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Glycaemic control and factors affecting it in type 1 diabetes in children: experience from a tertiary care centre in India

Kontrola glikemii i czynniki na nią wpływające w cukrzycy typu 1 u dzieci: doświadczenie z ośrodka trzeciego stopnia referencyjności w Indiach

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Abstract

Introduction: Optimal glycaemic control is essential for the prevention of future micro- and macrovascular complications in type 1 diabetes (T1D). The type of insulin, the type of insulin delivery device, the caregiver's knowledge, the patient's age, duration of diabetes, and self-monitoring of blood glucose affect glycaemic control in type 1 diabetes. In the present study, we analysed glycaemic control and factors affecting it at a tertiary care centre in northern India.

Material and methods: A retrospective review of records of patients registered between 2015 and 2018 was done. The data on demographic and disease-related factors were collected from the records. The different groups were compared with the t-test, one-way ANOVA, or Kruskal-Wallis test.

Results: The mean age at the time of evaluation was 10.43 ±4.04 years (2–21 years), and the mean disease duration was 46.61 ±28.49 months (16–141 months). Most of the patients were prepubertal and using a basal-bolus regimen. The mean glycated haemoglobin (HbA1c) was 7.96 ±1.46%, but only 24% had HbA_{1c} below the International Society of Paediatric and Adolescent Diabetes (ISPAD) recommended desirable level of below 7%. Forty-six patients suffered one or more micro-macrovascular complications, and dyslipidaemia was the most common complication. Children with a longer duration of disease (8.39 ±1.42% vs. 7.59 ±1.65%), an episode of DKA (diabetes ketoacidosis) within a year of evaluation (9.19 ±2.54% vs. 7.93 ±1.39%), lower maternal (8.22 ±1.37% vs. 7.56 ±1.45%) and paternal education (8.26 ±1.67% vs. 7.78 ±1.30%), and hyperthyroid state (9.43 ±2.28% vs. 7.91 ±1.45%) had higher HbA_{1c}.

Conclusions: Better diabetes education focusing on parents with lower education strata and children with longer disease duration and poor compliance can help improve glycaemic control in developing countries like India.

Key words:
type 1 diabetes, glycaemic control, glycated haemoglobin (HbA_{1c}), education.

Introduction

The famous Diabetes Control and Complication Trial (DCCT) unequivocally demonstrated the importance of prolonged reasonable glycaemic control to reduce the risk of microvascular and macrovascular complications in patients with type 1 diabetes [1]. According to the International Diabetes Federation (IDF) atlas, India has the highest number of children and adolescents living with diabetes in the age group 0–19 years (229,400), and 24,000 new cases are recognised in this pool annually [2]. Besides several management tools and diabetes education advancements, glycaemic control in a large population remains suboptimal [3]. Poor glycaemic control in the early years of disease adversely affects neurodevelopment and raises the risk for long-term complications [1, 4]. Standard of care, patient's age, disease duration, type of insulin, insulin delivery method, and personal and social factors could affect glycaemic control in paediatric TID [5]. Identifying and correcting modifiable factors will improve the delivery of diabetes care and glycaemic control. This study assessed glycaemic control and factors affecting it at our tertiary care hospital in Northern India.

Material and methods

This was a retrospective study of T1D children attending a tertiary care hospital in Northwest India between 2015 and 2018. The patients who had a follow-up of at least one year after registration in the clinic and one clinic visit in the year preceding the survey were eligible for inclusion in the study. The diagnosis of type T1D (symptoms suggestive of diabetes plus

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random plasma glucose ≥ 200 mg/dl (11.1 mmol/l) or fasting plasma glucose ≥ 126 mg/dl (7.0 mmol/l) or presenting with complications) was per ISPAD guidelines [6]. The data on age, sex, disease duration, insulin regimen, comorbidities, parental education, glycated haemoglobin (HbA_{1c}), frequency of diabetes ketoacidosis (DKA) in the last year, and severe hypoglycaemic episodes were extracted from the clinic records for the year preceding the survey. The insulin regimen is intensive if the patient receives insulin injections 3 or more times a day. The weight, height, and body mass index (BMI) Z scores were calculated according to national growth reference charts (IAP 2015) [7]. The pubertal status was assessed with Tanner staging. HbA_{1c} was assessed with the HPLC method. Glycaemic control was categorized into adequate control ($HbA_{1c} < 7.0\%$), suboptimal control ($7.0\% \leq HbA_{1c} < 9.0\%$), and poor control ($HbA_{1c} \geq 9.0\%$) groups. Dyslipidaemia was defined as fasting low-density lipoprotein (LDL) cholesterol of more than 100 mg/dl and triglyceride level greater than 170 mg/dl [8]. A severe hypoglycaemic episode was defined as a hypoglycaemic episode associated with severe cognitive impairment requiring external assistance for recovery. The parental education was categorised into illiterate, secondary, senior secondary, graduate, and postgraduate. The information on associated autoimmune diseases was also collected. The thyroid status was classified according to thyroid function test, and celiac disease was diagnosed based on duodenal biopsy. In total, 500 patients were screened during this period, and complete information was available for 281 patients. The patients were categorised and compared according to factors affecting glycaemic control such as age, sex, duration of diabetes, caregiver education, history of DKA or severe hypoglycaemic episodes in the last one year, and presence of an autoimmune condition. The continuous variables are reported as mean ±SD, and categorical variables are expressed as percentages. The normality of data was assessed with the Shapiro-Wilk test and visual inspection of the histogram. The various categories were compared with the t-test, ANOVA, and Kruskal-Wallis Test. After adjusting for other variables, multivariate and logistic regression were conducted to assess the significant factors, influencing glycaemic control. The data were analysed with IBM SPSS Statistics for Windows, Armonk, NY: IBM Corp. The departmental review board gave ethical clearance for the study.

Results

The mean age at the time of evaluation was 10.43 ±4.04 years (2–21 years), and the mean disease duration was 3.88 ±2.37 years (1.33–11.75 years). The mean height (1.04 ±1.180) and BMI Z scores (0.03 ±1.05) of the cohort were normal, but 19 patients (6.7%) were stunted (height < –2Z), and 6.8% were obese (BMI > 27 kg/m^2 adult equivalent according to IAP 2015 charts). The mean HbA_{1c} of the study cohort was 7.96 ±1.46%. Adequate control was found in 75 (24%) patients, while 159 (50.8%) had optimal and 79 (25.2%) were poorly controlled. The prevalence of hypothyroidism, hyperthyroidism, and celiac disease was 22 (7.2%), 6 (2%) and 46/263 (17.5%), respectively. Forty-six patients suffered one or more micro-macrovascular (dyslipidaemia 22, microalbuminuria 11, retinopathy 9, cataract 3, autoimmune hepatitis 1) complications, and dyslipidaemia was the most common complication. Most patients received a basal-bolus regimen with a mean insulin dose of 1.10 ±0.52 U/kg (basal 39%, bolus 61%; Table I). The mean HbA_{1c} was similar between males and females in different age groups and insulin regimens. The child's pubertal status, severe hypoglycaemic episodes, and comorbidities like hypothyroidism and celiac disease did not affect the mean HbA_{1c} values. However, the HbA_{1c} values were significantly higher in children with a longer duration of disease (8.39 ±1.42% vs. 7.59 ±1.65%, *p*-value 0.04), who had an episode of DKA within a year of evaluation (9.19 ±2.54% vs. 7.93 ±1.39% *p*-value < 0.01), and lower maternal education status (8.22 ±1.37% vs. 7.56 ±1.45%, *p*-value 0.01) and paternal education (8.26 ±1.67 vs. 7.78 ±1.30, *p*-value < 0.01) and hyperthyroid state (9.43 ±2.28 vs. 7.91 ±1.45, *p*-value 0.03; Table II) On multiple regression analysis, disease duration ($\beta = 0.39$, *p*-value = 0.007) was a significant predictor of HbA_{1c} after adjusting for age, age at diagnosis, gender, insulin regimen, and pubertal, thyroid, and celiac disease status. On multiple logistic regression analysis, the hyperthyroid status was associated with poor glycaemic control ($HbA_{1c} > 9\%$; *p*-value = 0.028, $\beta = 16.45$) after adjusting for age, gender, disease duration, insulin regimen, pubertal status, and thyroid and celiac disease status.

Discussion

Optimal glycaemic control is essential to decrease the risk of future microvascular complications in T1D. The recent multicountry study attainment of adequate glycaemic control according to guidelines is achievable in only a small proportion of patients. The SEARCH (USA) and YDR (India) registries study showed that only 45–50% of patients achieved adequate control in the USA with different insulin regimens, while the numbers dropped to 8.5–12% in the Indian registry [9]. A similar trend was observed in other countries also. The median HbA_{1c} in the cohort varied from 7.2 to 9.4%. Various factors influence diabetic control including age, gender, duration of disease, rural status, access to insurance and health care, and associated autoimmune diseases. However, the data on predictors affecting glycaemic control are scarce and variable [5, 10, 11].

Most of our patients used analogue insulins with insulin pens and had adequate control comparable to that seen in developed countries [9]. Most Indian patients are still using insulin syringes and older insulin, and the mean HbA_{1c} in these studies varied from 8.2 to 11% [9, 12, 13]. Our study participants had lower HbA_{1c} than previous Indian studies and reports from other developing countries due to better insulins and frequent blood sugar monitoring (4 times/day).

The duration of diabetes also affects glycaemic control. As the age and duration of the disease increase, the glycaemic control worsens, as shown by the recent study [10, 11]. The honeymoon phase and supervised parental care in the early years of diagnosis are factors associated with better glycaemic control in the early years after diagnosis. The present study

Table I. Clinical and demographic characteristics of the study cohort

Age (in years)	10.43 ±4.04	
Sex		
Male	163 (52%)	
Female	150 (48%)	
Age at diagnosis (years)	7.00 ±6.6	
Duration of disease (years)	3.88 ±2.37	
Parents' education	Mother (n = 304)	Father (n = 305)
Illiterate	17 (5.6%)	13 (4.3%)
Secondary	126 (41.3%)	111 (36.4%)
Senior secondary	64 (21%)	72 (23.6%)
Undergraduate	48 (15.8%)	83 (27.2%)
Postgraduate	49 (16.1%)	26 (8.5%)
Parents' occupation	Mother (n = 304)	Father (n = 297)
Govt Job	27 (8.9%)	57 (19.2%)
Pvt Job	18 (5.9%)	78 (26.3%)
Business	4 (1.3%)	66 (22.2%)
Farmer	7 (2.3%)	34 (11.4%)
Labourer		56 (18.9%)
Housewife	243(79.9%)	
Height, height Z score[#]	138 (34.4) – 0.18 (1.78), 19 stunted (10 male, 9 females)	
BMI Z core[#]	–0.06 (1.04) (6.8% obese, 19.5% overweight)	
Pubertal status		
Prepubertal	129 (41.2%)	
Pubertal	54 (17.3%)	
Post pubertal	58(18.5%)	
Not recorded	71 (22.7%)	
Insulin regimen		
Basal bolus	255 (81.5%)	
Mixed split	51 (16.3%)	
Pump	7 (2.2%)	
Insulin requirement (IU/kg/day)	1.10 ±0.52	
Basal dose (%)	38.87 ±13.79	
Bolus dose(%)	61.55 ±13.44	
Mean HbA_{1c} at diagnosis (%)	11.99 ±2.73	

Table I. Clinical and demographic characteristics of the study cohort (cont.)

Best HbA_{1c} during the year (%), range	7.15 ±1.42 (4.20–16.60)
Worst HbA_{1c} (%)	8.87 ±1.85 (5.80–16.20)
Mean HbA_{1c} (%)	7.96 ±1.46
Glycaemic control	Adequate – 75 (24%), optimal – 159 (50.8%), poor – 79 (25.2%)
Frequency of HbA_{1c} in last one year	1 (6.7%), 2 (17.8%), 3 (26.2%), 4 (40.9%)
Number of visits during last year	1 (3.8%), 2 (10.2%), 3 or more (80.2%)
DKA at presentation	17 (5.4%)
Thyroid status	
Euthyroid	271
Hypothyroid	22
Hyperthyroid	6
Celiac disease	46 (14.7%)
Microvascular and macrovascular complications	Cataract – 3, microalbuminuria – 11, autoimmune hepatitis – 1, retinopathy – 9, dyslipidaemia – 22
Severe hypoglycaemia episodes	60 (19.2%)
Serious infection	3 (1%)
Lipodystrophy	63 (20.1%)

Median (interquartile range)

showed significantly lower HbA_{1c} in the first 2 years of diagnosis. Similar results have been reported by Yazidi *et al*. [14].

The present study did not show any difference in glycaemic control in boys versus girls, but females had higher HbA_{1c}, similar to the observations in a cohort of Scottish T1D children [5]. The glycaemic control was identical in different age groups. Similar results have been reported by previous Indian field studies [3, 12]. In contrast, Noorani *et al*. reported better control in younger children due to supervised care by parents [15]. However, larger cohorts have shown poorer control in the female sex and older age groups (after 15 years of age) [10].The mother is the primary caregiver for T1D in most countries, and maternal education status is an essential determinant of glycaemic control in these children. We observed a better glycaemic control in children with mothers who had higher education, and the results were consistent with the study results of Husref *et al*. [16]. As in a previous Iranian study, we also found a positive impact on the father's education status in our cohort [17]. Our study showed that better compliance and parental education for a better understanding of diabetes and its management are more important than the insulin regimen used by the patient.

The children who suffered an episode of DKA in the year preceding the survey had higher HbA_{1c}, depicting better glycaemic control in this subgroup. Puberty is also associated with increased insulin resistance and poor glycaemic control [14]; we also found higher HbA_{1c} in pubertal children, but the difference was non-significant, probably due to the smaller sample size.

Autoimmune diseases are often associated with T1DM and usually worsen the glycaemic control in children. Hyperthyroid children in our study had significantly higher HbA_{1c} due to the metabolic effects of thyroid hormones on glucose metabolism. Celiac disease has also been reported to affect glycaemic control. Children with celiac disease had poorer control in our cohort, but the difference was non-significant [18–20].

Poor glycaemic control is associated with long-term complications. 11/69 (15.9%) and 9/67 (13.4%) of the eligible screened patients suffered from microalbuminuria and diabetic retinopathy in our cohort. This prevalence is higher than the previous recent reports. Inadequate control and possible glycaemic variability in our cohort might be responsible for these higher rates [21].

Conclusions

Parental education, disease duration, hyperthyroid state, and a DKA episode in the year preceding the survey are significant factors influencing HbA_{1c} in our study. Better diabetes education focusing on parents with lower education strata and children with longer disease duration and poor compliance can help improve glycaemic control in developing countries like India.

Table II. Comparison of the factors affecting glycaemic control in type 1 diabetes

Variable	Mean HbA_{1c} (%)	*p*-value
Age group*		0.103
0–6 years (*n* = 48)	7.78 ±1.21	
6–12 years (*n* = 139)	7.84 ±1.43	
> 12 years (*n* = 94)	8.21 ±1.59	
Duration of illness*		0.04
0–24 months (*n* = 67)	7.59 ±1.65	
25–60 months (*n* = 140)	7.90 ±1.33	
> 60 months (*n* = 74)	8.39 ±1.42	
Sex**		0.590
Male (*n* = 163)	7.91 ±1.38	
Female (*n* = 117)	8.01 ±1.57	
Thyroid status*		0.03
Euthyroid (*n* = 250)	7.91 ±1.45	
Hypothyroid (*n* = 19)	8.14 ±1.04	
Hyperthyroid (*n* = 6)	9.43 ±2.28	
Celiac status**		0.92
Yes (*n* = 44)	7.94 ±1.29	
No (*n* = 204)	7.90 ±1.41	
Insulin regimen*		0.153
Basal bolus (*n* = 231)	7.92 ±1.45	
Mixed split (*n* = 40)	8.20 ±1.56	
Insulin pump (*n* = 6)	7.86 ±1.07	

Variable	Mean HbA_{1c} (%)	*p*-value
Pubertal status at last visit#		0.13
Prepubertal (*n* = 129)	7.84 ±1.31.	
Pubertal (*n* = 54)	8.33 ±1.45	
Post pubertal (*n* = 58)	8.14 ±1.57	
Father's education**		0.008
Below secondary level (*n* = 102)	8.26 ±1.67	
Above secondary level (*n* = 179)	7.78 ±1.30	
Mother's education**		0.01
Below secondary level (*n* = 120)	8.21 ±1.45	
Above secondary level (*n* = 161)	7.76 ±1.44	
Diabetes ketoacidosis in last year**		0.007
Yes (*n* = 10)	9.19 ±2.54	
No (*n* = 267)	7.93 ±1.39	
Severe hypoglycaemia**		0.85
Yes (*n* = 46)	0.85	
No (*n* = 231)	7.97	
Visit to physician**		0.24
< 3 (*n* = 32)	8.25 ±1.76	
≥ 3 (*n* = 249)	7.92 ±1.42	

* ANOVA, ** t-test, # Kruskal-Wallis test

References

1. Diabetes Control and Complications Trial Research Group, Nathan DM, Genuth S, Lachin J, et al. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med 1993; 329: 977–86. doi: 10.1056/NEJM199309303291401.
2. IDF_Atlas_10th_Edition_2021.pdf [Internet]. [cited 2022 Apr 4]. Available from: https://diabetesatlas.org/idfawp/resource-files/2021/07/IDF_Atlas_10th_Edition_2021.pdf
3. Sudhanshu S, Nair VV, Godbole T, et al. Glycemic Control and Long-term Complications in Pediatric Onset Type 1 Diabetes Mellitus: A Single-center Experience from Northern India. Indian Pediatr 2019; 56: 191–195.
4. Liu S, Kuja-Halkola R, Larsson H, et al. Neurodevelopmental Disorders, Glycemic Control, and Diabetic Complications in Type 1 Diabetes: a Nationwide Cohort Study. J Clin Endocrinol Metab. 2021; 106: e4459–e4470. doi: 10.1210/clinem/dgab467
5. Mazarello Paes V, Barrett JK, Dunger DB, et al. Factors predicting poor glycemic control in the first two years of childhood onset type 1 diabetes in a cohort from East London, UK: Analyses using mixed effects fractional polynomial models. Pediatr Diabetes 2020; 21: 288–299. doi: 10.1111/pedi.12950.
6. Mayer-Davis EJ, Kahkoska AR, Jefferies C, et al. ISPAD Clinical Practice Consensus Guidelines 2018: Definition, epidemiology, and classification of diabetes in children and adolescents. Pediatr Diabetes 2018; 19 Suppl 27: 7–19. doi: 10.1111/pedi.12773.
7. 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: 470–476. doi: 10.4103/2230-8210.159028.
8. Donaghue KC, Marcovecchio ML, Wadwa RP, et al. ISPAD Clinical Practice Consensus Guidelines 2018: Microvascular and macrovascular complications in children and adolescents. Pediatr Diabetes 2018; 19 Suppl 27: 262–274. doi: 10.1111/pedi.12742.
9. Amutha A, Praveen PA, Hockett CW, Ong TC, Jensen ET, Isom SP, et al. Treatment regimens and glycosylated hemoglobin levels in youth with Type 1 and Type 2 diabetes: Data from SEARCH (United States) and YDR (India) registries. Pediatr Diabetes 2021; 22: 31–39. doi: 10.1111/pedi.13004.
10. Prigge R, McKnight JA, Wild SH, et al. International comparison of glycaemic control in people with type 1 diabetes: an update and extension. Diabet Med 2022; 39: e14766. doi: 10.1111/dme.14766.
11. Alsaheel AY, Alayed SI, Alotaibi YM, et al. Mean glycosylated hemoglobin in children with type 1 diabetes at King Fahad Medical City, Riyadh, Saudi Arabia. J Fam Community Med 2020; 27: 163–167. doi: 10.4103/jfcm.JFCM_173_20.
12. Mangla P, Gupta S, Chopra A, et al. Influence of Socio-Economic and Cultural Factors on Type 1 Diabetes Management: Report from a Tertiary Care Multidisciplinary Diabetes Management Center in India. Indian J Pediatr 2020; 87: 520–525. doi: 10.1007/s12098-020-03227-w.
13. Gupta S, Gupta JK, Kumar S, et al. Comprehensive Management of Type 1 Diabetes in a Marginalised Population in Northern India: a Seven Year Retrospective Review. J Diabetol 2016; 7.
14. Yazidi M, Chihaoui M, Chaker F, Rjeb O, Slimane H. Factors Predicting Glycemic Control in Type 1 Diabetic Patient. Open Med J 2016; 3: 153–158. doi: 10.2174/1874220301603010153.
15. Noorani M, Ramaiya K, Manji K. Glycaemic control in type 1 diabetes mellitus among children and adolescents in a resource limited setting in Dar es Salaam – Tanzania. BMC Endocr Disord 2016; 16: 29. doi: https://doi.org/10.1186/s12902-016-0113-y
16. Tahirovic H, Toromanovic A. Glycemic control in diabetic children: role of mother's knowledge and socioeconomic status. Eur J Pediatr 2010; 169: 961–964. doi: 10.1007/s00431-010-1156-0.
17. Baharvand P, Hormozi M. Can parents' educational level and occupation affect perceived parental support and metabolic control in adolescents with type 1 diabetes? J Educ Health Promot 2019; 8: 11. doi: 10.4103/jehp.jehp_215_18.
18. Amin R, Murphy N, Edge J, et al. A longitudinal study of the effects of a gluten-free diet on glycemic control and weight gain in subjects with type 1 diabetes and celiac disease. Diabetes Care 2002; 25: 1117–1122. doi: 10.2337/diacare.25.7.1117.
19. Andreelli F, Plotton I, Riou JP, Thivolet C. Diabetic instability and celiac disease. A frequent association to keep in mind. Diabetes Care 1998; 21: 2192–2193. doi: 10.2337/diacare.21.12.2192.
20. Krzewska A, Ben-Skowronek I. Effect of Associated Autoimmune Diseases on Type 1 Diabetes Mellitus Incidence and Metabolic Control in Children and Adolescents. BioMed Res Int 2016; 2016: 6219730. doi: 10.1155/2016/6219730.
21. Dabelea D, Sauder KA, Jensen ET, et al. Twenty years of pediatric diabetes surveillance: what do we know and why it matters. Ann N Y Acad Sci 2021; 1495: 99–120. doi: 10.1111/nyas.14573.

