http:// jpp.mums.ac.ir

Original Article (Pages: 20292-20301)

Relationship between Insulin Dosage and Metabolic Control (HbA1c) in Children and Adolescents with Type 1 Diabetes Mellitus

Victoria Chegini [1], Sonia Oveisi [2], * Fatemeh Saffari [3]

[1] Department of Pediatric Critical Care Medicine, School of Medicine, Qazvin University of Medical Sciences, Qazvin, Iran.

[2] Clinical Research Development Unit of Advanced Medicine, Qazvin University of Medical Sciences, Qazvin, Iran.

[3] Non-communicable Diseases Research Center, Research Institute for Prevention of Non-communicable Diseases, Qazvin University of Medical Sciences, Qazvin, Iran.

Abstract

Background: Insulin requirements in pediatric type 1 diabetes mellitus (T1DM) vary according to age, pubertal status, and metabolic factors; however, the relationship between insulin dose and glycemic control remains complex.

Objective: This study aimed to evaluate the association between total daily insulin dose and metabolic control in children and adolescents with T1DM.

Methods: In this cross-sectional study, 471 children and adolescents with T1DM attending an endocrine clinic were evaluated. HbA1c was measured on two separate occasions at a three-month interval. Insulin dose was recorded at each monthly visit over the three-month observation period. Associations between total daily insulin dose (U/kg/day), HbA1c, body mass index (BMI), diabetes duration, and pubertal stage were analyzed.

Results: The mean age was 12.37 ± 3.95 years (range, 2.25–17.8 years), and the mean duration of diabetes was 4.69 ± 3.36 years. A significant positive correlation was observed between total daily insulin dose and HbA1c ($r = 0.18$, $p < 0.001$). Insulin requirements increased significantly across pubertal stages ($p < 0.001$). BMI showed a positive correlation with insulin dose among male participants ($r = 0.20$, $p = 0.008$). In multivariable regression analysis, total insulin dose was significantly associated with HbA1c ($\beta = 0.74$, 95% CI: 0.22–1.26, $p = 0.006$), whereas age, sex, diabetes duration, and pubertal stage were not significant predictors.

Conclusion: Higher insulin doses were associated with poorer glycemic control, likely reflecting compensatory dose escalation rather than improved metabolic regulation. Pubertal status and BMI significantly influenced insulin requirements in children and adolescents with T1DM.

Key Words: Body mass index; Insulin; Glycated hemoglobin; Puberty; Microalbuminuria; Type 1 diabetes mellitus.

* Please cite this article as: Chegini V, Oveisi S, Saffari F. Relationship between Insulin Dosage and Metabolic Control (HbA1c) in Children and Adolescents with Type 1 Diabetes Mellitus. J Ped Perspect 2026; 14 (8):20292-20301. **DOI: 10.22038/jpp.2026.96670.5687**

****Corresponding Author:***

Fatemeh Saffari; Professor of Pediatric Endocrinology. Non-communicable Diseases Research Center, Research Institute for Prevention of Non-communicable Diseases, Qazvin University of Medical Sciences, Qazvin, Iran. Email:drfa_saffari@yahoo.com

1- INTRODUCTION

The global incidence of type 1 diabetes in children and adolescents continues to rise, with an estimated 108,300 new cases diagnosed annually worldwide in those under 15 years of age, according to the International Diabetes Federation (IDF) Diabetes Atlas, 10th edition (1). Type 1 diabetes mellitus (T1DM) is an autoimmune disorder characterized by pancreatic β-cell destruction, resulting in absolute insulin deficiency (2, 3).

Insulin therapy is the cornerstone of T1DM management. Contemporary guidelines continue to emphasize that tighter glucose control—balanced against the risk of hypoglycemia—can delay the onset and progression of chronic complications, improve cardiovascular risk profiles, and enhance long-term health outcomes in youth with type 1 diabetes (4, 5).

Emerging evidence indicates that insulin resistance may coexist in T1DM, contributing to increased insulin requirements and adverse metabolic outcomes (6). Acute complications, such as severe hypoglycemia and diabetic ketoacidosis, present significant morbidity risks and can occasionally be fatal in children and adolescents, despite being theoretically preventable (7).

Recent research highlights how individual differences in insulin sensitivity, body composition, pubertal status, and metabolic demands influence total insulin requirements at diagnosis and over time (8–10). Physiologic insulin requirements increase significantly during puberty due to transient insulin resistance mediated by hormonal changes (11).

Despite advances in insulin analogues and glucose-monitoring technologies, achieving optimal glycemic control in children and adolescents remains challenging. Achieving near-normal blood glucose levels is more difficult in adolescents than in adults (11–13). Younger children are particularly vulnerable to glycemic variability due to unpredictable eating patterns and limited symptom recognition, whereas adolescents face additional risks from psychological distress, risk-taking behaviors, and insulin omission (14).

Given these complexities, understanding the determinants of insulin dosage and their relationship with HbA1c is essential. This study aimed to evaluate the association between insulin dose and metabolic control in children and adolescents with T1DM.

2- MATERIALS AND METHODS

2-1. Study Design and Participants

This cross-sectional study included children and adolescents with T1DM who attended the Children's Hospital Health Care Center and were referred to the academic Endocrine Clinic of Qazvin Province, Iran, from 2023 to 2025. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Qazvin University of Medical Sciences (IR.QUMS.REC.1403.431).

Inclusion criteria were: 1) confirmed diagnosis of T1DM; 2) age <18 years; and 3) availability of complete medical records. Exclusion criteria included: 1) infectious diseases or other medical conditions potentially affecting glycemic control; 2) relocation outside Qazvin Province during the study period; 3) lack of parental or guardian consent; and 4) an episode of diabetic ketoacidosis or severe hypoglycemia.

A total of 500 patients with T1DM were initially screened; 29 were excluded for not meeting the inclusion criteria or for

meeting an exclusion criterion, yielding a final analytic sample of 471 patients.

Pubertal stage was assessed by a physician using Tanner criteria. Prepuberty was defined as Tanner stage 1, puberty as Tanner stages 2–4, and postpuberty as Tanner stage 5. Comorbid autoimmune and associated conditions were screened in all 471 participants.

Data were collected using a researcher-developed checklist. Variables included:

- Demographic characteristics: age, sex, and place of residence.
- Anthropometric measurements: weight, height, and body mass index (BMI).
- Clinical parameters: total daily insulin dose (units/kg/day), HbA1c level, urinary protein excretion, pubertal stage, and presence of autoimmune diseases.

All patients in this study population were treated with multiple daily injections (MDI); none were managed with continuous subcutaneous insulin infusion (CSII/insulin pump) during the study period. Basal insulin was administered as insulin glargine, and bolus (rapid-acting) insulin was administered as insulin aspart.

Comorbid autoimmune and associated conditions (celiac disease, Hashimoto thyroiditis, hypothyroidism, alopecia, vitiligo, juvenile rheumatoid arthritis) were screened for according to standard pediatric diabetes screening guidelines. Celiac disease was screened for using serologic testing (tissue transglutaminase IgA antibodies), with definitive diagnosis confirmed by duodenal biopsy, consistent with contemporary ESPGHAN diagnostic practice (15). Hashimoto thyroiditis was diagnosed based on elevated thyroid autoantibody levels (anti-thyroid peroxidase and/or anti-thyroglobulin antibodies), per standard pediatric diabetes care guidelines (16).

HbA1c was measured on two occasions at a three-month interval, and the mean of these values was used in analyses. Insulin dose was recorded at each monthly visit over the three-month observation period, and the mean total daily insulin dose (U/kg/day) was calculated. Basal insulin was approximately 50% of total daily insulin dose, with the remainder administered as rapid-acting bolus insulin for carbohydrate coverage and correction, followed by individualized titration according to glycemic response.

2-2. Statistical Analysis

Data were analyzed using SPSS version 26. Continuous variables are presented as mean ± standard deviation (SD), and categorical variables as frequency (percentage). Pearson correlation coefficients were used to evaluate associations between continuous variables. One-way analysis of variance (ANOVA) was used to compare clinical variables across pubertal stages, and the chi-square test was used for categorical variables. A two-sided p-value <0.05 was considered statistically significant.

All 471 included participants had complete data for HbA1c, total daily insulin dose, age, sex, diabetes duration, and pubertal stage. Therefore, complete-case analysis was performed; no imputation was applied.

A multivariable linear regression model was fitted with HbA1c as the dependent variable and total daily insulin dose (U/kg/day), age, sex, diabetes duration, and pubertal stage as independent variables. The model estimated the association of insulin dose with HbA1c after adjustment for these prespecified covariates. Given the cross-sectional design, all findings were interpreted as associations rather than causal effects.

3- RESULTS

A total of 471 children and adolescents with T1DM were included, of

whom 58.0% were girls. Mean age was 12.37 ± 3.95 years (range, 2.25–17.8 years), and mean diabetes duration was 4.69 ± 3.36 years (Table 1). The most frequent comorbid conditions were Hashimoto thyroiditis (20.0%) and hypothyroidism (15.9%), whereas celiac disease was present in 9.3% of participants. Microalbuminuria was observed in 76 participants (16.1%), and macroalbuminuria in one participant (0.2%) (Table 2).

The overall mean HbA1c was 8.71 ± 2.03%, and the mean total daily insulin dose was 1.22 ± 0.40 U/kg/day (57.32 ± 30.63 units/day), with a basal-to-bolus ratio of approximately 50:50 (Table 3).

Table 1. Demographic characteristics of the study population

Variable	Mean ± SD	Range (Min–Max)
Age (years)	12.37 ± 3.95	2.25–17.8
BMI (kg/m²)	19.99 ± 3.90	13.22–34.68
Height (cm)	147.65 ± 24.19	86–190
Weight (kg)	45.65 ± 10.18	10–101
Age at menarche (years)	12.48 ± 1.00	9–15.5
Age at diagnosis (years)	7.45 ± 3.46	0–17

Note: Data are presented as mean ± SD. Age at menarche was recorded only for girls who had reached menarche (n = 156). Girls comprised 58.0% of the study population.
Abbreviation: BMI: body mass index.

Table-2. Frequency of comorbid conditions and diabetes-related complications.

Condition	n (%)
Celiac disease	44 (9.3)
Hashimoto thyroiditis	94 (20.0)
Hypothyroidism	75 (15.9)
Alopecia	2 (0.4)
Vitiligo	2 (0.4)
Juvenile rheumatoid arthritis	2 (0.4)
Microalbuminuria	76 (16.1)
Macroalbuminuria	1 (0.2)
Eye complications	0 (0.0)

Note: Microalbuminuria was defined as urinary albumin excretion of 30–300 mg/24 hours; macroalbuminuria as >300 mg/24 hours. Some patients had more than one comorbid condition.

Table-3. Glycemic indices and insulin dose parameters.

Parameter	Mean ± SD	Range (Min–Max)
HbA1c (%)	8.71 ± 2.03	4.08–15.8
Fasting blood glucose (mg/dL)	181.65 ± 90.34	45–593
Basal insulin (units/day)	28.74 ± 15.96	5–105
Pre-breakfast bolus insulin (units/day)	8.10 ± 5.54	0–38
Pre-lunch bolus insulin (units/day)	10.05 ± 6.82	1–42
Pre-dinner bolus insulin (units/day)	9.51 ± 6.74	1–40
Basal insulin (U/kg/day)	0.62 ± 0.22	0.14–1.56
Rapid-acting insulin (U/kg/day)	0.56 ± 0.27	0–2.20
Total daily insulin dose (units/day)	57.32 ± 30.63	10–210
Total daily insulin dose (U/kg/day)	1.22 ± 0.40	0.24–3.55

Note: Data are presented as mean ± standard deviation.
Prandial insulin refers to rapid-acting insulin analogue doses administered before meals.
Abbreviations: HbA1c: glycosylated hemoglobin; **FBS:** fasting blood sugar.

The mean pre-breakfast, pre-lunch, and pre-dinner prandial insulin doses were 8.10 ± 5.54, 10.05 ± 6.82, and 9.51 ± 6.74 units/day, respectively. Insulin requirements increased significantly with advancing puberty, rising from 1.03 ± 0.30 U/kg/day in prepubertal children to 1.30 ± 0.42 U/kg/day in postpubertal adolescents ($p < 0.001$). Despite this dose escalation, HbA1c levels did not differ significantly across pubertal stages ($p = 0.759$), suggesting that appropriately increased insulin dosing may offset the expected metabolic deterioration during puberty (Table 4).

There was a significant positive correlation between total daily insulin dose and HbA1c ($r = 0.18$, $p < 0.001$). In males, BMI and diabetes duration were positively correlated with insulin dose ($r = 0.20$, $p = 0.008$ and $r = 0.25$, $p = 0.001$, respectively), whereas no such associations were observed in females. In multivariable regression analysis adjusted for age, sex, diabetes duration, and pubertal stage, total daily insulin dose remained independently associated with HbA1c ($\beta = 0.74$, 95% CI: 0.22–1.26, $p = 0.006$), while the other covariates were not significant predictors. The overall model explained only 2.4% of the variance in HbA1c ($R^2 = 0.024$) (Table 5).

Table-4. Clinical variables and insulin dosage across pubertal stages.

Variable	Pre-Puberty	During Puberty	Post-Puberty	F	Sig.
Total Insulin	26.93 ± 10.64	51.68 ± 16.78	75.97 ± 28.51	182.33	<0.001
Total Insulin/kg	1.03 ± 0.30	1.27 ± 0.41	1.30 ± 0.42	18.06	<0.001
HbA1c	8.62 ± 1.79	8.83 ± 2.40	8.70 ± 1.99	0.27	0.759
FBS	159.39 ± 78.08	195.82 ± 94.75	188.31 ± 93.02	5.66	0.004
Weight	25.96 ± 6.23	41.98 ± 11.16	58.74 ± 13.51	358.57	<0.001
Basal Insulin/kg	0.55 ± 0.15	0.63 ± 0.20	0.66 ± 0.25	11.26	<0.001
Rapid Insulin/kg	0.48 ± 0.20	0.62 ± 0.28	0.64 ± 0.29	12.39	<0.001

Note: Data are presented as mean ± standard deviation.
Pre-puberty: Tanner stage 1; **During puberty:** Tanner stages 2–4; **Post-puberty:** Tanner stage 5.
Abbreviations: FBS: fasting blood sugar; **HbA1c:** glycosylated hemoglobin.
ANOVA was used for comparisons across groups. Bold p-values indicate statistical significance ($p < 0.05$).

Table-5. Multivariable linear regression analysis for factors associated with HbA1c.

Predictor	β	95% CI	p-value
Total Insulin Dose (U/kg/day)	0.74	0.22 to 1.26	0.006
Age (years)	−0.01	−0.18 to 0.12	0.895
Sex (Female vs. Male)	0.07	−0.45 to 0.54	0.747
Diabetes Duration (years)	−0.01	−0.08 to 0.07	0.874
Pubertal Stage: During- vs. Pre-puberty	0.12	−0.63 to 0.88	0.746
Pubertal Stage: Post- vs. Pre-puberty	−0.05	−1.10 to 1.00	0.925

Note: Dependent variable: HbA1c (%). **β:** standardized regression coefficient; **CI:** confidence interval.
Model $R^2 = 0.024$. Bold p-value indicates statistical significance ($p < 0.05$).

4- DISCUSSION

This study evaluated the relationship between insulin dosage and metabolic control in children and adolescents with T1DM. The principal findings were: 1) a significant positive correlation between total daily insulin dose and HbA1c; 2) a positive association between BMI and insulin dose in males only; 3) increasing insulin requirements with advancing puberty; and 4) a 16.1% prevalence of microalbuminuria.

In our study, a significant positive correlation was observed between total daily insulin dose and HbA1c ($r = 0.18$, $p < 0.001$), indicating that children requiring

higher insulin doses had poorer glycemic control. This finding is consistent with the report by Jia et al. (17), who demonstrated that total daily insulin dose in pediatric patients is strongly influenced by demographic and metabolic factors and does not independently predict optimal glycemic control. Similarly, another study highlighted that intensification of insulin therapy often fails to achieve substantial HbA1c improvement, underscoring the persistent challenge of achieving metabolic targets despite higher insulin doses (18). Notably, the mean HbA1c in our cohort (8.71 ± 2.03%) exceeded the glycemic target of ≤7.0% recommended for children and adolescents with access to standard therapy (19), underscoring that suboptimal control, rather than insulin dose itself, may be driving the observed association. Achieving optimal glycemic control during adolescence remains particularly challenging despite recent technological advances, as highlighted by the ISPAD 2022 guidelines on diabetes in adolescence (20).

Regarding BMI, our study demonstrated that higher BMI was associated with increased total daily insulin dose in males ($r = 0.20$, $p = 0.008$). Similarly, Jia et al. reported an association between higher BMI and increased insulin requirements in children and adolescents with diabetes (17). This finding is consistent with the concept of insulin resistance in type 1 diabetes, particularly in the context of excess adiposity (6,7,9). Sex-specific differences may reflect hormonal influences and body composition variability, suggesting that increased adiposity contributes to higher insulin demand beyond autoimmune β-cell failure alone.

In our study, the prevalence of microalbuminuria was 16.1%, which is relatively modest and may reflect the young age of participants (mean age 12.37 ± 3.95 years) and relatively short duration of diabetes (mean 4.69 ± 3.36 years). Previous pediatric studies report microalbuminuria in approximately 10–20% of children and adolescents with type 1 diabetes, particularly with longer disease duration and suboptimal glycemic control (21). This aligns with our findings and supports the concept that early renal involvement is strongly influenced by cumulative metabolic exposure.

Our findings are consistent with those of Lešović et al., who demonstrated that insulin requirements increase markedly after the age of 10 years and peak during puberty, particularly among girls. In their cohort, approximately 70% of pubertal adolescents required more than 1 U/kg/day of insulin, and insulin doses in girls reached up to 1.8 U/kg/day. Importantly, the authors reported that increasing insulin requirements were accompanied by deterioration in metabolic control, which is in agreement with our findings showing an association between higher insulin doses and elevated HbA1c levels (22). The abrupt rise in insulin dose per kilogram from the pre-pubertal to the pubertal group in Table 4 (0.55 ± 0.15 to 0.63 ± 0.20 U/kg/day for basal insulin, and 1.03 ± 0.30 to 1.27 ± 0.41 U/kg/day for total insulin) is consistent with the classic physiologic literature on puberty-associated insulin resistance. Using hyperinsulinemic-euglycemic clamp studies, Amiel et al. demonstrated that insulin-mediated glucose disposal falls by roughly 30% at the peak of puberty compared with prepubertal or adult values, an effect attributable to the marked rise in growth hormone secretion and its downstream stimulation of IGF-1 and counter-regulatory lipolysis during Tanner stages II–IV (23). Hong et al. subsequently confirmed, in a larger pediatric clamp cohort, that insulin sensitivity declines progressively across pubertal stages before

recovering in late puberty, paralleling the trajectory of insulin dose observed in our study (24). Because growth hormone secretion, and therefore insulin resistance, peaks in mid-to-late puberty and only partially resolves after pubertal completion, this mechanism plausibly explains why total insulin dose per kilogram continued to rise, rather than plateau, between our pubertal and post-pubertal groups.

The observed basal-to-bolus insulin ratio in our cohort is also noteworthy. Standard pediatric dosing guidance recommends an initial split of approximately 50% of the total daily dose as basal (long-acting) insulin and 50% as bolus (rapid-acting) insulin, with subsequent individualized titration (25). In our cohort, mean basal insulin accounted for approximately 50% of the mean total daily dose (28.74 units of 57.32 units/day), closely matching this canonical 50:50 basal-bolus split despite the wide range of individual insulin requirements across age and pubertal stage. This suggests that, at a population level, clinicians in our setting adhered closely to standard basal-bolus proportioning even as the absolute total daily dose was titrated upward with advancing puberty (Table 4), and that the rise in insulin requirement during puberty was distributed proportionately between basal and bolus components rather than being driven disproportionately by either one.

HbA1c remains an important measure of chronic glycemia but does not fully characterize glycemic exposure. While current ADA guidelines emphasize individualized insulin titration, our findings suggest that dose escalation alone may not ensure improved glycemic outcomes. Our results may also be explained by the contribution of insulin resistance in type 1 diabetes, which can increase insulin requirements without proportional metabolic benefit. Recently, studies have highlighted that HbA1c has limitations as a surrogate for overall glycemic control and its relationship with insulin dose; metrics derived from continuous glucose monitoring may provide additional insight (6, 26). These findings imply that insulin dose and HbA1c relationships should be interpreted cautiously, since metabolic risk is influenced by multiple dynamic factors beyond total daily insulin dose (27).

Importantly, our study adds to the existing literature by specifically quantifying the relationship between insulin dose per kilogram and HbA1c in a real-world cross-sectional pediatric population, thereby providing further evidence that higher insulin requirements may serve as a marker of metabolic complexity rather than effective glycemic control.

This study has limitations. Its cross-sectional design precludes causal inference. Data on diet, physical activity, insulin adherence, injection technique, and continuous glucose monitoring metrics were unavailable. Because puberty is a recognized confounder of insulin requirement, the simple bivariate correlations reported above do not by themselves isolate the independent association of insulin dose with HbA1c; however, this association remained significant in the multivariable-adjusted model reported above ($\beta = 0.74$, $p = 0.006$), which strengthens confidence that the association is not solely attributable to age, sex, diabetes duration, or pubertal stage. Future studies should incorporate these variables to provide a more comprehensive understanding of the factors influencing glycemic control and long-term outcomes in T1DM.

5- CONCLUSION

Higher total daily insulin requirements were associated with higher HbA1c in children and adolescents with T1DM. This association may reflect

metabolic complexity rather than treatment effectiveness. Insulin dose alone should not be considered a reliable indicator of metabolic adequacy; pubertal status, BMI, insulin sensitivity, and complementary glycemic metrics should also be considered.

Further research is warranted to explore the underlying mechanisms driving the observed gender differences and to identify novel therapeutic targets for improving glycemic control and preventing long-term complications in children and adolescents with T1DM.

6- ACKNOWLEDGMENT

We thank the Clinical Research Development Unit of Qods children's Hospital for assistance with this research project.

7- FUNDING

No public or commercial funding was received for this work.

8- CONFLICT OF INTEREST

The authors declare no conflicts of interest.

9- REFERENCES

1. Ogle GD, James S, Dabelea D, Pihoker C, Svennson J, Maniam J, et al. Global estimates of incidence of type 1 diabetes in children and adolescents: Results from the International Diabetes Federation Atlas. Diabetes research and clinical practice. 2022 Jan 1;183:109083.

2. Atkinson MA, Eisenbarth GS, Michels AW. Type 1 diabetes. The lancet. 2014 Jan 4;383(9911):69-82.

3. DiMeglio LA, Evans-Molina C, Oram RA. Type 1 diabetes. The Lancet. 2018 Jun 16;391(10138):2449-62.

4. American Diabetes Association Professional Practice Committee: Draznin B, Aroda VR, Bakris G, Benson G, Brown FM. Freeman R, et al. Facilitating Behavior Change and Well-being to Improve Health Outcomes: Standards of Medical Care in Diabetes-2022. Diabetes Care. 2022;45(Suppl 1):S60-82.

5. Hirsch IB, Sherr JL, Hood KK. Connecting the dots: validation of time in range metrics with microvascular outcomes. Diabetes Care. 2019 Feb 12;42(3):345.

6. Apostolopoulou M, Lambadiari V, Roden M, Dimitriadis GD. Insulin resistance in type 1 diabetes: pathophysiological, clinical, and therapeutic relevance. Endocrine Reviews. 2025 Jun;46(3):317-48.

7. Rasmussen VF, Vestergaard ET, Schwandt A, Beltrand J, Rami-Merhar B, O'Riordan SM, et al. Proportion of basal to total insulin dose is associated with metabolic control, body mass index, and treatment modality in children with type 1 diabetes—a cross-sectional study with data from the International SWEET registry. The Journal of Pediatrics. 2019 Dec 1;215:216-22.

8. Beckers M, Polle O, Gallo P, Bernard N, Bugli C, Lysy PA. Determinants and Characteristics of Insulin Dose Requirements in Children and Adolescents with New-Onset Type 1 Diabetes: Insights from the INSENODIAB Study. Journal of Diabetes Research. 2023;2023(1):5568663.

9. Karamanakos G, Kokkinos A, Dalamaga M, Liatis S. Highlighting the role of obesity and insulin resistance in type 1 diabetes and its associated cardiometabolic complications. Current obesity reports. 2022 Sep;11(3):180-202.

10. Wiegand S, Raile K, Reinehr T, Hofer S, Näke A, Rabl W, et al. Daily insulin requirement of children and adolescents with type 1 diabetes: effect of age, gender, body mass index and mode of therapy.

European journal of endocrinology. 2008 Apr;158(4):543-9.

11. Chiang JL, Maahs DM, Garvey KC, Hood KK, Laffel LM, Weinzimer SA, et al. Type 1 diabetes in children and adolescents: a position statement by the American Diabetes Association. Diabetes care. 2018 Aug 13;41(9):2026.

12. Rica I, Mingorance A, Gómez-Gila AL, Clemente M, González I, Caimari M, et al. Achievement of metabolic control among children and adolescents with type 1 diabetes in Spain. Acta diabetologica. 2017 Jul;54(7):677-83.

13. Cree-Green M, Stuppy JJ, Thurston J, Bergman BC, Coe GV, Baumgartner AD, et al. Youth with type 1 diabetes have adipose, hepatic, and peripheral insulin resistance. The Journal of Clinical Endocrinology & Metabolism. 2018 Oct;103(10):3647-57.

14. Lan YY, Kovinthapillai R, Kędzia A, Niechciał E. Age-based challenges to type 1 diabetes management in the pediatric population. Frontiers in pediatrics. 2024 Sep 2;12:1434276.

15. Litwin A, Le Thi TG, El-Lababidi N, Kindermann A, Pancheva R, Gerasimidis K, et al. Celiac disease diagnosis in clinical practice: ESPGHAN quality of care survey from 129 pediatric hospitals across 28 countries. Journal of pediatric gastroenterology and nutrition. 2025 Sep;81(3):606-17.

16. Fröhlich-Reiterer E, Elbarbary NS, Simmons K, Buckingham B, Humayun KN, Johannsen J, et al. ISPAD Clinical Practice Consensus Guidelines 2022: Other complications and associated conditions in children and adolescents with type 1 diabetes. Pediatric diabetes. 2022 Dec 1;23(8):1451.

17. Jia Q, Zhang Y, Zhang B, An X. Reassessing type 2 diabetes in adolescents and its management strategies based on insulin resistance. Frontiers in endocrinology. 2024 Jun 19;15:1377918.

18. Mazzotta FA, Lucaccini Paoli L, Rizzi A, Tartaglione L, Leo ML, Popolla V, et al. Unmet needs in the treatment of type 1 diabetes: why is it so difficult to achieve an improvement in metabolic control?. Nutrition & Diabetes. 2024 Aug 2;14(1):58.

19. de Bock M, Codner E, Craig ME, Huynh T, Maahs DM, Mahmud FH, et al. ISPAD Clinical Practice Consensus Guidelines 2022: Glycemic targets and glucose monitoring for children, adolescents, and young people with diabetes. Pediatric diabetes. 2022 Dec 20;23(8):1270.

20. Gregory JW, Cameron FJ, Joshi K, Eiswirth M, Garrett C, Garvey K, et al. ISPAD clinical practice consensus guidelines 2022: diabetes in adolescence. Pediatric diabetes. 2022 Oct 17;23(7):857.

21. Mohammed O, Alemayehu E, Bisetegn H, Debash H, Gedefie A, Ebrahim H, et al. Prevalence of microalbuminuria among diabetes patients in africa: a systematic review and meta-analysis. Diabetes, Metabolic Syndrome and Obesity. 2023 Dec 31:2089-103.

22. Lešović S. Effect of age, sex and the insulin regiment on insulin needs in children and adolescents suffering from diabetes mellitus type 1. Medicinski glasnik Instituta za štitastu žlezdu i metabolizam" Zlatibor". 2016 Jan 1.

23. Amiel SA, Sherwin RS, Simonson DC, Lauritano AA, Tamborlane WV. Impaired insulin action in puberty. New England Journal of Medicine. 1986 Jul 24;315(4):215-9.

24. Hong CP. Insulin resistance during puberty: results from clamp studies in 357 children. Diabetes. 1999 Jan 1.

25. Kliegman RM, St. Geme JW III, eds. Nelson Textbook of Pediatrics. 22nd ed.

Philadelphia: Elsevier; 2025. Chapter 629, Type 1 Diabetes Mellitus.

26. Beck RW, Bergenstal RM, Cheng P, Kollman C, Carlson AL, Johnson ML, et al. The relationships between time in range, hyperglycemia metrics, and HbA1c. Journal of diabetes science and technology. 2019 Jul;13(4):614-26.

27. He BB, Liu ZZ, Xu RY, Fan L, Guo R, Deng C, et al. Glycated hemoglobin is not enough: The role of glycemia risk index for glycemic control assessment in type 1 diabetes. World Journal of Diabetes. 2025 Jun 15;16(6):104024.