diabetesresearchandclinicalpractice 238 (2026) 113369

Contents lists available at ScienceDirect

Brazilian Journal of Health and Clinical Approaches

journal homepage: www.journals.elsevier.com/bjhca

GLP-1 receptor agonist adjunct therapy stabilises Ramadan dysglycaemia in insulin-treated diabetes: a CGM-based study

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ARTICLE INFO

Keywords:
Ramadan fasting
Type 2 diabetes
Type 1 diabetes
Continuous glucose monitoring
GLP-1 receptor agonist
GLP-1/GIP dual agonist
Tirzepatide
Semaglutide
Post-iftar hyperglycaemia
Time in Range

ABSTRACT

Background: Patients with type 1 and insulin-treated type 2 diabetes are at higher risk of hypo- and hyperglycaemia during Ramadan fasting. The role of incretin-based add-on therapy (GLP-1 receptor agonist semaglutide and the GLP-1/GIP dual agonist tirzepatide) in attenuating Ramadan dysglycaemia in insulin-treated type 2 diabetes has not been characterised using continuous glucose monitoring. Emerging evidence indicates that exaggerated post-iftar hyperglycaemia, drives Ramadan dysglycaemia in insulin-treated individuals.
Aims: To use continuous glucose monitoring (CGM) to characterise glycaemic control in patients with type 1 and type 2 diabetes on intensive insulin during Ramadan fasting, and to evaluate the role of add-on semaglutide or tirzepatide in attenuating post-iftar hyperglycaemia.
Methods: Adults with type 1 or type 2 diabetes using FreeStyle Libre CGM who completed ≥ 14 full fasting days during Ramadan 2025 were included. Of 140 participants screened pre-Ramadan, 54 met all inclusion criteria and were analysed: type 2 diabetes on basal–bolus insulin alone (BB, n = 18), type 2 diabetes on basal–bolus plus tirzepatide or semaglutide (BB+, n = 18) – matched 1:1 by age, baseline HbA1c and BMI – and type 1 diabetes on basal–bolus insulin (T1DM, n = 18). CGM metrics were collected over 28 days pre-Ramadan (1–28 February 2025) and 29 days during Ramadan (1–29 March 2025) and compared within and between groups, and across fasting versus non-fasting windows.
Results: Dysglycaemia was driven predominantly by the post-iftar period. BB participants showed marked deterioration during non-fasting hours. Adjunctive therapy attenuated this effect: time in range 74.4 % vs 36.8 % (p = 0.007), glucose management indicator 6.9 % vs 8.3 % (p = 0.004), and > 2-fold (≈61 %) reduction in incremental post-iftar area under the curve (102,014 vs 260,578 mg/dL·min over the 4-h post-iftar window).
Conclusion: In matched insulin-treated type 2 diabetes cohorts, add-on semaglutide or tirzepatide stabilised Ramadan glycaemia and reduced post-iftar hyperglycaemia without increasing hypoglycaemia, and was well tolerated with no treatment discontinuations during Ramadan.

1. Introduction

Ramadan fasting (RF) is observed for a full lunar month annually and entails abstinence from food and drink from dawn to sunset [1,2]. The main meal (iftar) is taken at sunset and often consists of carbohydrate-rich food [3,4]. For individuals living with diabetes, these abrupt shifts in nutritional timing and composition pose significant metabolic challenges [5–7]. International guidelines have been developed to stratify risk and support safe fasting, with an emphasis on preventing hypoglycaemia, particularly among those treated with insulin or insulin secretagogues [8–10]. The IDF-DAR risk assessment tool categorises patients into low, moderate-, and higher-risk groups to guide individualised treatment plans [11,12].

While this framework has been essential for patient safety, emerging evidence suggests that the dominant glycaemic challenge during Ramadan may not be hypoglycaemia per se, but also exaggerated post-iftar hyperglycaemia and nocturnal variability phenomena that are incompletely captured by conventional measures such as glycated haemoglobin (HbA1c) [13–16]. HbA1c reflects average glucose over 2–3 months and fails to detect the prominent post-meal glucose spikes and

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https://doi.org/10.1016/j.diabres.2026.113369
Received 6 April 2026; Received in revised form 4 June 2026; Accepted 9 June 2026
Available online 10 June 2026

glycaemic variability patterns that occur specifically during Ramadan fasting [17–19]. CGM-based studies have therefore become essential for characterising Ramadan glycaemic dynamics [20,21].

Continuous glucose monitoring (CGM) provides clinically actionable metrics — time in range (TIR), time above range (TAR), time below range (TBR) and glycaemic variability — and the Ambulatory Glucose Profile (AGP) standardises their visualisation; a 10 % increase in TIR is associated with lower microvascular risk in type 2 diabetes [7,16,19–21].

CGM studies during Ramadan have shown that fasting alters the glycaemic pattern more than its mean, with a rapid post-sunset rise — the 'iftar effect' — that is most pronounced in insulin-treated patients [15,17,20,21]. A subsequent intermittently scanned CGM (isCGM) study in insulin-treated patients identified post-iftar excursions as a key therapeutic target [9], and Alguwaihes et al. reported persistent post-iftar hyperglycaemia in T1DM lasting at least one month after Ramadan [17].

CGM systems such as FreeStyle Libre have enabled real-world glucometric assessment during Ramadan [4,9,15,20], and automated insulin delivery (AID) and tight-range CGM analyses in T1DM have demonstrated feasibility during fasting [10,20,21].

Subsequent work has confirmed that while hypoglycaemia remains a concern during prolonged fasting [22], the predominant glycaemic burden often occurs in the evening and early night, driven by large, high-glycaemic-index meals, late-night snacking, and conservative insulin dosing to avoid hypoglycaemia [8,10,21–23]. Specifically in insulin-treated type 2 diabetes, insulin management strategies — including dose reduction by approximately 30 %, use of rapid-acting analogues, and structured pre-Ramadan education [24] — can mitigate these risks but remain underutilised.

In parallel, incretin-based therapies, particularly glucagon-like peptide-1 receptor agonists (GLP-1RAs), have emerged as cornerstone treatments in T2DM, offering glucose-dependent insulinotropic effects, suppression of inappropriate glucagon secretion, delayed gastric emptying, and clinically meaningful reductions in postprandial glycaemia and body weight. Delayed gastric emptying induced by GLP-1RAs contributes to postprandial glucose modulation. Published evidence on the use of GLP-1 receptor agonists during Ramadan in individuals with and without diabetes underscores their metabolic advantages and low likelihood of causing hypoglycaemia [25–29]. During Ramadan, GLP-1RAs have demonstrated favourable safety and efficacy profiles, with reduced hypoglycaemia risk and preserved or improved metabolic outcomes compared with sulphonylureas and other oral agents [25,28–30]; recent fixed-ratio data from the SoliRam sub-analysis support concomitant use of iGlarLixi and an SGLT-2i in T2DM during Ramadan [29]. The LixiRam trial showed superiority of lixisenatide over sulphonylurea during Ramadan, and lixisenatide plus basal insulin has demonstrated safety and efficacy [28].

Real-world studies of injectable and oral semaglutide during Ramadan have reported improved HbA1c, weight reduction, and high treatment adherence without excess hypoglycaemia [28,30]. A study by Pathan et al. documented real-world metabolic improvements associated with semaglutide use during Ramadan in Bangladesh [28]. The O-SEMA-FAST study evaluated oral semaglutide in 257 adults with T2DM who were fasting during Ramadan across the UAE, Saudi Arabia, and Kuwait, reporting significant HbA1c reductions (0.2–0.3 percentage points), weight loss (2.6–3.2 kg), and 68.4 % dosing adherence [30]. Tirzepatide, a dual GLP-1/GIP receptor agonist, was evaluated in 109 patients with T2DM fasting during Ramadan in Bangladesh, showing HbA1c reduction from 7.6 % (60 mmol/mol) to 6.5 % (48 mmol/mol), weight loss of 5.3 kg, significant reductions in fasting and postprandial glucose, and no hypoglycaemia [31–33]. A 2025 systematic review and *meta*-analysis confirmed the safety and efficacy of GLP-1RAs during Ramadan [31].

However, these investigations have largely relied on conventional endpoints and have rarely incorporated CGM-derived metrics, leaving an important gap in understanding how semaglutide or tirzepatide therapy modulates diurnal glycaemic patterns during fasting [30–32]. Studies using CGM in T2DM during Ramadan have documented glucometric changes but have not evaluated GLP-1RA adjunct therapy to intensive insulin regimens.

2. Methods

2.1. Design and setting

The study was conducted at the Imperial College London Diabetes and Endocrine Centre (ICLDEC) in Abu Dhabi. The observational design was chosen to reflect routine clinical practice and to minimise interference with participants' fasting intentions and daily activities. Data were collected over two contiguous 28–29-day windows: 1–28 February 2025 (pre-Ramadan) and 1–29 March 2025, corresponding to Ramadan 1446 AH — the year of the Islamic Hijri calendar, which is the lunar calendar followed by Muslims worldwide.

2.2. Participant Eligibility and Recruitment

Adults (≥18 years) with type 1 or type 2 diabetes who were using a CGM device (FreeStyle Libre™) and intended to complete at least 14 full fasting days during Ramadan (dawn to sunset, with no breaking of the fast outside iftar/suhoor) were eligible for inclusion. Days on which the fast was broken before sunset for any reason were not counted as fasting days. Exclusion criteria included pregnancy, advanced chronic kidney disease, unwillingness to fast, or insufficient CGM validity (defined as ≥ 14 days with ≥ 70 % wear time), in line with international consensus guidelines [15].

A total of 140 patients were approached and consented to participate during the pre-Ramadan screening. After Ramadan, follow-up phone calls were made to collect information on the actual number of fasting days. Patients were excluded if they:

- Fasted for fewer than 14 days,
- Were not connected to the LibreView™ CGM platform (making data unavailable),
- Had incomplete or missing pre-Ramadan CGM data.

Of 140 patients consented at pre-Ramadan screening, 54 fulfilled all inclusion criteria and were analysed: 36 adults with type 2 diabetes and 18 adults with type 1 diabetes. The two T2DM groups (BB, n = 18; BB + tirzepatide or semaglutide, n = 18) were optimally matched 1:1 on age, baseline HbA1c and BMI. The 18 T1DM participants on basal-bolus insulin were analysed in parallel as a physiologically distinct comparator cohort.

2.3. Power analysis

The study was powered based on the primary continuous glucose monitoring (CGM) endpoints assessed during Ramadan, including time in range (TIR; 70–180 mg/dL), time above range (TAR; >180 mg/dL), and time below range (TBR; <70 mg/dL), comparing patients with type 2 diabetes treated with basal-bolus insulin alone versus BB + therapy.

Prior CGM-based Ramadan studies in T2DM report between-group differences in TIR of approximately 15–20 percentage points (20). Assuming a conservative standard deviation of 25 % for TIR and a two-sided α of 0.05, a standardised effect size (Cohen's d) of 0.75 was selected to avoid overestimation. Under these assumptions, a minimum of 17 participants per group is required to achieve 80 % power for a two-group comparison.

2.4. Data collection and definitions

Participants used their usual CGM systems (FreeStyle Libre™). CGM

Table 1
Patients' characteristics (n = 54).

Variable	T2DM BB n = 18	T2DM BB+ n = 18	T1DM n = 18	p-value
HbA1c % mmol/mol	7.7 [7.0–8.9] 61 [7.0–8.9]	7.3 [7.0–8.0] 56 [7.0–8.0]	7.1 [6.3–7.9] 54 [6.3–7.9]	0.115
BMI Kg/m^2	27.7 [25.3–33.3]	27.2 [26.1–34.0]	27.5 [26.1–33.6]	0.996
Age years	55.0 [41.0–59.0]	57.0 [49.0–62.0]	32.0 [26.0–44.0]	0.001
Gender	Male = 7 (39 %)	Male = 9 (50 %)	Male = 12 (67 %)	0.286
	Female = 11 (61 %)	Female = 9 (50 %)	Female = 6 (33 %)	

BB group: Type 2 diabetes patients on Basal-bolus insulin alone.
BB + group: Type 2 diabetes patients on Basal-bolus + Tirzepatide or Semaglutide.
T1DM: Type 1 diabetes patients on Basal Bolus-insulin alone.
Data are presented as median values with interquartile ranges (Q1–Q3). Comparisons of continuous variables (HbA1c, BMI, and age) were performed using the Mann–Whitney U test. Gender distribution was compared using Fisher's Exact Test due to the small sample size.

downloads spanning 1–28 February 2025 (pre-Ramadan, 28 days) and 1–29 March 2025 (Ramadan, 29 days) were retrieved from LibreView™. Fasting hours were defined as the dawn-to-sunset window in Abu Dhabi during Ramadan (approximately 05:30–18:00; Fajr to Maghrib) [34], and non-fasting hours as the complementary 18:00–05:30 window. The post-iftar period (18:00–22:00) was pre-specified for incremental area under the curve (iAUC) analyses. Consensus thresholds defined primary endpoints: TIR (70–180 mg/dL), TAR (>180 mg/dL), and TBR (<70 mg/dL) (7). Where available, level 1/2 breakdowns were recorded. CGM validity adhered to established wear-time and data-completeness thresholds to ensure robust estimates.

2.5. CGM data characteristics and statistical Approach

CGM-derived mean and median glucose values reflect interstitial glucose concentrations rather than blood glucose measurements, consistent with prior validation studies. Continuous variables were summarised using medians and interquartile ranges (IQR), while categorical variables were presented as counts and percentages. CGM-derived metrics exhibit skewed and bounded distributions, as widely reported in CGM literature (5–7). Accordingly, all continuous variables were analysed using non-parametric methods. Glycaemic metrics were analysed using non-parametric tests, including the Wilcoxon signed-rank test for within-group comparisons (pre-Ramadan vs Ramadan, and fasting vs non-fasting), and the Mann–Whitney *U* test for between-group comparisons.

In addition to the primary analyses, within-group and between-group comparisons of CGM metrics **during Ramadan** were also performed separately for fasting hours vs non-fasting hours. All tests were two-sided with a significance level of $p < 0.05$, and analyses were conducted using RStudio (Version-2025.09.1 + 401; Posit Software, USA). All pairwise and non-parametric comparisons were adjusted using the Benjamini–Hochberg false discovery rate (FDR) correction.

The study adhered to STROBE reporting principles. The research ethics committee of ICLDEC approved the protocol, and all participants provided informed consent (approval number: IREC110).

3. Results

3.1. Patient demographics

Baseline characteristics of the matched study cohort are summarised in Table 1. A total of 54 participants were included, comprising three matched groups: T2DM on basal–bolus insulin alone (BB, n = 18), T2DM on basal–bolus plus semaglutide or tirzepatide therapy (BB+, n = 18), and T1DM on basal–bolus insulin (T1DM, n = 18). Median HbA1c values were comparable across cohorts (BB: 7.7 % (61 mmol/mol) [7.00–8.90 (53–74 mmol/mol)]; BB + GLP-1: 7.3 % (56 mmol/mol) [7.00–8.00] (53–64 mmol/mol); T1DM: 7.1 % (54 mmol/mol) [6.30–7.90] (45–63 mmol/mol); p = 0.115, Kruskal–Wallis). BMI was also similar between groups (medians 27.2–27.7 kg/m^2; p = 0.996).

Age differed significantly between cohorts (p = 0.001), driven by the younger T1DM group (32.0 years [26.0–44.0]) compared with the two T2DM cohorts (55.0 years [41.0–59.0] in BB and 57.0 years [49.0–62.0] in BB + GLP-1). Gender distribution did not differ significantly (p = 0.286, Fisher's exact test).

Table 2
CGM Metrics: Pre-Ramadan vs Ramadan.

Within-group changes

Cohort	Metric	Pre-Ramadan	*Ramadan*	*p value (within)*
BB	GMI (%)	7.8 [7.0–8.1]	8.3 [7.2–9.1]	0.070
	TAR (%)	53.2 [33.3–60.9]	63.0 [28.4–77.2]	0.070
	TIR (%)	43.8 [38.3–59.7]	36.8 [22.4–71.3]	0.070
	TBR (%)	0.4 [0.0–2.0]	0.1 [0.0–0.5]	0.140
	CV (%)	30.61 [27.92–35.71]	30.51 [26.44–34.59]	0.302
BB+	GMI (%)	6.8 [6.4–7.3]	6.9 [6.3–7.6]	0.877
	TAR (%)	20.5 [9.8–41.0]	24.7 [7.0–46.5]	0.877
	TIR (%)	77.6 [56.9–87.4]	74.4 [51.0–90.1]	0.923
	TBR (%)	1.2 [0.1–2.9]	0.6 [0.2–1.9]	0.349
	CV (%)	29.62 [25.46–32.71]	29.34 [26.87–32.02]	0.965
T1DM	GMI (%)	7.8 [7.0–8.5]	8.3 [7.2–9.1]	0.192
	TAR (%)	48.8 [25.8–65.0]	63.0 [36.1–71.0]	0.129
	TIR (%)	47.8 [33.1–69.9]	36.9 [26.4–60.8]	0.129
	TBR (%)	2.0 [0.0–4.5]	0.7 [0.0–2.8]	0.110
	CV (%)	34.63 [30.89–41.35]	30.91 [29.03–36.50]	0.248

(b) Between-group comparisons

Metric	Comparison	Pre-Ramadan p value	Ramadan p value
GMI (%)	BB vs BB+	0.038	0.004
	BB vs T1DM	0.937	0.790
	BB + vs T1DM	0.039	0.004
TAR (%)	BB vs BB+	0.021	0.008
	BB vs T1DM	0.889	0.879
	BB + vs T1DM	0.021	0.008
TIR (%)	BB vs BB+	0.026	0.007
	BB vs T1DM	0.984	0.820
	BB + vs T1DM	0.026	0.007
TBR (%)	BB vs BB+	0.514	0.021
	BB vs T1DM	0.514	0.351
	BB + vs T1DM	0.633	0.594
CV (%)	BB vs BB+	0.364	0.692
	BB vs T1DM	0.351	0.605
	BB + vs T1DM	0.126	0.497

BB group: Type 2 diabetes patients on Basal-bolus insulin alone.
BB + group: Type 2 diabetes patients on Basal-bolus + Tirzepatide or Semaglutide.
T1DM: Type 1 diabetes patients on Basal Bolus-insulin alone.
(Median [Q1, Q3]) CV: Coefficient of Variation, GMI: Glucose Management Indicator, TAR: Time Above Range, TBR: Time Below Range, TIR: Time In Range.
*p < 0.05 after Benjamini–Hochberg FDR correction.

Table 3
Ramadan period; fasting hours vs non-fasting hours within each group.

Cohort	n_pairs	Metric	Fasting hours Median [IQR]	Non-Fasting hours Median [IQR]	p (BH-FDR)	Sig
BB	18	median_glucose (mg/dL)	200.9 [154.6, 238.8]	235.0 [188.2, 268.3]	0.007	**
BB	18	TIR (%)	40.4 [19.9, 80.5]	22.9 [10.1, 43.7]	0.004	**
BB	18	TAR (%)	59.5 [18.3, 79.6]	77.0 [56.2, 89.9]	0.004	**
BB	18	TBR (%)	0.0 [0.0, 0.4]	0.0 [0.0, 0.1]	1.000	ns
BB	18	CV (%)	26.78 [23.23, 30.59]	28.12 [24.00, 31.66]	1.000	ns
BB+	18	median_glucose (mg/dL)	140.8 [120.0, 172.0]	163.5 [139.1, 191.6]	<0.001	***
BB+	18	TIR (%)	82.2 [55.8, 97.3]	64.3 [40.5, 86.5]	0.002	**
BB+	18	TAR (%)	16.1 [1.6, 43.0]	34.4 [13.1, 56.4]	<0.001	***
BB+	18	TBR (%)	0.5 [0.0, 2.0]	0.9 [0.2, 1.1]	1.000	ns
BB+	18	CV (%)	26.03 [19.69, 30.07]	28.39 [26.89, 32.89]	0.399	ns

BB group: Type 2 diabetes patients on Basal-bolus insulin alone.
BB + group: Type 2 diabetes patients on Basal-bolus + Tirzepatide or Semaglutide.
* $p < 0.05$ after Benjamini–Hochberg FDR correction.

3.2. Pre-Ramadan vs. Ramadan: Within-Group glycaemic changes

Median CGM metrics for each cohort during the pre-Ramadan (February) and Ramadan (March) periods, together with within-group comparisons, are presented in Table 2.

3.2.1. T2DM Basal-bolus (BB)

In the T2DM basal–bolus group, no statistically significant differences were observed in glycaemic metrics during Ramadan compared with the pre-Ramadan period (Table 2A). Median values showed no significant changes in time in range (TIR; 43.8 % vs 36.8 %, p = 0.070), time above range (TAR; 53.2 % vs 63.0 %, p = 0.070) or glucose management indicator (GMI; 7.8 % vs 8.3 %, p = 0.070).

Likewise, the coefficient of variation (CV; 30.61 % vs 30.51 %, p = 0.302) was unchanged, and the trend in time below range (TBR; 0.4 % vs 0.1 %, p = 0.140) did not reach statistical significance (Table 2A).

3.2.2. T2DM Basal-bolus + Tirzepatide or semaglutide (BB +)

In the T2DM BB + group, glycaemic metrics during Ramadan remained comparable to pre-Ramadan values (Table 2A), with no significant changes in TIR (77.6 % vs 74.4 %, p = 0.923), TAR (20.5 % vs 24.7 %, p = 0.877) or GMI (6.8 % vs 6.9 %, p = 0.877).

No significant changes were observed in CV (29.62 % vs 29.34 %, p = 0.965) or TBR (1.2 % vs 0.6 %, p = 0.349) between the pre-Ramadan and Ramadan periods (Table 2A).

3.2.3. T1DM Basal-bolus

In participants with T1DM, no statistically significant differences were observed between the pre-Ramadan and Ramadan periods (Table 2A): TIR (47.8 % vs 36.9 %, p = 0.129), TAR (48.8 % vs 63.0 %, p = 0.129), GMI (7.8 % vs 8.3 %, p = 0.192), CV (34.6 % vs 30.9 %, p = 0.248) and TBR (2.0 % vs 0.7 %, p = 0.110).

3.3. Between-group comparisons: pre-ramadan and ramadan (Table 2)

3.3.1. Pre-Ramadan

Before Ramadan, the BB + group exhibited significantly superior glycaemic control compared with the BB group (Table 2B): TIR was markedly higher (77.6 % vs 43.8 %, p = 0.026), TAR substantially lower (20.5 % vs 53.2 %, p = 0.021) and GMI reduced (6.8 % vs 7.8 %, p = 0.038). No significant differences were observed for CV (p = 0.364) or TBR (p = 0.514).

3.3.2. Ramadan

During Ramadan, the glycaemic advantage of BB + over BB persisted and strengthened (Table 2B): TIR remained higher (74.4 % vs 36.8 %, p = 0.007), TAR lower (24.7 % vs 63.0 %, p = 0.008) and GMI reduced (6.9 % vs 8.3 %, p = 0.004). TBR was significantly lower in BB than in BB+ (0.10 % vs 0.6 %, p = 0.021), while CV remained comparable (p = 0.692).

3.4. Within-Ramadan 'fasting hours vs non-fasting hours' (Table 3)

To explore within-day glycaemic variability during Ramadan, paired analyses compared CGM metrics between fasting and non-fasting windows within the matched T2DM cohorts receiving basal–bolus insulin alone (BB) or basal–bolus plus tirzepatide or semaglutide (BB +).

3.4.1. Basal-bolus (BB)

In the BB cohort (n = 18), median glucose increased from 200.9 mg/dL during fasting hours to 235.0 mg/dL during non-fasting hours (p = 0.007). TIR decreased from 40.4 % to 22.9 % (p = 0.004), while TAR increased from 59.5 % to 77.0 % (p = 0.004). TBR (0.0 % vs 0.0 %, p = 1.000) and the coefficient of variation (CV; 26.78 % vs 28.12 %, p = 1.000) did not differ between periods (Table 3).

3.4.1.1. Basal-bolus + Tirzepatide or semaglutide (BB +). In the BB + cohort (n = 18), median glucose increased from 140.8 mg/dL during fasting hours to 163.5 mg/dL during non-fasting hours (p < 0.001). TIR decreased from 82.2 % to 64.3 % (p = 0.002), while TAR increased from 16.1 % to 34.4 % (p < 0.001). TBR (0.5 % vs 0.9 %, p = 1.000) and CV (26.03 % vs 28.39 %, p = 0.399) did not differ between fasting and non-fasting periods (Table 3).

3.4.1.2. Between-group. Between-group comparisons during Ramadan demonstrated significantly better glycaemic outcomes in the BB + cohort compared with BB across both time windows (Table 3). During fasting hours, BB + showed lower median glucose (140.8 vs 200.9 mg/dL, p = 0.001), higher TIR (82.2 % vs 40.4 %, p = 0.007) and lower TAR (16.1 % vs 59.5 %, p = 0.004). During non-fasting hours, BB + similarly demonstrated lower median glucose (163.5 vs 235.0 mg/dL, p = 0.002), higher TIR (64.3 % vs 22.9 %, p = 0.003) and lower TAR (34.4 % vs 77.0 %, p = 0.006). Between-group differences in TBR were not observed during fasting hours (p = 0.115) but emerged during non-fasting hours (p = 0.001), while CV remained similar between groups in both periods (p = 1.000 for both).

3.5. Pre-Ramadan day–night glycaemic comparisons

To contextualise the Ramadan findings, pre-Ramadan within-day glycaemic variability were examined using paired day–night comparisons.

In the BB cohort (n = 18), no statistically significant differences were observed between day and night periods. Median glucose was 178.0 mg/dL [143.0–185.0] during the day and 195.0 mg/dL [165.0–230.0] at

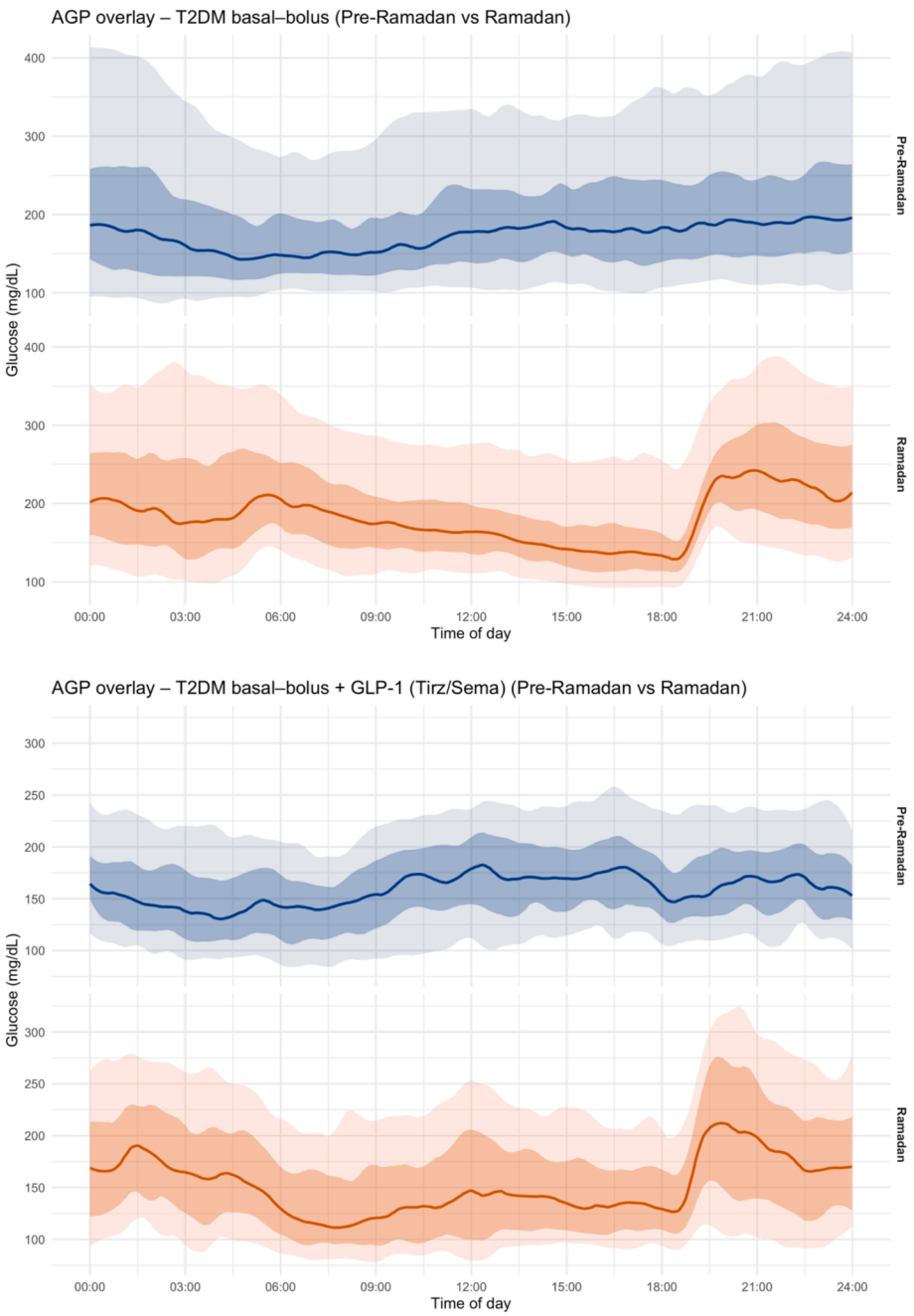


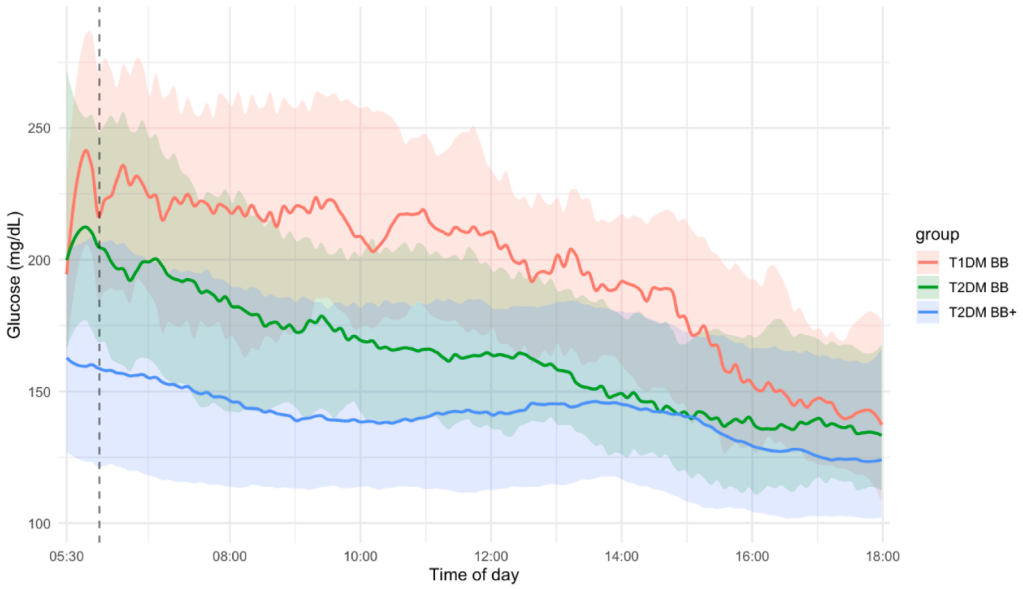
Fig. 1. Ambulatory Glucose Profile (AGP) overlays of T2DM patients comparing Basal–Bolus (BB) and Basal–Bolus plus GLP-1 receptor agonist (BB +) groups before and during Ramadan fasting. Each panel depicts the composite 24-hour ambulatory glucose profile (AGP) for 18 participants within each treatment group. For each cohort, the upper sub-panel represents the pre-Ramadan period and the lower sub-panel represents the Ramadan period. The solid dark line denotes the median glucose (50th percentile). The darker shaded band corresponds to the interquartile range (25th–75th percentiles), while the lighter outer band represents the 5th–95th percentile envelope, illustrating overall glycaemic dispersion. Pre-Ramadan profiles are shown in blue and Ramadan profiles in orange. The x-axis indicates time of day (00:00–24:00), and the y-axis denotes interstitial glucose concentration (mg/dL). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

night (p = 0.332). TIR was 51.1 % [45.9–61.7] during the day and 38.2 % [24.1–59.3] at night (p = 0.340). TAR was 48.8 % [32.4–54.0] during the day and 56.6 % [39.02–75.55] at night (p = 0.330). TBR (0.3 % [0.0–1.0] vs 0.2 % [0.0–1.8]; p = 0.712) and coefficient of variation (CV) (29.97 % [27.13–35.54] vs 29.33 % [26.91–31.74]; p = 0.951) also did not differ between periods.

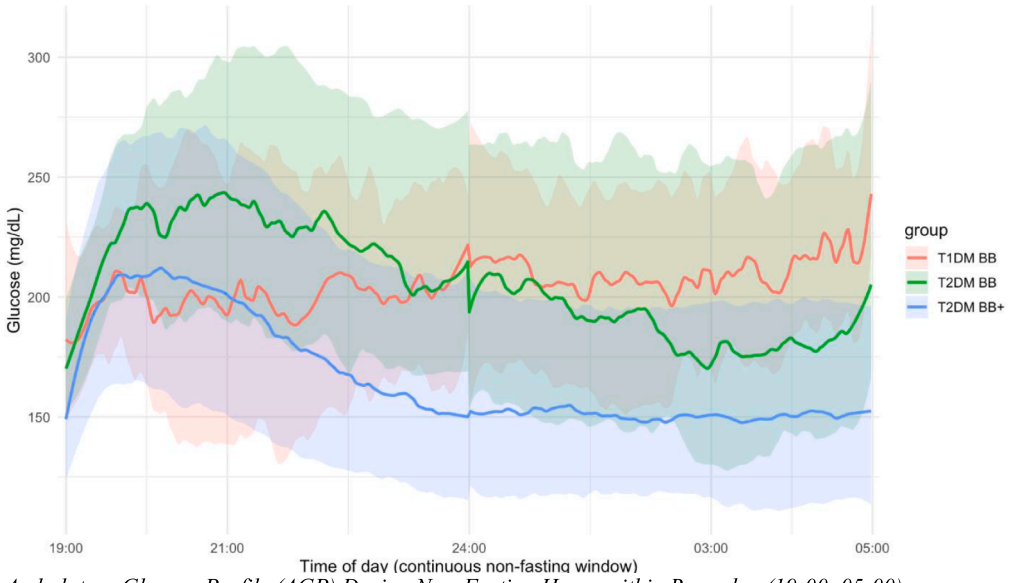
Similarly, in the BB + cohort (n = 18), no statistically significant day–night differences were observed. Median glucose was 143.5 mg/dL [126.0–156.5] during the day and 143.0 mg/dL [119.3–171.6] at night (p = 0.760). TIR was 79.6 % [61.9–86.5] during the day and 77.9 % [49.2–88.2] at night (p = 0.705), and TAR was 18.6 % [11.3–37.2] vs 21.2 % [8.4–42.5] (p = 0.765). TBR (1.2 % [0.0–2.9] vs 0.8 % [0.0–3.1]; p = 0.760) and CV (26.75 % [24.43–31.12] vs 30.81 % [27.42–33.53]; p = 0.460) were also comparable between day and night periods.

4. Discussion

Fasting during Ramadan for patients with diabetes carries risks of hypoglycaemia and hyperglycaemia. In our previous work, we have shown that this risk is highest in insulin-treated patients [9,15]. Work



Ambulatory Glucose Profile (AGP) During Fasting Hours within Ramadan (05:30–18:00).



Ambulatory Glucose Profile (AGP) During Non-Fasting Hours within Ramadan (19:00–05:00).

Median glucose (solid lines) and glycaemic variability (shaded percentile bands) are shown for T1DM BB (red), T2DM BB (green), and T2DM BB+ (blue).

Fig. 2. Ambulatory Glucose Profile (AGP) During Fasting Hours within Ramadan (05:30–18:00) vs Ambulatory Glucose Profile (AGP) During Non-Fasting Hours within Ramadan (19:00–05:00). Ambulatory Glucose Profile (AGP) During Fasting Hours within Ramadan (05:30–18:00). Ambulatory Glucose Profile (AGP) During Non-Fasting Hours within Ramadan (19:00–05:00). Median glucose (solid lines) and glycaemic variability (shaded percentile bands) are shown for T1DM BB (red), T2DM BB (green), and T2DM BB+ (blue). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

from our group and others has shown that a major contributor to Ramadan dysglycaemia is the rapid rise in glucose after iftar [4,9,10,15,19], and that this is more pronounced in insulin-treated patients, regardless of insulin type or regimen [10,15,17,21,35–37].

This real-world CGM-based analysis delineates the distinctive glycaemic challenges imposed by Ramadan fasting in such individuals and demonstrates clinically meaningful benefits of adjunctive semaglutide or tirzepatide therapy. We have shown that Ramadan-associated dysglycaemia is driven predominantly by post-iftar hyperglycaemia. Hypoglycaemia during fasting hours was infrequent in our study population, particularly in the GLP-1RA/Tirzepatide arm. Across cohorts, deterioration in glycaemic control during Ramadan was largely attributable to the non-fasting hours. In BB-treated individuals, TAR and GMI increased and TIR declined (Table 2), with AGP overlays (Fig. 1–4) demonstrating pronounced post-iftar surges and broad evening dispersion. These findings align with prior CGM studies [4,9,10,13,17–19,31,33].

GLP-1 receptor agonists have been available since the approval of exenatide in 2005 and are now established add-on therapies in type 2 diabetes [32]. The dual GLP-1/GIP receptor agonist tirzepatide [38], is the most recent addition to therapeutic options in type 2 diabetes. Both treatment groups have several advantages over older treatment options, including cardiac and renal protection. More important considerations in the context of Ramadan fasting are the positive effects on glycaemic

control and weight reduction. GLP-1RAs and tirzepatide have a specific effect in reducing postprandial glucose excursions, making them an attractive option in individuals with diabetes who practise Ramadan fasting [25,26,30,31,33].

Lixisenatide, oral semaglutide, and tirzepatide have all been studied in the context of Ramadan, showing comparable or superior glycaemic efficacy to sulphonylureas, as measured by HbA1c or fructosamine, with less hypoglycaemia [25,28–31,33,39]. Building on this evidence base, the present study directly compared basal-bolus insulin alone with basal-bolus plus a GLP-1 receptor agonist (semaglutide) or a dual GLP-1/GIP receptor agonist (tirzepatide) in matched insulin-treated T2DM cohorts using CGM-derived metrics.

In the current study, we have examined the nature of the iftar-time glucose excursion more closely through CGM and CGM-derived glucose metrics. There is general acceptance that this iftar effect is at least in part due to dietary factors, particularly carbohydrate-rich, high-glycaemic-index foods consumed at this time. However, other factors may be contributing to this rapid excursion. We postulate that the body may be "primed" through hormonal mechanisms to respond to food in an exaggerated manner at iftar, following a period of prolonged fasting. We have investigated the effect of GLP-1RA or the GLP-1/GIP dual agonist tirzepatide on this effect. Our data confirm that the iftar glucose excursion is blunted when these drugs are added to background basal–bolus insulin treatment.

The BB + group maintained stable TIR and GMI throughout Ramadan and exhibited consistently lower TAR than the BB alone group, with marked attenuation of post-iftar peaks and no excess hypoglycaemia. The incremental post-iftar AUC (iAUC) was reduced by approximately 61 % in BB + versus BB, corresponding to a between-group standardised effect size of approximately 1.0. The known effects of GLP-1RAs on gastric emptying, glucagon suppression and glucose-dependent insulin secretion provide a plausible mechanistic basis for this postprandial blunting. Safety and tolerability of the add-on therapies during Ramadan were favourable in this real-world cohort. There were no episodes of severe (level 3) hypoglycaemia in either group, and the BB + group showed a numerically lower incidence of clinically significant (level 2) hypoglycaemia. No participant in the BB + group discontinued semaglutide or tirzepatide during Ramadan; transient gastrointestinal symptoms (nausea, mild dyspepsia) were occasionally reported but did not lead to dose interruption or impair fasting completion. These observations are consistent with previous Ramadan studies of GLP-1 receptor agonists and dual GLP-1/GIP agonists, which have reported a low risk of hypoglycaemia and predominantly mild, self-limiting gastrointestinal effects [25,28,30,31,33].

Comparison with the T1DM cohort contextualised these findings. T1DM participants displayed intermediate variability, with AGP profiles showing the same post-iftar pattern (Fig. 2), underscoring the universality of evening dysglycaemia during Ramadan. The BB + group outperformed both the T2DM BB-alone and T1DM cohorts in TIR, TAR, and GMI during the pre-Ramadan and Ramadan periods, indicating that pharmacological modulation of postprandial physiology can surpass insulin intensification alone. Pre-Ramadan analyses demonstrate that circadian patterns are not unique to fasting: basal–bolus-treated individuals exhibited greater nocturnal and postprandial instability even before Ramadan, whereas those receiving adjunctive semaglutide or tirzepatide showed minimal day–night divergence. Ramadan therefore amplifies an existing evening vulnerability in insulin-only regimens.

It has to be borne in mind that this study was non-randomised by design and, as such, was prone to potential residual confounding from unmeasured factors such as dietary composition, physical activity, and patient-driven insulin adjustments. The observation window was limited to one pre-Ramadan month and the Ramadan period itself. Patient-reported outcomes and detailed dietary data were not collected. These limitations can be addressed in future studies. It is also important to emphasise that although in the settings of the study hypoglycaemic episodes were infrequent, hypoglycaemia does remain a major concern in patients with diabetes opting to fast during Ramadan, and in particular needs preventative measures in insulin and/or sulphonylurea patients, as per recent guidelines by the Diabetes and Ramadan Alliance, International Diabetes Federation, and the American Diabetes Association [1,5,6,40].

To our knowledge, this is the first CGM-based evaluation of semaglutide or tirzepatide as adjuncts to basal–bolus insulin during Ramadan. Key strengths include the pragmatic, real-world design using routine-care CGM, the explicit partitioning of glycaemia into fasting and non-fasting windows during Ramadan, matched cohorts for primary comparisons of T2DM, and the integration of conventional CGM metrics with AGP visualisation. The demonstration that GLP-1RA co-therapy attenuates post-iftar excursions without increasing hypoglycaemia supports clinical adoption.

In conclusion, this real-world CGM analysis demonstrates that Ramadan-associated dysglycaemia in insulin-treated patients is driven predominantly by post-iftar hyperglycaemia, and that adjunctive semaglutide or tirzepatide therapy confers substantial protection against evening excursions without excess hypoglycaemia. These results provide actionable guidance for clinicians and support the integration of GLP-1RA co-therapy into personalised Ramadan care pathways for individuals requiring intensive insulin therapy.

CRediT authorship contribution statement

Tanveer Ashraf: Writing – original draft, Visualization, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Nader Lessan:** Writing – review & editing, Supervision, Project administration, Conceptualization.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The authors would like to thank the Imperial College London Diabetes and Endocrine Centre (ICLDEC), Abu Dhabi, UAE, for providing the infrastructure and institutional support that made this study possible. We are grateful to all study participants for their commitment and cooperation during both the pre-Ramadan and Ramadan phases, and the patient recruitment team.

Dalia Haj: Patient recruitment.
Haya AlKarbi: Patient recruitment.
Magda Alfukaha: Patient recruitment.
Sameera AlAhmed: Patient recruitment.

Ethics approval

The research ethics committee of ICLDEC approved the protocol (approval number: IREC110). All participants provided informed consent.

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