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Original Research

Assessment of Clinical Factors Influencing Glucose Management Indicator and Glycated Hemoglobin Discordance in Children With Type 1 Diabetes: A 1-Year, Real-world Data Observation

Grażyna Deja PhD [a,*]; Aleksandra Brudzińska [b]; Łukasz Wybrańczyk [b]; Rafał Deja PhD [c]; Przemysława Jarosz-Chobot PhD [a]

[a] *Department of Children's Diabetology and Lifestyle Medicine, Medical University of Silesia, Katowice, Poland*

[b] *Students' Scientific Association in the Department of Children's Diabetology, Department of Children's Diabetology and Lifestyle Medicine, Medical University of Silesia, Katowice, Poland*

[c] *Department of Computer Science, WSB University, Dabrowa Gornicza, Poland*

Key Messages

- Discordances between glucose management indicator (GMI) coming from continuous glucose monitoring (CGM) report and laboratory glycated hemoglobin (A1C) still exist.
- Our 1-year study shows a greater difference is more likely to occur in individuals with a higher A1C value, longer diabetes duration, and less stable glycemic management.
- Individual discordance between A1C and GMI from 90 days of data was stable in two-thirds of patients, although with varying degrees of difference.
- Our observations can provide practical guidance during ongoing treatment evaluation.

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ABSTRACT

Objectives: Published data still highlight discordances between glucose management indicator (GMI; the parameter estimating glycated hemoglobin [A1C] from continuous glucose monitoring [CGM] reporting) and laboratory A1C, for reasons yet to be explored. In our study we aimed to identify potential clinical factors contributing to these discordances.

Methods: A retrospective study of 99 children (mean 12.92±4.03 years) was conducted using CGM devices (Dexcom G6-31, FreeStyle Libre 2-30, and Guardian 3-38). Inclusion criteria for patients were type 1 diabetes (T1D), continuous use of one type of CGM (with >70% sensor activity) over the previous year, and quarterly visits. At each visit, we collected data for age, sex, body mass index, diabetes duration, daily insulin dose, CGM report (14 of 90 days), and laboratory A1C.

Results: We confirmed linear dependency between A1C and GMI—that is, higher A1C led to more A1C–GMI differences. The A1C–GMI 90-day discordance was categorized into 4 thresholds: 48.7% at <0.25, 20.1% between 0.25 and 0.5, 22.4% between 0.5 and 0.75, and 8.7% at >0.75. Children with A1C–GMI 90 discordance <0.5% had significantly lower A1C (6.80% vs 7.59%), shorter T1D duration (<5 years), and more stable A1C (differences <0.4 between results). The analysis of participants' stability based on comparing A1C–GMI 90 discordances at subsequent follow-up visits confirmed an individual variability of <0.25 in two-thirds of participants. Other factors were not associated with the A1C–GMI discordance.

Conclusions: One-year, real-world data show that clinically significant discordances (A1C–GMI 90 >0.5%) occurred in <30% of the children. A greater difference is more likely in individuals with higher A1C, longer diabetes duration, and less stable glycemic management. Individual A1C–GMI 90 discordance was mostly stable, although with varying degrees of difference.

* Address for correspondence: Grażyna Deja PhD, Department of Children's Diabetology and Lifestyle Medicine, Medical University of Silesia, Medykow 16 Street, Katowice 40-752, Poland.
Email address: gdeja@sum.edu.pl

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Mots clés:
GMI
indicateur de gestion du glucose
MCG
systèmes de surveillance continue du glucose
HbA1c

R É S U M É

Objectifs : Les données publiées soulignent toujours des discordances entre le GMI (paramètre estimant l'hémoglobine glyquée HbA1c à partir des rapports issus de la mesure continue du glucose – MCG) et l'HbA1c mesurée en laboratoire, dont les causes restent à explorer. Cette étude visait à identifier les facteurs cliniques potentiels contribuant à ces discordances.
Méthodologie : Une étude rétrospective a été menée auprès de 99 enfants âgés de 12,92 ans (écart-type 4,03) utilisant des appareils CGM (Dexcom G6-31, Libre 2-30, Guardian 3-38). Les critères d'inclusion étaient les suivants : diabète de type 1, utilisation continue d'un type de CGM (avec une activité du capteur supérieure à 70 %) au cours de l'année écoulée, visites trimestrielles. À chaque visite, nous avons recueilli les données suivantes : âge, sexe, IMC, durée du diabète, dose quotidienne d'insuline, rapport CGM (14/90 jours) et HbA1c mesurée en laboratoire.
Résultats : Nous avons confirmé une relation linéaire entre l'HbA1c et le GMI : plus l'HbA1c était élevée, plus les différences entre l'HbA1c et le GMI étaient importantes. La discordance HbA1c-GMI sur 90 jours a été classée en quatre seuils : 48,7 % < 0,25 ; 20,1 % dans la fourchette 0,25-0,5 ; 22,4 % dans la fourchette 0,5-0,75 ; et 8,7 % > 0,75. Les enfants présentant une discordance HbA1c-GMI 90 < 0,5 % avaient un taux d'HbA1c significativement plus bas (6,80 contre 7,59 %), une durée du DT1 plus courte (< 5 ans) et un taux d'HbA1c plus stable (différences < 0,4 entre deux mesures). L'analyse de la stabilité du bilan des participants, basée sur la comparaison des discordances HbA1c-GMI 90 lors des visites de suivi ultérieures, a confirmé une variabilité individuelle < 0,25 pour deux tiers des participants. Aucun autre facteur n'était associé à la discordance HbA1c-GMI.
Conclusion : Les données en conditions réelles sur un an ont montré que des discordances cliniquement significatives (HbA1c-GMI 90 > 0,5 %) sont survenues chez moins de 30 % des enfants. Une différence plus importante est plus probable chez les personnes ayant des taux d'HbA1c plus élevées, une durée du diabète plus longue et un contrôle glycémique moins stable. La discordance individuelle HbA1c-GMI 90 tend à rester stable, bien que l'ampleur de la différence soit variable.

Introduction

Glycated hemoglobin (A1C) and the glucose management indicator (GMI) are now commonly used in people with diabetes (PwD) as the gold standard for assessing the effectiveness of therapy. GMI is a form of continuous glucose monitoring (CGM) that provides an estimation of A1C for a 3-month period using CGM data [1]. It was confirmed in large studies that >70% of sensor usage over 10 to 14 days represents a good estimate of CGM metrics for a 3-month period [1]. Thus, GMI is now recommended by an international consensus group as a useful part of CGM reporting [2] and a supplementary glucose monitoring indicator. Although it is a valuable tool when it comes to assessment in PwD, both literature data and clinical practice have shown discordances between GMI and laboratory A1C, which cannot be ignored. Unfortunately, there is not much scientific data on the potential factors influencing this discordance. Commonly known factors influencing A1C measurement and red blood cell turnover, such as anemia, hemoglobinopathies, and certain medications, may play roles in the discordance, but are too rare in everyday practice to explain the discrepancy of 0.5% to 1% reported in the literature [3,4]. As we presented in our latest literature review [5], there are clinical factors associated with A1C–GMI discordance, such as ethnic and racial genotype, adipose tissue (body mass index [BMI]), glycemic variability, age, pregnancy, and chronic kidney disease [3,5]. However, this still does not fully describe the phenomenon.

We believe that this topic is extremely important for PwD and clinicians, especially in the era of increased CGM usage. Nowadays, CGM systems are becoming the primary way of measuring glycemia, particularly in children and adolescents with type 1 diabetes (T1D), significantly improving treatment management [2]. A very important element of an individual's ongoing self-monitoring is correct interpretation of the results, along with other GMI parameters.

Unfortunately, not every potential factor influencing GMI has been properly examined. Some studies have presented interesting results, but the study cohorts were rather small or did not include children. Therefore, to expand our knowledge on this topic, we conducted our own analysis. We focussed on individual factors influencing diabetes management that are controlled in everyday clinical practice and that are easily accessible during routine visits.

We assessed age, sex, BMI, duration of diabetes, A1C values, daily insulin dose, type of CGM, and CGM metrics with the goal of identifying new clinical factors that may lead to discordances between laboratory measurements of A1C and GMI.

Methods

We conducted a retrospective study of 99 children and adolescents with T1D using 3 different CGM systems. All patients were treated in the Department of Children's Diabetology, Medical University of Silesia, Katowice, Poland, a diabetologic regional Better control in Pediatric and Adolescent diabeteS: Working to crEate CEnTers of Reference (SWEET) international reference centre.

Inclusion criteria for participants were as follows: age 2 to 18 years, a diagnosis of T1D for >1 year, continuous use of 1 type of CGM device (Dexcom G6 [DexCom, San Diego, California, United States], FreeStyle Libre 2 [Abbott Laboratories, North Chicago, Illinois, United States], or Guardian 3 [Medtronic, Minneapolis, Minnesota, United States]) over the past year of treatment, and regular visits to the outpatient clinic (every 3 to 4 months). Data were collected from March to June 2023 and covered the period of January 2022 to June 2023.

This was a real-life study; that is, we collected clinical data from routine visits of children and adolescents in the outpatient clinic, including age, sex, height, weight, duration of diabetes, daily insulin dose, sensor type, and CGM report, as well as laboratory measurement of A1C. Each study participant was assessed up to 1 year earlier to compare a wide range of clinical data with multiple CGM reports. We enrolled only individuals with ≥70% sensor activity. From among the initially researched children using CGM systems, 50% did not meet these demanding inclusion criteria (change of CGM system, no A1C results, no complete CGM reports during the past year).

The following data were selected from the CGM reports for further analysis: sensor activity, mean glycemia, glycemic variability, time in range, GMI from 14 days (GMI 14) of data, and GMI from 90 days (GMI 90) of data. GMI was calculated automatically by the appropriate system (Medtronic, DexCom, or Abbott). A1C tests were performed for all participants in a certified laboratory in our hospital using high-performance liquid chromatography. The basic characteristics of the study group are shown in Table 1. All children and adolescents were of Polish nationality, an ethnically homogeneous Caucasian race.

The absolute differences between A1C and GMI were calculated for each patient for 14 days and 90 days and for all consecutive visits, with this difference being reported as A1C–GMI discordance. The mean absolute relative differences (GMI MARDs) for 14 days and 90 days were calculated. A1C–GMI discordance was categorized according to the following thresholds: <0.25, 0.25 to 0.5, 0.5 to 0.75, and >0.75, to define the clinical relevance of these differences. Next, we analyzed whether there was an A1C–GMI discordance relationship when compared with clinical factors such as age, sex, BMI, duration of diabetes, daily insulin dose, A1C value, and parameters of CGM reports. Finally, we assessed the stability of discordance between A1C and GMI 90 over time. For each patient, we calculated the absolute difference between these 2 values at each follow-up visit, ensuring that both parameters were obtained on the same day and referred to the same analysis period. These discordance values were then grouped into 4 predefined intervals noted earlier: <0.25, 0.25 to 0.5, 0.5 to 0.75, and >0.75. Finally, we identified patients whose discordance measurements consistently fell within the same bin across all follow-up visits.

Statistics

Categorical variables are presented as number and percent and continuous variables as mean and standard deviation (SD). Verification of normality of the distribution was carried out using the Shapiro–Wilk test. Because most of the variables did not follow a normal distribution and we were interested in comparing the groups within different categories, the nonparametric chi-square test was applied in this study. $p<0.05$ was considered statistically significant. Analyses were performed using SciPy statistical libraries for Python. All charts were plotted using the Seaborn Python visualization library.

Ethics approval

This study was conducted in accordance with the Declaration of Helsinki ("Ethical Principles for Medical Research in Humans," July 9, 2018). Both the study protocol and consent procedure were approved by the institutional bioethics committees at the Medical University of Silesia, Katowice, Poland.

Results

The GMI MARD calculated for 14 and 90 days revealed high compliance with A1C laboratory results. The MARD reached 5.55 for 14-day and 5.21 for 90-day GMI analysis, respectively.

We confirmed a linear relation when we assessed dependency between the noted parameters. Moreover, we found that the higher the A1C result, the more differences between A1C and GMI (Figure 1A and B). Due to the presence of multiple measurements in the same patient, we applied mixed linear regression to avoid a within-subject correlation. The mixed linear regression analyses for both GMI 14 and GMI 90 revealed strong, statistically significant. positive associations with A1C levels. For GMI 14, each unit increase was associated with a 0.932-unit rise in A1C ($p<0.001$), whereas GMI 90 showed an even stronger relationship, with a 1.077-unit increase in A1C per unit of GMI 90 ($p<0.001$). In both models, the variance attributed to the random effect (grouping factor) was negligible, indicating that differences between groups contributed little additional variability after accounting for GMI values. These findings suggest that both GMI 14 and GMI 90 are robust predictors of A1C, with GMI 90 showing a slightly stronger association.

As shown in Table 2, A1C–GMI discordance in our study group was not very high, both overall and after taking CGM type into account. No significant differences between different types of CGM systems were observed.

As described earlier, A1C–GMI discordance was categorized into 4 thresholds according to clinical significance: <0.25, 0.25 to 0.5, 0.5 to 0.75, and >0.75. We noted relatively many consistent results: 48.7% at <0.25, 20.1% at 0.25 to 0.5, 22.4% at 0.5 to 0.75, and only 8.7% at >0.75, respectively (Table 2). The detailed analysis of clinical factors potentially influencing A1C–GMI discordance showed a significant relationship with the A1C value, duration of diabetes, and the individual's A1C stabilization during the 1-year follow-up. The same results were observed for both GMI 14 and GMI 90. We confirmed that children with an A1C–GMI 90 discordance <0.5 had significantly lower A1C: 6.80±0.49 vs 7.59±1.14 ($p<0.01$; Figure 2A). A similar trend was observed for GMI 90, which is important in clinical practice when replacing A1C with GMI without results of laboratory A1C—a lower GMI 90 may indicate lower noncompliance ($p<0.01$; Figure 2B). The duration of diabetes also had an impact on A1C–GMI 90 discordance: children living with T1D for >5 years had differences >0.5 significantly more often ($p<0.01$; Figure 2C). Moreover, the stability of A1C values (similar A1C results in subsequent measurements during the 1-year follow-up) was also important. Study participants with a difference in subsequent A1C results of <0.4% were significantly less likely to have A1C–GMI 90 discordance of >0.5 ($p<0.01$;

Table 1
Basic characteristics of patients on enrolment into the study (n=99)

	Overall (n=99)	Dexcom G6 (n=31)	FreeStyle Libre 2 (n=30)	Medtronic Guardian 3 (n=38)
Age, years, mean (SD)	12.92 (4.03)	12.71 (3.71)	15.22 (3.46)	11.28 (3.92)
Girls, n (%)	47 (47.5%)	15 (48.4%)	12 (40%)	20 (52.6%)
Boys, n (%)	52 (52.5%)	16 (51.6%)	18 (60%)	18 (47.4%)
Duration of diabetes, years, mean (SD)	4.23 (3.37)	4.46 (3.34)	5.2 (3.98)	3.2 (2.51)
BMI, mean (SD)	18.74 (3.04)	18.09 (2.65)	19.92 (2.97)	18.45 (3.22)
BMI *Z* score (girls/boys)	0.24/−0.07	0.24/−0.43	0.21/0.23	0.26/−0.03
Daily insulin dose, IU/kg (SD)	0.73 (0.23)	0.76 (0.23)	0.67 (0.28)	0.70 (0.20)
A1C%, mean (SD)	6.94 (0.65)	6.96 (0.70)	6.82 (0.61)	7.01 (0.63)
A1C, mmol/mmol, mean (SD)	52 (0.7)	53 (0.7)	51 (0.6)	53 (0.6)

A1C, glycated hemoglobin; *BMI*, body mass index; *SD*, standard deviation.

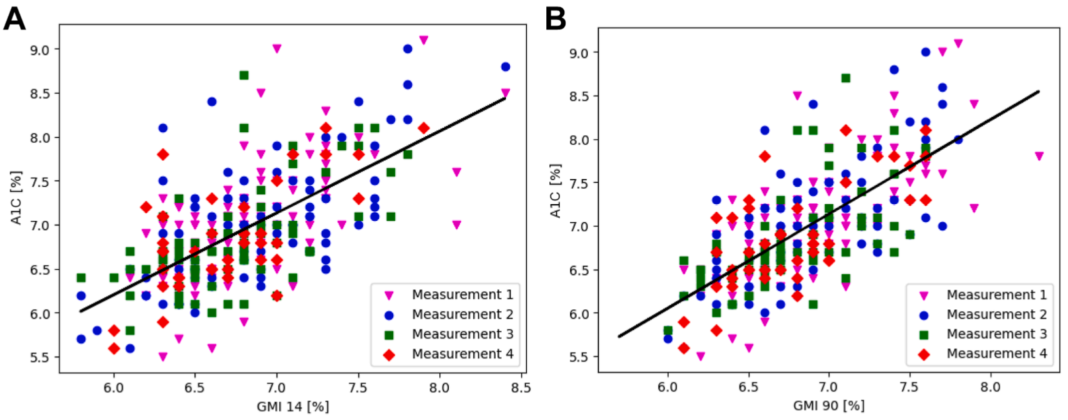

Figure 1. Linear regression between glucose management indicator (GMI) 14 days and glycated hemoglobin (A) and between GMI 90 days and glycated hemoglobin (B) (n=308). The results from subsequent visits are marked in different colors. *A1C*, glycated hemoglobin.

Figure 2D). The other clinical factors assessed, including sex, age, BMI, daily insulin dose, and CGM parameters, were not associated with A1C–GMI 90 discordance.

A unique result of our analysis came from assessing the stability of discordance between A1C and GMI 90 over time. As described in the Methods section, for each patient we compared the absolute difference between these 2 values at different visits. The analysis of individual participants' stability, based on comparing A1C–GMI 90 discordances at subsequent follow-up visits, confirmed a relatively low variability in the results in two-thirds of the participants. We observed consistent discordances in 49% of children with values <0.25, in 6% of those in the range 0.25 to 0.5, in 8% in the range 0.5 to 0.75, in 6% of those with values >0.75, and no consistency in 31% of children (Figure 3).

Discussion

To our knowledge, this study is the first to analyze the problem of A1C–GMI discordance in a long-term, real-world setting in a select group of children with T1D, based on clinical data from regular, routine outpatient care. We have shown that, during constant use of the same CGM system, differences in the results occur at <0.25 and >0.5, respectively, in less than half and one third of children. The results of our study are consistent with the data underlying the definition of GMI put forth by Bergenstal et al [1]. Data from several randomized trials conducted in different patient populations that used Dexcom sensors showed discordance between A1C and GMI in 51% of cases by ≥0.3% and in 28% of cases by ≥0.5% [1].

The differences between GMI and A1C >0.5 seem to be clinically significant, and the persistence in differences in various populations of approximately 30% is still a major problem that requires explanation. Several studies were performed to establish potential clinical factors influencing the observed differences. The relationship was demonstrated for the factors of ethnicity [6], adipose tissue (BMI) [7], glycemic variability [8], age [9], pregnancy [10], and chronic kidney disease [11]. Most of these studies were performed in adults, who are physiologically different from children. When it comes to the pediatric population, the only extensive study was performed by Piona et al [4]. The authors investigated a large cohort of children and adolescents using CGM and looked for discordance between GMI and A1C measurements. They stratified individuals with a discordance according to factors such as age, gender, BMI, CGM type, insulin therapy, hemoglobin, anemia, and coexistent autoimmune diseases. Their general results about A1C–GMI discordance were similar to ours, concluding that GMI could be meaningfully discordant (>0.5%) with respect to A1C in more than a third of children/adolescents with T1D and >1% discordant in one-tenth of them. None of the aforementioned factors explained the A1C–GMI differences in regression analyses. It is worth emphasizing that we obtained similar results in these areas; that is, we did not demonstrate a relationship between greater A1C–GMI discordance and CGM type, gender, age, BMI, or daily insulin dose. Another real-world study from Italy of a pediatric population addressed A1C–GMI differences in the context of blood count parameters and typical CGM metrics [12]. The authors revealed a higher coefficient of variation and time

Table 2
Data from CGM reports and results of A1C–GMI discordance (all records, n=308, no significant differences between users of different sensors)

	Overall (n=308)	Dexcom G6 (n=107)	FreeStyle Libre 2 (n=89)	Medtronic Guardian 3 (n=112)
A1C%, mean (SD)	6.94 (0.6)	6.96 (0.7)	6.82 (0.6)	7.01 (0.6)
GMI 14, %, mean (SD)	6.79 (0.5)	6.89 (0.5)	6.85 (0.5)	6.76 (0.4)
GMI 90, %, mean (SD)	6.82 (0.4)	6.85 (0.5)	6.78 (0.5)	6.76 (0.3)
TIR, %, mean (SD)	72 (12)	70 (12)	70 (15)	75 (9)
Glycemia, mg/dL, mean (SD)	147 (18)	149 (19)	148 (21)	143 (14)
CV% (SD)	37 (7)	39 (7)	38 (9)	35 (4)
A1C–GMI 14 discordance, mean (SD)	0.38 (0.3)	0.34 (0.3)	0.38 (0.2)	0.41 (0.3)
A1C–GMI 90 discordance, mean (SD)	0.35 (0.3)	0.36 (0.3)	0.30 (0.2)	0.39 (0.3)
A1C–GMI 90 discordance <0.25 (% of all records)	48.7%	46.7%	49.4%	50.0%
A1C–GMI 90 discordance 0.25–0.5 (% of all records)	20.1%	22.4%	27.0%	14.6%
A1C–GMI 90 discordance 0.5–0.75 (% of all records)	22.4%	22.4%	18.9%	22.8%
A1C–GMI 90 discordance >0.75 (% of all records)	8.7%	8.4%	4.5%	12.5%

A1C, glycated hemoglobin; *CGM*, continuous glucose monitoring; *CV*, coefficient of variation; *GMI*, glucose management indicator; *SD*, standard deviation; *TIR*, time in range.

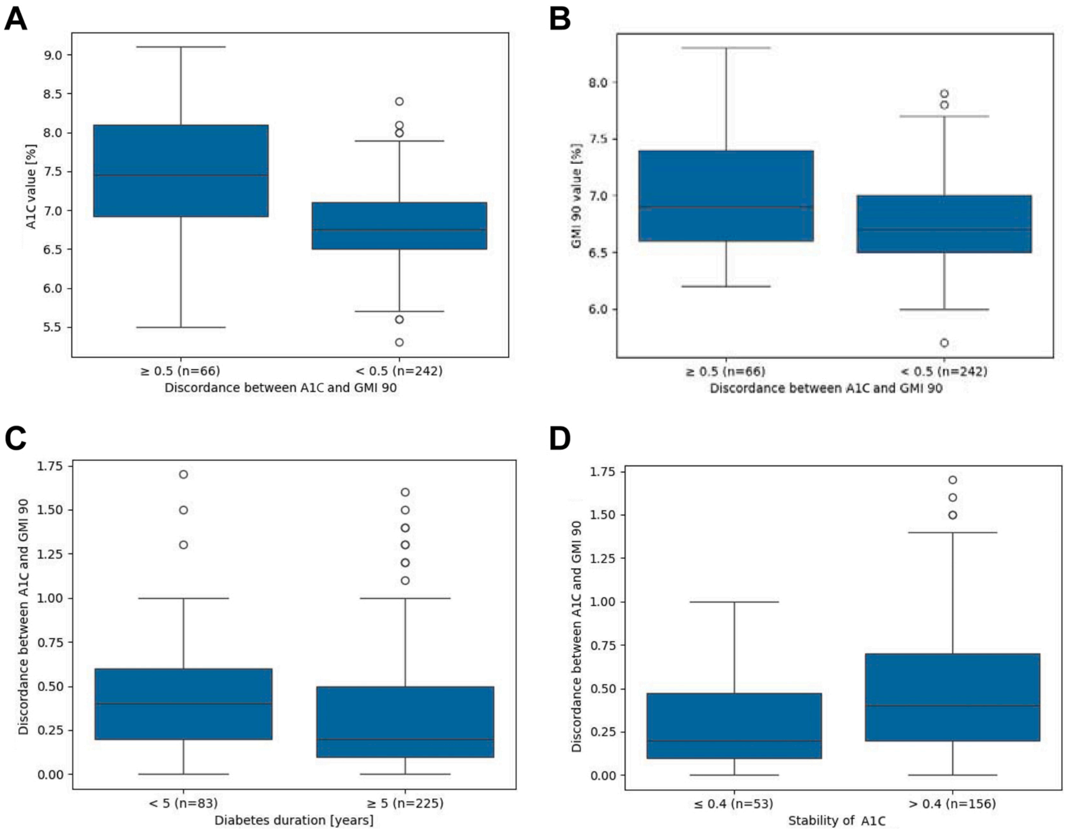

Figure 2. Correlation between factors influencing the glycated hemoglobin (A1C)–glucose management indicator (GMI) 90 discordance with statistically significance levels. (A) Discordance <0.5% in relation to A1C value (chi-square test, p<0.005). (B) Discordance <0.5% in relation to GMI value (chi-square test, p<0.005). (C) Patients with >5 years of diabetes duration (chi-square test, p<0.005). (D) Stability of patient metabolic control–difference in subsequent results of A1C <0.4 (chi-square test, p<0.005).

above range >250 mg/dL in those with an A1C–GMI discordance >0.3% and no association between blood count parameters and A1C–GMI discordance.

Several studies on A1C–GMI discordance in the pediatric population were also presented at the 2023 ISPAD conference (materials currently available only in the Abstract Book). The authors emphasized the importance of a high frequency of A1C–GMI discordance with an unidentified cause [13,14]. They presented other data as well: in some ethnic groups (non-Caucasian), there were higher A1C values in relation to GMI [15]; smaller differences correlated positively with duration of use of the CGM system [16]; CGM reports generated from different time periods (14, 30, 60, and 90 days) did not differ significantly when compared with A1C [17]; and there were differences between different CGM systems [18].

In our 1-year analysis of real-world data from PwD who regularly and continuously used the same type of CGM (i.e. >70% of the time), with more clinical data disposal, we observed that the differences between A1C for GMI 14 days and GMI 90 days were similar and had a linear relationship, which coincides with observations of other authors [19]. Moreover, we also found that greater differences in A1C–GMI 90 (differences >0.5%) were more likely to occur in individuals with higher A1C, longer disease duration, and less stable A1C values during subsequent visits. Our results confirm those of Díaz-Soto et al [8] and Randazzese et al [12], who showed an association of greater A1C–GMI discordance with higher coefficient of variation and longer time above range at >250 mg/dL in PwD with less optimal glycemic metrics and instability.

Our unique analysis on the stability of participants with regard to A1C–GMI discordance observed at subsequent visits has shown that this difference remains at a constant, individual level in as many as two-thirds of cases. This may be the result of differing abilities to glycate hemoglobin. Although our results should be considered as preliminary and require confirmation in a larger group of patients, this is important information for both the clinician and the patient in the context of taking further therapeutic actions.

A limitation of our study is that we assessed a select group of children and adolescents—those with stable treatment and monitoring—who consistently and regularly used the same type of CGM throughout the year at a single centre. However, according to data from other studies on the usefulness of CGM [18], and perhaps thanks to this, our children achieved relatively good metabolic management, as reflected by the low A1C values. This, in turn, allowed for the clinical dependence described earlier. A second limitation of our work is the relatively small size of the study group. This was partly due to the specificity of the study methodology, which included select inclusion criteria as well as a long observation period in a pediatric population with typically high variability. Therefore, our observations should be treated with caution.

Recognizing and understanding the factors that cause differences between A1C and GMI is an important clinical skill. As a rule, evaluation of these 2 parameters should be personalized. Undoubtedly, red blood cell lifespan and individual glycation rates are the main factors determining A1C formation. Clinicians should exercise caution when using GMI to evaluate treatment outcomes, especially those with high A1C–GMI discordance. For example, for situations in which A1C is elevated above GMI, further attempts at intensification of therapy based solely on the A1C value may increase the risk of hypoglycemia [20]. It is worth remembering that, when A1C is consistently higher than the GMI, these individuals are likely to be “high” glycators as opposed to “low” glycators, whose A1C is consistently lower than the GMI. This is very important, because it

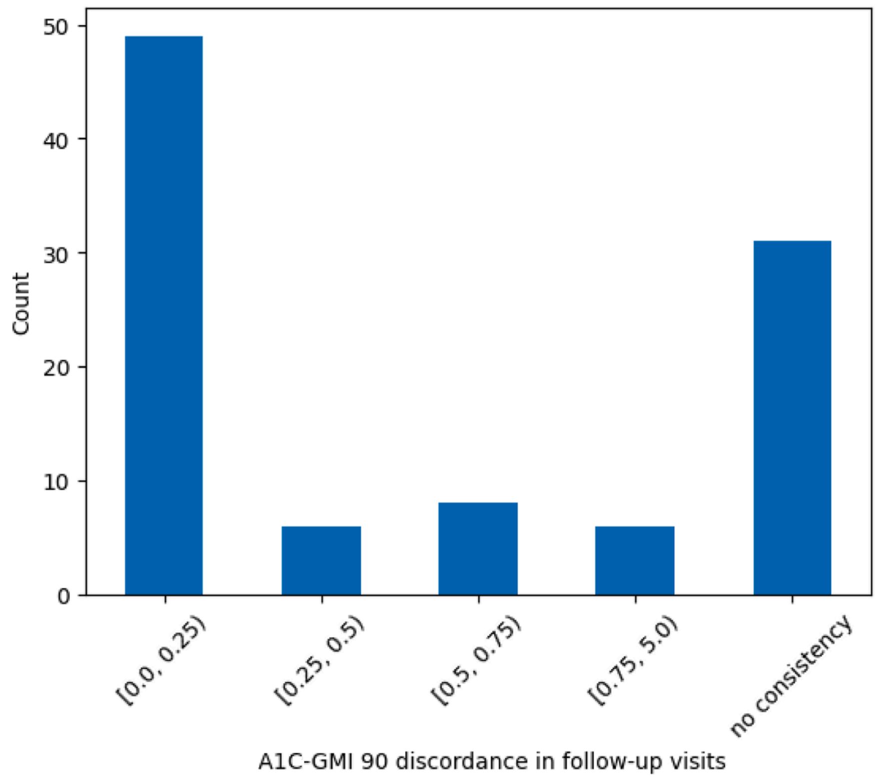

Figure 3. Variability of glycated hemoglobin (A1C)–glucose management indicator (GMI) 90 discordance—comparison of absolute difference between these 2 values at each visit and grouped into 4 predefined intervals.

was confirmed in many studies that high glycators have the potential for more glucose-mediated organ damage despite the same average glucose levels [3,20]. In a recent study, Selvin [3], concluded that, due to these large differences, the use of GMI should be discontinued and the focus should be more on mean level of glycemia. Relying on CGM mean glucose, rather than GMI, would reduce patient and provider confusion. We strongly agree with Bergenstal [21], who noted, in response to Selvin, that at this time most patients and many clinicians do not have a perspective on how to interpret mean glucose or the clinical meaningfulness of the change mean glucose. We could see the GMI as the bridge to move from using primarily A1C for diabetes management to using CGM metrics and profiles, along with A1C level [21].

To our knowledge, this study is the first to undertake long-term observation of children and adolescents in a real-life setting and show how information from analysis of commonly available clinical data could be interpreted in a practical manner. We believe that continued use of one system in PwD who understand the principles of monitoring and achieving optimal and stable treatment outcomes offers real, practical benefits. In such a carefully selected group of study participants, GMI usually correlates better with laboratory A1C, giving the clinician quick and direct insight into the current treatment. Individual A1C–GMI 90 discordance remains rather stable, although with varying degrees of difference. However, in those with insufficient and unstable control and longer disease duration, laboratory A1C testing remains a very important parameter and is still the gold standard in the overall assessment of diabetes treatment.

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Author Disclosures

Conflicts of interest: None.

Author Contributions

G.D.: Conceptualization, Investigation, Writing – original draft, Formal analysis, Methodology, Review, Editing. A.B.: Data collection, Investigation, Writing – original draft, Review, Editing. Ł.W.: Data collection, Investigation, Writing – original draft, Review, Editing. R.D.: Statistical analysis, Formal analysis, Methodology, Review. P.J.-C.: Review, Acceptance. All authors reviewed and approved the final manuscript.

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