

## The Relationship Between HbA1c and GMI and Glucose Metrics in Children and Adolescents with Type 1 Diabetes Using AID

Arslan E et al. The Relationship Between HbA1c and GMI

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### What is already known on this topic?

• HbA1c remains the most widely used biomarker for long-term glycemic control, but it does not fully reflect short-term glucose variability or CGMS-derived parameters in children with T1D.

### What this study adds?

• HbA1c showed the strongest correlation with GMI calculated over the last six weeks ( $r = 0.728$ ,  $p < 0.001$ ), suggesting that HbA1c mainly reflects recent rather than cumulative glycemic trends.

• GMI demonstrated stronger associations than HbA1c with key CGMS-derived metrics, including TIR, TAR, and TBR. Compared with HbA1c, GMI values were more stable across similar TIR levels, supporting its reliability for personalized diabetes management.

• Incorporating GMI alongside CGMS-derived parameters may provide a more accurate and clinically actionable assessment of glycemic control in pediatric AID users.

### ABSTRACT

**Introduction:** HbA1c remains the standard biomarker for long-term glycemic control, but it lacks precision in capturing short-term glucose variability and acute excursions. This limitation is especially relevant in children with type 1 diabetes (T1D) who use continuous glucose monitoring systems (CGMS) and automated insulin delivery (AID) systems.

**Aim:** To evaluate the temporal relationship between HbA1c and the glucose management indicator (GMI), and their associations with CGMS-derived glycemic parameters over 12-week period in children and adolescents with T1D using AID systems.

**Material-methods:** In this retrospective cross-sectional observational study, 81 children and adolescents with T1D on the Medtronic MiniMed 780G™ system were included. CGMS data covering 12 weeks prior to HbA1c measurement were analyzed in two-week intervals. Correlations between HbA1c, GMI, and CGMS metrics were assessed.

**Results:** HbA1c was positively correlated with all GMI values, with the strongest correlation observed for the last six-week GMI ( $r=0.728, p<0.001$ ). The mean difference between HbA1c and last 12-week GMI was 0.57% (95%CI: -1.13 to 2.27). GMI demonstrated stronger correlations than HbA1c with time in range (TIR), time above range (TAR), and time below range (TBR). Notably, in individuals with similar TIR (~70%), HbA1c values varied widely (6.6–9.6% / 48–84 mmol/mol), while GMI remained stable (6.8–7.1%).

**Discussion:** HbA1c exhibited the strongest correlation with GMI calculated over the last six weeks, suggesting that it primarily reflects recent glycemic trends rather than cumulative exposure. GMI also showed closer alignment with CGMS-derived indices such as TIR, TAR, and TBR, indicating its enhanced sensitivity in capturing day-to-day glycemic variability, especially in suboptimally controlled individuals.

**Conclusion:** Given its temporal limitations, HbA1c may not reliably capture 12-week glycemic patterns in pediatric AID users. GMI, as CGMS-derived metric, offers a more consistent and clinically actionable estimate of glycemic control, supporting its integration into routine care for children with T1D.

**Keywords:** T1D, AID, CGMS, GMI, sampling period

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### INTRODUCTION

Type 1 diabetes (T1D) is the most common chronic autoimmune disorder in childhood, characterized by insulin deficiency and persistent hyperglycemia. Achieving and maintaining optimal glycemic control is crucial in reducing the risk of both acute and long-term complications, particularly microvascular damage (1,2).

Glycosylated hemoglobin (HbA1c) remains the primary indirect measuring method for glycemic control, and its correlation with microvascular complications is well-established (3). Although HbA1c is acknowledged as a predictor of glucose exposure in the three months preceding sampling, utilizing HbA1c alone is insufficient to optimize and personalize treatment decisions. However, HbA1c alone does not capture short-term glucose fluctuations or provide information about glycemic variability, hypoglycemic episodes, or postprandial excursions (3). Moreover, its accuracy may be compromised in individuals with conditions such as anemia, iron deficiency, or hemoglobinopathies, which are not uncommon in pediatric populations (4).

The increasing use of continuous glucose monitoring systems (CGMS) systems has highlighted the limitations of HbA1c.

CGMS systems assess glucose levels in the interstitial compartment, which closely correlate with plasma glucose, thereby enabling continuous evaluation of glycemic patterns (5–7). CGMS provides real-time data on glucose dynamics, including time in range (TIR), time below range (TBR), time above range (TAR), and glycemic variability. In response to these advancements, the glucose management indicator (GMI) was introduced to estimate average glucose levels based on CGMS data. While GMI and HbA1c are intended to represent similar aspects of glycemic control, studies have shown that they often differ substantially, and this discrepancy appears to remain relatively stable for individuals over time (8). Several physiological factors contribute to the divergence between HbA1c and GMI, including interindividual differences in erythrocyte lifespan, rates of glycation, and glucose exposure. The commonly assumed erythrocyte lifespan of

120 days is not universally applicable, and newer evidence suggests that the average age of circulating erythrocytes may be significantly shorter, particularly in individuals with higher mean glucose levels.

Although a 14-day CGMS sampling period is considered sufficient to estimate glycemic patterns in adults, there is limited evidence supporting this recommendation in pediatric populations using advanced technologies such as automated insulin delivery (AID) systems. It remains unclear how well HbA1c reflects mean blood glucose over time, and how closely GMI aligns with HbA1c and other CGMS metrics, particularly in children with T1D (9).

In this study, we aimed to examine the relationship between HbA1c and GMI, explore the temporal evolution of this relationship, and assess their associations with CGMS-derived parameters in children and adolescents with T1D using an AID system. By analyzing biweekly CGMS data over a 12-week period, we sought to clarify the clinical relevance and reliability of these metrics in the context of modern diabetes management.

### Materials and Methods

In this retrospective cross-sectional observational study, 81 children and adolescents with T1D on Medtronic MiniMed 780G™ were enrolled in the study. The sample size was not calculated because our study is designed to encompass all T1D children and adolescents who are monitored in our clinic and utilize AID. The data of children and adolescents with T1D who met the inclusion criteria and accepted to participate in the study were retrospectively examined during the six-month study period. Children and adolescents with type 1 diabetes who were followed up at the Department of Pediatric Endocrinology and Diabetes, Ege University Faculty of Medicine were evaluated for inclusion in the study. Inclusion criteria were; age between 2 and 18 years (both inclusive); diagnosis of T1D for at least 1 year; at least 6 months of current use of automated insulin delivery system with MiniMed 780G™- The Guardian™ Sensor (3). Exclusion criteria were; people with T1D with a diagnosis of chronic disease as glucose-6-phosphate dehydrogenase deficiency (G6PDD), hemoglobinopathies (i.e., thalassemia, Sickle cell disease) and/or anemia of any cause.

Data for this study were obtained from a dataset approved by the E. University Ethics Committee (Approval No. 249T/38). This dataset was obtained retrospectively from children and adolescents with T1D using AHCL. Another study derived from this dataset discussing the temporal relationship of TIR and TITR is currently in the process of being published in a journal.

The study protocol was approved by the Ege University Ethics Committee (Approval No. 24-9T/38). The parents of all people with diabetes and from people with diabetes over 18 years of age provided written informed consent. We confirm that this study complied with the Declaration of Helsinki.

Anthropometric data (height, weight) and HbA1c levels were collected from the people with diabetes files. Height was measured to the nearest millimeter with Seca 264® stadiometer and weight to the nearest 100 grams by an electronic scale (Delsit Model KW®). Standard deviation scores (SDS) for weight, height, and BMI were calculated based on age and gender (10). Normal weight is defined as BMI-SDS  $\geq -1$  to  $< +1$  for children and adolescents and a BMI of 18.5–24.9 kg/m<sup>2</sup> for young adults. HbA1c was measured using a turbidimetric inhibition immunoassay (TINIA, Roche cobas c513, Tina-quant HbA1c Gen.3). This method is traceable to the IFCC reference system and NGSP-certified. Previous comparative studies have shown excellent agreement between the Roche TINIA method and IFCC-aligned HPLC systems ( $r > 0.98$ , mean bias  $< 0.2\%$  HbA1c).

Glucose ranges are presented in mg/dL with SI unit equivalents (mmol/L) given in parentheses. CGMS data for the entire study duration from each people with T1D were extracted from CareLink™. TIR 70–180 mg/dL, time above range (TAR)  $>180$  mg/dL, and time below range (TBR)  $<70$  mg/dL, mean glucose, mean glucose SD and CV and Glucose management indicator (GMI) were defined per the 2024 international consensus guidance on TIR and other CGMS metrics (11).

### Data Analysis

Six CGMS reports for the three months prior to the HbA1c measurement were obtained. For each CGMS report, a minimum sensor wear time of 80% was required. People with T1D who did not have at least five valid reports fulfilling this criterion were excluded from the study. Each report covered two-week intervals, beginning from the date of the HbA1c measurement. The first CGMS report included data from the two weeks leading up to the HbA1c measurement, the second CGMS report covered data from weeks three and four, and the third CGMS report captured data from weeks five and six. We then restructured the data to display a continuous timeline leading up to the HbA1c measurement date. (e.g., GMILastTwoWeeks, GMILastFourWeeks, and GMILastSixWeeks represent the 2-, 4-, and 6-week periods immediately preceding the HbA1c measurement, respectively).

The timeline diagram has been included as supplementary material to provide clearer clarification of the definitions.

### Statistical Analysis

Statistical analyses were performed by the Statistical Package for the Social Sciences version 25.0® (SPSS Inc., Chicago, IL, USA). The significance level was defined as  $p < 0.05$ . The sample size was not calculated because our study is designed to encompass all T1D children and adolescents who are monitored in our clinic and utilize AID. Categorical variables were represented as counts and percentages. Normal distribution for quantitative variables were assessed. Continuous variables with normal or skewed distributions were presented as mean  $\pm$  SD or median (IQR), respectively. Group differences were assessed using the independent t-test for normally distributed data and the Mann-Whitney U test for skewed data. We analyzed the differences in repeated measures using the repeated measures ANOVA for normally distributed data and the Friedman test for skewed data. 12-week data from each sampling period were used to compare the values with the squared value of the Pearson correlation coefficient (R<sup>2</sup>). We evaluated the concordance between the 12 weeks of CGMS data and each of the six biweekly CGMS reports using Bland-Altman plots and linear regression. The correlation between TIR values of GMI and HbA1c was assessed using the Williams' t-test for testing the significance of two related correlations. To control for multiple comparisons, p-values were adjusted using the Benjamini-Hochberg false discovery rate (FDR) correction.

### RESULTS

The study included 81 people with diabetes; 46 (57%) were female. There were 12 type 1 diabetics who used the AID system off-label because they were under 7 years old. The median age at diagnosis was 8.1 years (IQR: 4.3–10.8), the median age at AID initiation was 11.4 years (IQR: 9.3–15.2), and the median age at the time of the study was 13.6 years (IQR: 11.3–17). At the time of AID initiation, median BMI SDS was 0.21 (IQR: -0.37/0.74). All CGMS data, with the exception of TBR, exhibited a normal distribution (Table 1).

To evaluate the adequacy of our findings, a post hoc power analysis was conducted based on the observed effect sizes. This analysis revealed a statistical power of 87% ( $\alpha = 0.05$ ), indicating that the study was sufficiently powered to detect the differences observed and supporting the robustness of our results.

Glucose management indicator (GMI<sub>Last two weeks</sub>, GMI<sub>Last Four weeks</sub>, GMI<sub>Last Six weeks</sub>, and etc.) had a strong correlation with each other, and there was no significant difference among these correlations ( $p = 0.26$ ) (Table 2). HbA1c showed a strong positive correlation with all GMI values. HbA1c and GMI<sub>Last Twelve weeks</sub> / GMI<sub>Last Six week</sub> measurements were compared using the Bland-Altman statistical method. Average difference of 0.57 units was found between HbA1c and GMI<sub>Last Twelve weeks</sub> (95% CI: between -1.13 and 2.27,  $p < 0.001$ ), and average difference of 0.51 units was found between HbA1c and GMI<sub>Last Six weeks</sub> (95% CI: between -0.61 and 1.12,  $p < 0.001$ ). These plots suggest that the discrepancy between these two parameters increases particularly among individuals with poor glycemic control. A multiple linear regression analysis was performed in SPSS to identify the factors influencing the difference between HbA1c and GMI values (HbA1c–GMI difference). The model was statistically significant ( $F(6, 70) = 6.43$ ,  $p < .001$ ), explaining 35.5% of the variance ( $R^2 = 0.355$ , adjusted  $R^2 = 0.300$ ). Higher TITR ( $\beta = -0.415$ ,  $p = 0.025$ ) was significantly associated with a smaller HbA1c–GMI difference.

The relationship between HbA1c and  $\text{GMI}_{\text{Last two weeks}}$  shows the weakest association ( $r: 0.595, p < 0.001$ ) (Table 2). The strongest association between HbA1c and GMI was observed in the last six weeks ( $r: 0.728, p < 0.001$ ). The correlation of HbA1c with  $\text{GMI}_{\text{Last Six weeks}}$  was significantly stronger than with  $\text{GMI}_{\text{Last two weeks}}$  ( $t: 3.51; p < 0.001$ ) (Figure 2).

Table 3 summarizes the correlations between CGMS data and both HbA1c and GMI. All CGMS parameters, except for CV, showed a correlation with both HbA1c and GMI. In each of these associations, GMI exhibited a higher correlation coefficient. The correlation between TBR and HbA1C was not significant, but both  $\text{GMI}_{\text{Last two weeks}}$  and  $\text{GMI}_{\text{Last Twelve weeks}}$  showed a negative correlation with TBR. The correlation coefficients for the last two weeks with HbA1c and GMI indicated a significantly stronger correlation ( $t = 2.81, df = 78, p = 0.014; 95\% \text{ CI for } r_1-r_2 = 0.05 \text{ to } 0.29$ ) between TIR and GMI (Figure 3). In cases with a TIR of approximately 70%, HbA1c levels ranged from 6.6% to 9.6, while GMI values varied from 6.8% to 7.1%. The correlations of  $\text{GMI}_{\text{Last Twelve weeks}}$  with  $\text{TIR}_{\text{Last Twelve weeks}}$  ( $t = 5.20, df = 78, p < 0.001; 95\% \text{ CI for } r_1-r_2 = 0.17 \text{ to } 0.37$ ) and  $\text{TAR}_{\text{Last Twelve weeks}}$  ( $t = 6.00, df = 78, p < 0.001; 95\% \text{ CI for } r_1-r_2 = 0.20 \text{ to } 0.40$ ) were significantly higher than the correlation of  $\text{GMI}_{\text{Last two weeks}}$  with these parameters.  $\text{TBR}_{\text{Last twelve weeks}}$  showed a moderate correlation with both  $\text{GMI}_{\text{Last two weeks}}$  ( $r = -0.415, p = 0.007$ ) and  $\text{GMI}_{\text{Last twelve weeks}}$  ( $r = -0.5, p < 0.001$ ). Furthermore, no statistically significant difference was observed between the strengths of these two correlations ( $p > 0.47$ ) (Table 3).

There were no clinically significant correlations between CV and HbA1c or any GMI measures ( $r = 0.15-0.17, p = 0.15-0.22$ ).

## DISCUSSION

This study demonstrated that the last six weeks of GMI correlated well with HbA1c; however, the 12-week GMI exhibited a lack of similar consistency with HbA1c. GMI demonstrates a narrower variability than HbA1c and shows stronger correlations with metrics reflecting good glycemic control, such as TIR, TITR, and TBR, emphasizing its value as an indicator of optimal glycemic management.

GMI is determined using a method that generates a regression line from a plot of mean glucose concentration points on the x-axis and HbA1c values on the y-axis. Minimed Medtronic 780G™ continuous insulin infusion system calculates GMI by combining data from two trials that lasted an average of 48 days (with a range of 13 to 89 days)(3,12). The regression equation for calculating GMI (%) is  $3.31 + 0.02392 \times [\text{mean glucose in mg/dL}]$ , or  $\text{GMI} (\text{mmol/mol}) = 12.71 + 4.70587 \times [\text{mean glucose in mmol/L glucose}]$ . In a study where 528 people with diabetes were included, 19% of GMI and HbA1c levels were the same, while 51% diverged by 0.3% or more, and 28% differed by 0.5%(3). In the study by Perlman et al., which predominantly included adults with type 1 diabetes, the discrepancy between GMI and HbA1c reached  $\geq 0.5\%$  in approximately half of the people with diabetes, and exceeded 1% in nearly 22% of cases(13). Our data revealed a significant difference of 0.57% between HbA1c and GMI after twelve weeks, confirming the notion that HbA1c does not accurately reflect 12-week blood glucose in real-life conditions. Another finding supporting this notion, indicating that while HbA1c exhibited a strong correlation with all GMIs, the magnitude of these correlations varied significantly ( $t: 3.51; p < 0.001$ ). There was a strong correlation between GMIs reflecting different periods, and there was no significant difference between these correlations ( $p = 0.26$ ) (Table 2). Therefore, we attributed the difference in correlations between HbA1c and GMI values reflecting different periods to the fact that HbA1c did not reflect the 12-week period equally. Although numerous studies have examined the correlation between HbA1c and GMI, few have investigated how this relationship changes over time. A recent large cohort study in individuals with T1D evaluated correlations between HbA1c and CGMS data collected over last 4- and 12-week periods, demonstrating strong associations in both time frames—findings consistent with our results(14). However, because the study did not directly compare the strength of the correlations between HbA1c and the last 4- and 12-week CGMS datasets, a potential temporal difference in this relationship may have gone unnoticed. By identifying this difference, our study provides new insight and contributes to a more nuanced understanding of the time-dependent nature of the HbA1c–GMI relationship.

Several studies have suggested that the difference between GMI and HbA1c varies considerably among individuals and may be influenced by factors such as pubertal stage, the type of CGMS device used, and the mode of insulin therapy (12–15). Although no consensus has been established regarding what constitutes a clinically meaningful GMI–HbA1c discrepancy, Westra et al. recently emphasized that differences of 0.8% or greater should be interpreted with caution (15). In our study, we suggest that differences of 0.55% or greater (as presented in Figure 1) should prompt more cautious interpretation of glycemic control.

$\text{GMI}_{\text{Last Six weeks}}$  showed the strongest correlation with HbA1c, suggesting that blood glucose significantly influenced circulating red blood cells in the final six weeks. The fact that HbA1c did not consistently reflect the 12-week period leads credence to the theory that GMI reflects temporal changes in average blood glucose better than HbA1c. The literature shows that the difference between HbA1c and GMI remains relatively constant for each individual over time, possibly due to the individuals having a different erythrocyte lifespan or erythrocyte glycation rate than the average, making GMI useful in personalized diabetes treatment (3,8,16). Recent research has shown that erythrocyte lifespan varies greatly even in healthy people (17,18). The homogenous erythrocyte survival model, which predicts an erythrocyte lifespan of about 120 days, has led to a wrong understanding of HbA1c. Beltran et al. created HbA1c-MBG curves with the probability of maximum erythrocyte lifespan (MEL) in circulation being 90–117 and 140 days. Individuals with higher MBG have a shorter MEL (90 days), whereas those with lower MBG have a longer MEL (140 days). The authors interpreted this as a shortening effect of hyperglycemia on erythrocyte lifetimes, leading to clinically significant variations in HbA1c interpretation. They also suggested that the variability in HbA1c at the same MBG value may be larger than reported in the literature (19). Cohen et al. found that while the MEL was  $117 \pm 12$  days, the average lifespan of erythrocytes was  $80 \pm 11$  days, much shorter than the widely recognized 120 days. They presented this as evidence that age does not affect the clearing of erythrocytes from circulation. The study found that age-related clearance cleared only  $38 \pm 9.6\%$  of erythrocytes from circulation and reached MEL. The average age of circulating erythrocytes was  $49 \pm 6$  days, and the authors estimated the HbA1c half-life to be 25–35 days (16). A lot of people agree that the changing relationship between HbA1c and MBG is due in part to reticulocyte glycation in the bone marrow, the rate at which glucose separates from hemoglobin, and how high blood sugar affects the lifespan of circulating erythrocytes (16,20). In our study, HbA1c had the strongest correlation with  $\text{GMI}_{\text{Last six weeks}}$ , which confirms the two studies findings. The finding that HbA1c shows the strongest correlation with the last 6-week data will contribute to the interpretation of which time frame HbA1c best reflects in routine clinical practice. In addition, it will raise the discussion on the necessity of evaluating 6-week CGM data instead of 2-week CGM data.

Many investigations have demonstrated that, despite a strong association between TIR and HbA1c, a wide range of HbA1c for the same TIR value leads to inaccurate case prediction (21,22). Bosoni et al. observed that a lower TIR maintains HbA1c  $\leq 7\%$ ; nevertheless, another group needed a high TIR to achieve the same aim (22). In our study, given the identical TIR values, HbA1c had a substantially broader distribution than GMI. This showed that human factors have less influence on GMI, allowing it to predict the TIR within a more limited range.

Furthermore, as shown in Figure 1, the widening gap between GMI and HbA1c in individuals with suboptimally managed people with diabetes underscores the necessity of personalized diabetes management using CGMS data, particularly GMI, in this population. As demonstrated in this study, GMI correlates more strongly with TIR, TAR, and TBR than HbA1c, indicating that GMI is superior to HbA1c in measuring glycemic control. Though the use of CGMS technology in children with T1D is increasing, the efficient use of CGMS data remains low (23). This is primarily due to the difficulty in interpreting CGMS data and the lack of standardization (24). To achieve consistency, a recently published international agreement on the use of CGMS proposed that CGMS be sampled for 10 to 14 days, with glycemic control targets of  $\text{TIR} > 70\%$ ,  $\text{TAR} < 25\%$ , and  $\text{TBR} < 4\%$  (9,25). Based on research indicating that a longer sampling period does not increase correlation, this guideline recommends a 14-day sampling period. However, it's important to note that these studies primarily involved adults with diabetes with minimal use of insulin infusion pumps. Several studies have found that a 14-day sampling interval might be highly deceptive, especially when monitoring hypoglycemic objectives (26–28).

In our research, GMI data in CGMS reports from various sampling times revealed a significant correlation. However,  $TIR_{Last\ Twelve\ weeks}$  and  $TAR_{Last\ Twelve\ weeks}$  had differing levels of correlation with  $GMI_{Last\ two\ weeks}$  and  $GMI_{Last\ Twelve\ weeks}$ , highlighting the need to evaluate the 14-day sampling period's reliability.

Another area in which CGMS shows a clear advantage over HbA1c is its ability to facilitate remote monitoring through telemedicine, thereby enabling more frequent and responsive evaluation of glycemic control. During the COVID-19 pandemic, Kaushal et al. observed significant improvements in mean CGMS glucose and GMI among youth with T1D despite a reduction in face-to-face encounters (29). Consistently, Plachy et al. demonstrated that telemedicine follow-up was non-inferior to traditional in-person visits in maintaining glycemic outcomes, while allowing continuous assessment of CGMS-derived indices such as TIR (30). In addition, Ferber et al. reported short-term improvements in TIR and GMI following both telemedicine and on-site consultations, emphasizing the stability of glycemic management when CGMS data are accessible remotely (31). Collectively, these findings suggest that CGMS metrics, particularly GMI, enable real-time remote evaluation and timely treatment adjustments—an advantage that is inherently absent in HbA1c-based assessment.

## CONCLUSION

Our findings underscore the limitations of HbA1c as a standalone measure of glycemic control in children and adolescents with type 1 diabetes, particularly those using automated insulin delivery systems. Although HbA1c remains a widely used clinical tool, its variability and limited sensitivity to glycemic fluctuations reduce its reliability in personalized diabetes care.

In contrast, GMI, derived from continuous glucose monitoring data, demonstrated more stable and consistent associations with key glycemic metrics, including time in range and time in tight range. GMI was less influenced by physiological variability and more accurately reflected recent glucose exposure, particularly over the six- to twelve-week period.

Incorporating GMI and other CGMS-based metrics into routine clinical assessment may enhance treatment decisions and optimize outcomes, especially in pediatric populations utilizing advanced diabetes technologies. Future guidelines should consider greater emphasis on CGMS-derived measures alongside or in place of HbA1c to support individualized, data-driven management strategies in T1D.

## Study Limitations

This study has limitations. First, it was conducted at a single center with a relatively small sample size, which may limit the generalizability of the findings. Second, all individuals were using the same AID system, and results may not extend to those using other insulin delivery methods. Although HbA1c was measured using the TINIA method rather than HPLC, both assays are IFCC-aligned, and their results are considered interchangeable within clinically acceptable limits. Therefore, potential assay-related bias is unlikely to have affected the main findings.

## Disclosure

This study was presented at the Turkish National Pediatric Endocrinology Congress in May 2024

## Conflicts of Interest

The authors declare no conflicts of interest.

## Author Contributions

E.A., H.G.B., D.Ö.K., S.D., S.Ö. and D.G. contributed to the study design and data interpretation. E.A., G.D. acquired data. E.A. performed statistical analysis and drafted the manuscript. All authors have critically read, revised, and approved the final manuscript. E.A. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

## Availability of data and materials

The datasets generated and analyzed during the current study are not publicly available due to institutional and ethical restrictions but are securely stored on the personal computers of the corresponding author (Damla Gökşen) and co-author (Emrullah Arslan). The de-identified summary dataset generated and analyzed during the current study is available from the corresponding author upon reasonable request.

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**Table1: Summary of CGM Data**

Number of patients:81	Mean $\pm$ SD	Median, IQR
HbA1c, %	7.26 $\pm$ 0.67	
MBG <sub>Last two weeks</sub> , mg/dl	139.2 $\pm$ 12.3	
MBG <sub>Last twelve weeks</sub> , mg/dl	140.0 $\pm$ 11.3	
Sensor usege rate, %	90.8 $\pm$ 8.3	
GMI <sub>Last two weeks</sub> , %	6.6 $\pm$ 0.29	
GMI <sub>Last twelve weeks</sub> , %	6.6 $\pm$ 0.25	
TIR <sub>Last two weeks</sub> , %	77.4 $\pm$ 7.3	
TIR <sub>Last twelve weeks</sub> , %	76.8 $\pm$ 7.0	
*TBR <sub>Last two weeks</sub> , %		2(1-4)
*TBR <sub>Last twelve weeks</sub> , %		2(1-4)
TAR <sub>Last two weeks</sub> , %	17.2 $\pm$ 4.7	
TAR <sub>Last twelve weeks</sub> , %	16.9 $\pm$ 5.1	
CV <sub>Last two weeks</sub> , %	34.5 $\pm$ 3.8	
CV <sub>Last twelve weeks</sub> , %	35.2 $\pm$ 4.9	

CGM: Continuous glucose monitoring system, SD: Standard deviation, IQR: Interquartile range, HbA1C: Glycosylated hemoglobin, MBG: Mean blood glucose, GMI: Glucose management indicator, TIR: Time in range, TBR: Time below range, TAR: Time above range, CV: Coefficient of variation

**Table2: Correlation HbA1c and GMIs of different periods**

Number of patients: 81	GMI <sub>Last two weeks</sub>	GMI <sub>Four weeks</sub>	GMI <sub>Last Six weeks</sub>	GMI <sub>Last eight weeks</sub>	GMI <sub>Last ten weeks</sub>	GMI <sub>Last twelve weeks</sub>
HbA1c	r:0.595* <b>p&lt;0.001*</b>	r:0.697* <b>p&lt;0.001*</b>	r:0.728* <b>p&lt;0.001*</b>	r:0.714* <b>p&lt;0.001*</b>	r:0.718* <b>p&lt;0.001*</b>	r:0.704* <b>p&lt;0.001*</b>
GMI <sub>Last two weeks</sub>	1	r:0.892* <b>p&lt;0.001*</b>	r:0.890* <b>p&lt;0.001*</b>	r:0.848* <b>p&lt;0.001*</b>	r:0.819* <b>p&lt;0.001*</b>	r:0.776* <b>p&lt;0.001*</b>
GMI <sub>Twelve weeks</sub>	r:0.776* <b>p&lt;0.001*</b>	r:0.916* <b>p&lt;0.001*</b>	r:0.949* <b>p&lt;0.001*</b>	r:0.973* <b>p&lt;0.001*</b>	r:0.989* <b>p&lt;0.001*</b>	1

\*To control for multiple comparisons, p-values were adjusted using the Benjamini-Hochberg false discovery rate (FDR) correction.

HbA1C: Glycosylated hemoglobin, GMI: Glucose management indicator

**Reinterpreted combined datasets:**

- CGMS<sub>Last two weeks</sub>: 0 → -2 weeks
- CGMS<sub>Last four weeks</sub>: 0 → -4 weeks
- CGMS<sub>Last six weeks</sub>: 0 → -6 weeks
- CGMS<sub>Last eight weeks</sub>: 0 → -8 weeks
- CGMS<sub>Last ten weeks</sub>: 0 → -10 weeks
- CGMS<sub>Last twelve weeks</sub>: 0 → -12 weeks

**Table 3: Correlation HbA1c and GMI with other CGM data**

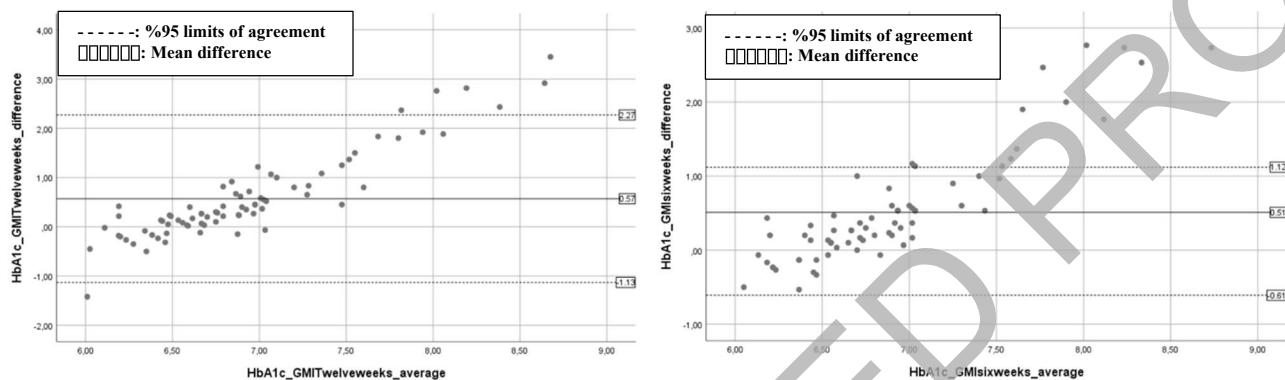
Number of patients: 81	MBG Last two weeks	MBG Last Twelve weeks	TIR Last two weeks	TIR Last Twelve weeks	TAR Last two weeks	TAR Last Twelve weeks	TBR Last two weeks	TBR Last Twelve weeks	CV Last two weeks	CV Last Twelve weeks
HbA1c	r:0.635* <b>p&lt;0.001*</b>	r:0.721* <b>p&lt;0.001*</b>	r:-0.583* <b>p&lt;0.001*</b>	r:-0.558* <b>p&lt;0.001*</b>	r:0.558* <b>p&lt;0.001*</b>	r:0.532* <b>p&lt;0.001*</b>	r:-0.12 p:0.31	r:-0.283* p:0.013	r:0.15 p:0.22	r:0.07 p:0.52
GMI Last two weeks	r:0.993* <b>p&lt;0.001*</b>	r:0.777* <b>p&lt;0.001*</b>	r:-0.762* <b>p&lt;0.001*</b>	r:-0.473* <b>p&lt;0.001*</b>	r:0.831* <b>p&lt;0.001*</b>	r:0.605* <b>p&lt;0.001*</b>	r:-0.533* <b>p&lt;0.001*</b>	r:-0.415* <b>p: 0.007*</b>	r:0.168 p:0.18	r:0.028 p:0.8
GMI Last Twelve weeks	r:0.803* <b>p&lt;0.001*</b>	r:0.987* <b>p&lt;0.001*</b>	r:-0.647* <b>p&lt;0.001*</b>	r:-0.749* <b>p&lt;0.001*</b>	r:0.706* <b>p&lt;0.001*</b>	r:0.845* <b>p&lt;0.001*</b>	r:-0.397* <b>p&lt;0.001*</b>	r:-0.500* <b>p&lt;0.001*</b>	r:0.173 p:0.15	r:0.194 p:0.11

\*To control for multiple comparisons, p-values were adjusted using the Benjamini-Hochberg false discovery rate (FDR) correction.

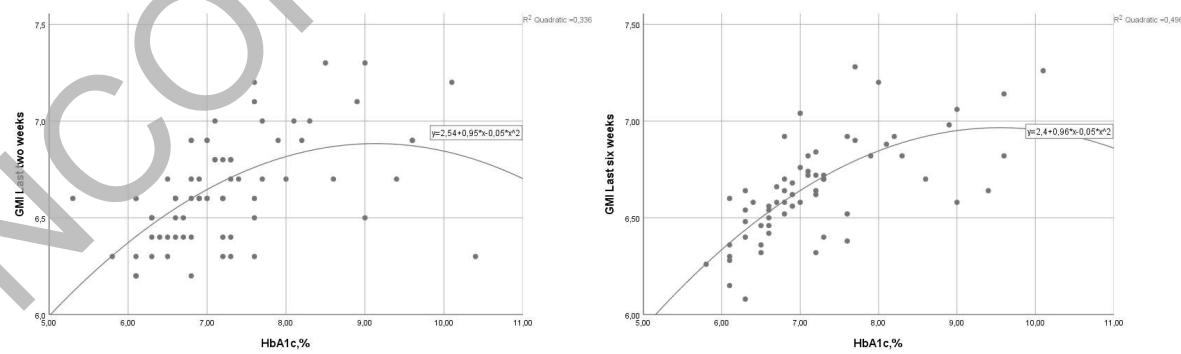
HbA1C: Glycosylated hemoglobin, GMI: Glucose management indicator, CGM: Continuous glucose monitoring system, MBG: Mean blood glucose, TIR: Time in range, TAR: Time above range, TBR: Time below range, CV: Coefficient of variation

**Reinterpreted combined datasets:**

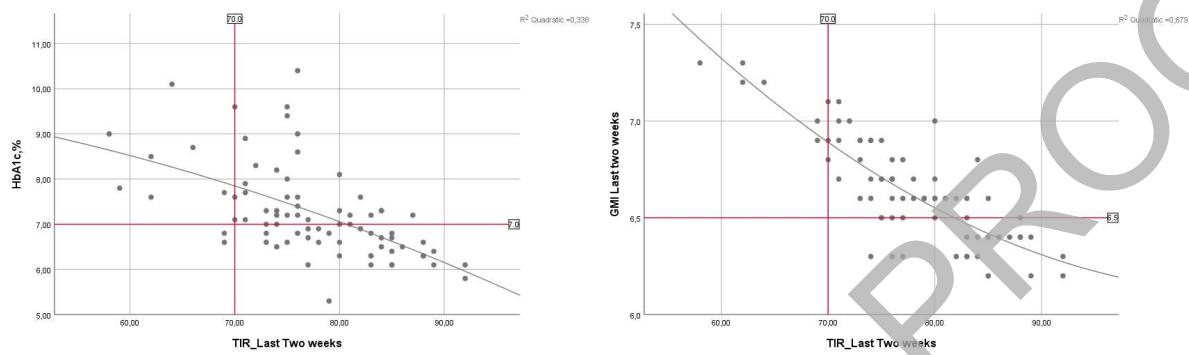
- CGMS<sub>Last two weeks</sub>: 0 → -2 weeks
- CGMS<sub>Last four weeks</sub>: 0 → -4 weeks
- CGMS<sub>Last six weeks</sub>: 0 → -6 weeks
- CGMS<sub>Last eight weeks</sub>: 0 → -8 weeks
- CGMS<sub>Last ten weeks</sub>: 0 → -10 weeks
- CGMS<sub>Last twelve weeks</sub>: 0 → -12 weeks



**Figure 1: Comparing HbA1c and GMI<sub>Twelve weeks</sub> and GMI<sub>Six weeks</sub> with the Bland-Altman Plots Test.** HbA1c and GMI<sub>Twelve weeks</sub> / GMI<sub>Six week</sub> measurements were compared using the Bland-Altman statistical method. Average difference of 0.51 units was found between HbA1c and GMI<sub>Twelve weeks</sub> (95% CI: between -1.13 and 2.27,  $p<0.001$ ), and average difference of 0.61 units was found between HbA1c and GMI<sub>Six weeks</sub> (95% CI: between -0.61 and 1.12,  $p<0.001$ ). These plots suggest that the discrepancy between these two parameters increases particularly among individuals with poor glycemic control.



**Figure 2: Comparison of HbA1c with GMI<sub>Last two weeks</sub> and GMI<sub>Six weeks</sub> ( $t:3,51$ ;  $p<0,001$ ).** HbA1c shows a strong correlation with both GMI<sub>Last two weeks</sub> and GMI<sub>Six weeks</sub>. When these two correlations are compared using the method of testing the significance of two related correlations, it is observed that GMI<sub>Six weeks</sub> correlates better with HbA1c. ( $t:2,9$ ,  $p:0,037$ ).



**Figure 3: Comparison of  $TIR_{Last\ two\ weeks}$  with  $HbA1c$  and  $GMI_{Last\ two\ weeks}$  ( $t:2,81$ ;  $p:0,014$ ).** The correlation of  $TIR_{Last\ two\ weeks}$  with  $HbA1c$  and  $GMI_{Last\ two\ weeks}$  were compared. The graph shows that  $TIR_{Last\ two\ weeks}$  has a better correlation with  $GMI_{Last\ two\ weeks}$  ( $t:2,81$ ;  $p:0,014$ ).

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