7 ± 3.5
Duration of disease (years), (median, IQR)	3.5 (2.1-7.0)
BMI z-score, (median, IQR)	0.9 (0.0-1.4)
History of long bone fractures, n (%)	3 (4.4%)
Regular participation in sports, n (%)	37 (54.4%)
Disease control	
Average HbA1c levels (%), (mean, S.D.)	7.3 ± 1.0
Medications, n (%)	
○ Multiple daily injections of insulin	53 (77.9%)
○ Insulin pump	15 (22.1%)
Biochemistry, mean (s.d.)	
Serum calcium (mmol/L) (2.31-2.64 mmol/L)	2.4 ± 0.1
Serum phosphate (mmol/L) (1.00-1.70 mmol/L)	1.5 ± 0.2
Alkaline phosphatase (IU/L), median (IQR)	229.0 (119.0-292.0)
25(OH)vitamin D (nmol/L)	50.9 ± 19.5
Bone health measurements	
TBS	
TBS z-score, median (IQR)	0.3 (-0.2 to 0.9)
TBS z-score ≤ -2, n (%)	3 (4.8 %)
Bone health index	
BHI SDS, median (IQR)	-0.8 (-1.7 to -0.3)
BHI z-score ≤ -2, n (%)	11 (19.6 %)
DXA parameters, median (IQR)	
TBLH z-score	-1.2 (-2.0 to -0.4)
LS z-score	-0.3 (-0.9 to 0.6)
BMD z-score ≤ -2, n (%)	
TBLH z-score ≤ -2	17 (25.8%)
LS z-score ≤ -2	2 (2.9%)

TBS = Trabecular bone score; BHI SDS = Bone health index standard deviation score; DXA = Dual-energy X-ray absorptiometry; TBLH = Total body less head; LS = Lumbar spine; BMD = Bone mineral density; SD = Standard deviation ; IQR = Interquartile range

Table 2 : Bone health measurements in children with HbA1c ≤ 7% vs HbA1c >7%

Indexes of Bone Health:	HbA1c ≤ 7%			HbA1c >7%			*P*-value
	n	median	IQR	n	median	IQR	
BHI SDS	21	-0.82	(-1.54, -0.36)	35	-0.85	(-1.74, -0.31)	0.89
TBLH Z- score	24	-1.55	(-1.80, -0.73)	42	-1.05	(-2.18, -0.30)	0.50

LS Z-score	26	-0.30	(-0.75, 0.38)	42	-0.30	(-0.9, 0.6)	0.93
TBS Z- score	24	0.25	(0.01, 0.92)	38	0.28	(-0.49, 0.94)	0.44
BHI SDS = Bone health index standard deviation score; TBLH = Total body less head; LS = Lumbar spine; TBS = Trabecular bone score; IQR = Interquartile range							

Table 3: Bone health measurements in pre-pubertal vs pubertal subjects

Indexes of Bone Health:	Pre-pubertal (N=30)				Pubertal (N=38)				*P*-value
	n	median	IQR		n	median	IQR		
BHI SDS	28	-1.11	(-1.76, -0.6)		35	-0.55	(-1.42, -0.08)		0.055
TBLH Z-score	29	-1.10	(-1.6, -0.4)		42	-1.70	(-2.1, -0.8)		0.11
LS Z-score	30	-0.30	(-0.7, 0.68)		42	-0.30	(-1.05, 0.28)		0.34
TBS Z-score	26	0.47	(0.18, 1.22)		38	-0.01	(-0.53, 0.62)		0.012
BHI SDS = Bone health index standard deviation score; TBLH = Total body less head; LS = Lumbar spine; TBS = Trabecular bone score; IQR = Interquartile range									

Table 4: Bone health measurements in children who had regular physical activity vs no regular physical activity

Indexes of Bone Health:	No physical activity (n=31)				Regular physical activity (n=37)				*P*-value
	n	median	IQR		n	median	IQR		
BHI SDS	22	-1.29	(-2.08, -0.65)		34	-0.62	(-1.34, -0.09)		0.020
TBLH Z- score	30	-1.70	(-2.3, -1.5)		36	-0.75	(-1.32, -0.3)		<0.001
LS Z-score	31	-0.50	(-1.1, 0.25)		37	-0.20	(-0.6, 0.8)		0.043
TBS Z-score	29	0.03	(-0.63, 0.51)		33	0.52	(0.13, 1.24)		0.009
BHI SDS = Bone health index standard deviation score; TBLH = Total body less head; LS = Lumbar spine; TBS = Trabecular bone score; IQR = Interquartile range									

Table 5: Multiple regression models for TBLH Z-score (R^2 =0.415, adjusted R^2 =0.376, F(4,61)=10.81, p<0.001.), TBS Z-score (R^2 =0.279, adjusted R^2 =0.279, F(3,57)=8.73, p<0.001.), and LS Z-score (R^2 =0.330, adjusted R^2 =0.287, F(4,62)=7.64, p<0.001.)

Outcome	Predictor	B	SE	t	*P*-value	95% CI lower	95% CI upper	Semi-partial r^2
TBLH Z-score	Disease duration	-0.141	0.045	-3.138	0.003	-0.231	-0.051	0.095
	Lean mass (g)	0.0001	0.00001	3.798	<0.001	0.00003	0.00009	0.138
LS Z-score	Disease duration	-0.134	0.040	-3.376	0.001	-0.213	-0.055	0.123
	Lean mass (g)	0.0001	0.00001	4.069	<0.001	0.00003	0.00009	0.179
TBS Z-score	Disease duration	-0.227	0.046	-4.960	<0.001	-0.319	-0.135	0.296

	Lean mass (g)	0.0001	0.00002	3.648	<0.001	0.00003	0.00009	0.160

Values are unstandardized regression coefficients (B), standard errors (SE), t-statistics, p-values, 95% confidence intervals, and squared semi-partial correlations (sr^2). sr^2 represents the unique proportion of variance in the outcome explained by each predictor after accounting for the other predictors in the model.
*Variables included in the stepwise model: Age, pubertal stage, disease duration, HbA1c, insulin delivery modality, vitamin D status, physical activity, lean mass
TBLH = Total body less head; LS = Lumbar spine; TBS = Trabecular bone score

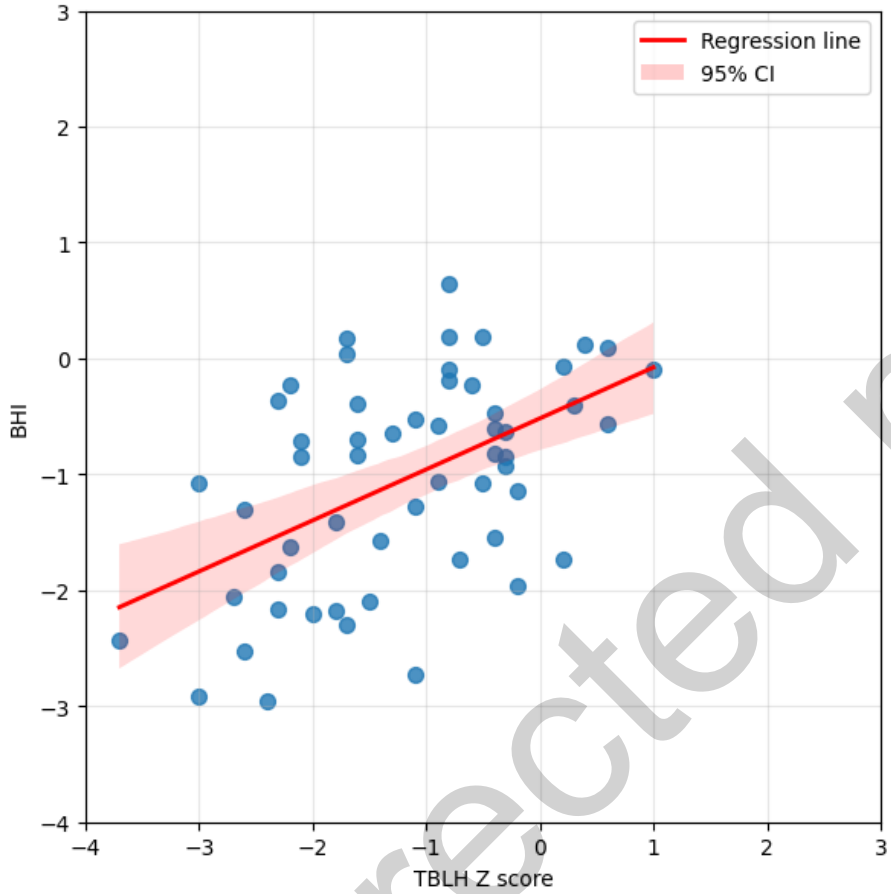

Figure 1: Correlation between BHI Z-score and TBLH Z-score
BHI = Bone health index; TBLH = Total body less head

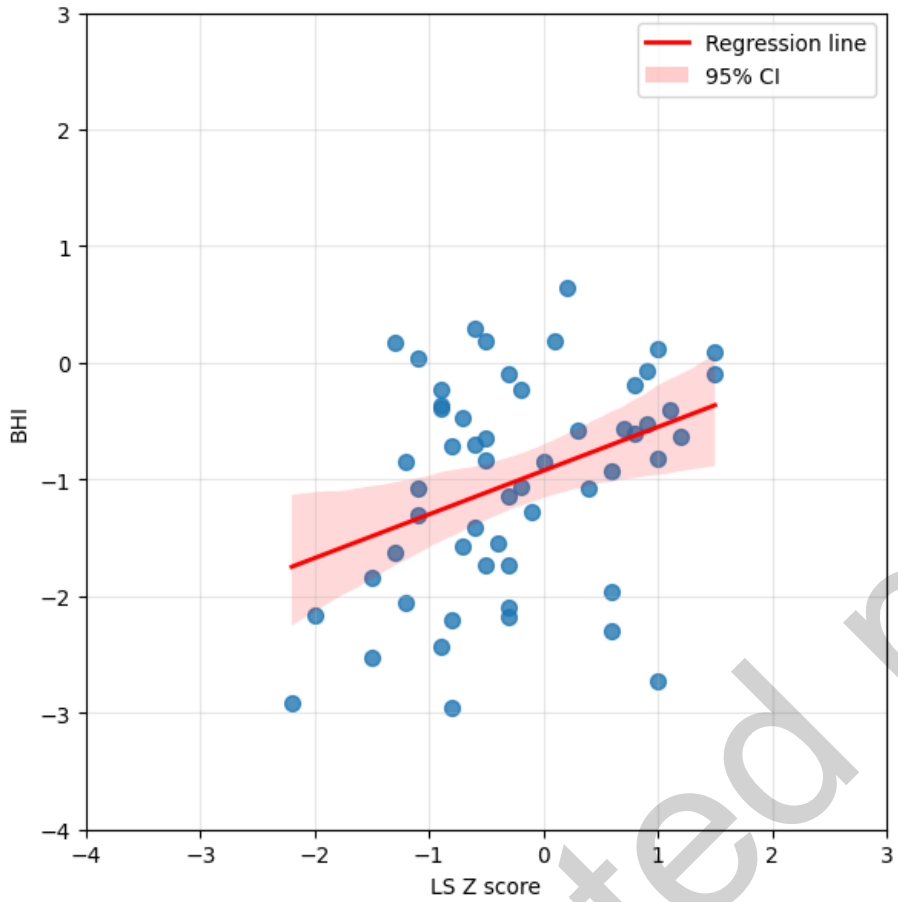

Figure 2: Correlation between BHI Z-score and LS Z-score
BHI = Bone health index; LS = Lumbar spine