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Investigating physiological glucose excursions before, during, and after Ramadan in adults without diabetes mellitus

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ABSTRACT

Aim: The study aimed to investigate physiological effects of Ramadan fasting on continuously monitored glucose levels in relation to Ramadan in young non-diabetic adults.

Methods: Continuous glucose monitoring was employed to measure interstitial glucose for several days 1–2 weeks before Ramadan, in the middle of Ramadan, and 4–6 weeks after Ramadan to assess glucose exposure and glucose variability.

Results: A total of 34,182 accurate glucose sensor readings and 438 capillary blood glucose values [mean absolute difference median (interquartile range) 8.5 (6.9–11.1)%] were obtained from 18 non-diabetic adults [13 females; aged 24 (21–27) years; baseline body mass index 23.9 (20.6–28.9) kg/m^2]. The continuous glucose monitoring profiles showed an increase in the hyperglycemic (above 140 mg/dL) area under the curve after Ramadan compared to both before ($P = 0.004$) and during Ramadan ($P = 0.003$), along with an increased glucose variability after Ramadan ($P = 0.014$). Both the area under the interstitial glucose concentration curve for the entire day and the average glucose were positively associated with body mass index during ($P = 0.004$ and $P = 0.005$, respectively) and after Ramadan ($P = 0.013$ and $P = 0.01$, respectively). Atypical continuous glucose patterns were recognized in 11% of subjects, distinguished by a prolonged increased glucose exposure, particularly in response to a meal.

Conclusion: The time-point 4–6 weeks after Ramadan was distinguished by greater glucose exposure and wider glucose variability that may reflect ongoing changes in insulin sensitivity in response to altering lifestyle patterns in non-diabetic young adults across the spectrum of body weight.

1. Introduction

Fasting (Sawm) is practiced globally during the Islamic holy month of Ramadan by many healthy post-pubertal followers of Islam, the world's second largest religion with an estimated 1.6 billion followers [1]. During Ramadan, there is complete abstinence from eating and drinking from dawn until sunset, and no food or fluid restriction between sunset and dawn. At sunset, the daily fast is broken at Iftar, the evening meal. While Iftar usually replaces the traditional three meals spread across the day, meals are also often consumed after Iftar, later during the night [2]. Prior to sunrise, Muslims have the morning meal (Suhur), which is the last meal eaten before fasting from dawn to sunset. Because of the use of the lunar calendar, the dates for Ramadan change annually. Also, the duration of the daily fast varies across the globe with differences in timings of dawn and sunset.

There are several social and biological changes observed during Ramadan, including alterations in chronobiology [3], sleep [2], diet [4], and physical activity. The biological changes observed with Ramadan are influenced by social practices that determine work, activity, eating, and sleeping behaviors. The most widely studied changes with

Abbreviations: AUC, area under the curve; $AUC_{above140}$, the hyperglycemic area under the interstitial glucose concentration curve (above 140 mg/dL) normalized for a 24-hour period; $AUC_{below70}$, the hypoglycemic area under the interstitial glucose concentration curve (below 70 mg/dL) normalized for a 24-hour period; BMI, body mass index; CGM, continuous glucose monitoring; CI, confidence interval; CV, coefficient of variation; DEXA, dual energy X-ray absorptiometry; HbA1c, glycated hemoglobin; LAGE, largest amplitude of glycemic excursion; SD, standard deviation; total AUC, the area under the interstitial glucose concentration curve for the entire day

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Ramadan include alterations in body weight, fasting blood glucose, and lipid profile. With respect to glucose levels, there has been a research focus on those with type 2 diabetes mellitus. There is much less evidence surrounding the potential glycemic alterations during Ramadan in a non-diabetic population.

To gain insight into physiological changes with Ramadan and potential effects beyond Ramadan, the aim of this study was to investigate glucose excursions, using continuous glucose monitoring, in non-diabetic healthy young fasting adults across three time-points: (I) before Ramadan, (II) during Ramadan, and (III) after Ramadan. To date, there are no studies that have continuously monitored glucose levels and glucose variability before, during and after Ramadan in non-diabetic individuals.

2. Subjects, materials and methods

2.1. Study design and setting

The study was part of a study to examine the impact of Ramadan fasting on body weight and composition. This was a single-center, prospective, observational study conducted at the Qatar Biobank in Doha, Qatar in 2014. The study incorporated the following three data collection time-points (from 15 June 2014 to 18 September 2014): (i) 1–2 weeks before Ramadan, (ii) in the middle of Ramadan, and (iii) 4–6 weeks after Ramadan.

The study participants were recruited from within Qatar through multimedia advertisement, and by providing study information to interested individuals in local shopping malls. All subjects provided written informed consent before participating in the study. The study was approved by the Weill Cornell Medicine-Qatar and Hamad Medical Corporation Joint Institutional Review Board. The research has been carried out in accordance with the principles of the Declaration of Helsinki.

2.2. Participants

The study included young Muslim adult (18–40 years old) men and women without diabetes mellitus who planned to fast during Ramadan. Shift workers, pregnant women, those with severe obesity (body mass index, BMI $\geq$ 35 kg/m^2), obesity-related complications, chronic diseases, terminal illness, and conditions that precluded accurate assessment of continuously monitored glucose response to fasting were excluded.

During the recruitment visit (during the month before Ramadan), prospective subjects attended the Qatar Biobank where details of the study were discussed and written informed consent was obtained. Recruited subjects were assessed for eligibility through several assessments, including measurements of body weight, body height, blood pressure, fasting or random blood glucose, obtaining medical history, and completing an interviewer-administered screening questionnaire to obtain demographics and lifestyle information. Study participants were selected on the basis of having no history of diabetes and a fasting glucose level $\leq$ 100 mg/dL or non-fasting blood glucose level $\leq$ 140 mg/dL.

2.3. Continuous glucose monitoring and outcomes

The study participants underwent continuous glucose monitoring (CGM) using the iPro2 Professional retrospective CGM system (Medtronic MiniMed; Northridge, CA). Based on previous experience, CGM sensor was inserted subcutaneously to the lower back to avoid any interference with Muslim prayers. The CGM system was employed to measure and record blinded interstitial glucose values for a minimum of three consecutive days 1–2 weeks before Ramadan, in the middle of Ramadan, and 4–6 weeks after Ramadan. The sensor calibration was accomplished during CGM data upload by entering self-monitored blood glucose values measured by One Touch Ultra 2 blood glucose meter (LifeScan, Inc., Milpitas, CA). Participants were instructed to measure and record their finger stick glucose levels at least three times a day (approximately every 8 h) for calibration purposes, complete a brief food/activity log, and return to the research center on assigned dates for the CGM data upload.

The performance and accuracy of the iPro2 CGM system was assessed using the Optimal accuracy criteria for CGM glucose data [5] calculated by CGM software from glucose sensor and glucose meter data for each day the sensor was worn. The investigated CGM measures and indicators included the area under the interstitial glucose concentration curve (AUC) for the entire day (total AUC), the hypo- (below 70 mg/dL) and hyperglycemic (above 140 mg/dL) AUCs normalized for a 24-hour period, the average and ranges of the sensor glucose readings, largest amplitude of glycemic excursion (LAGE, *maximum glucose-minimum glucose*), the J-index, $J\text{-}index = 0.001 \times (mean + SD)^2$ [6], and continuous glucose variability as indicated by glucose standard deviation (SD) and coefficient of variation (CV).

2.4. Dual energy X-ray absorptiometry

At each of the study visit, participants underwent a full body dual energy X-ray absorptiometry (a DEXA scan). A range of body composition outcomes were assessed at each time-point, including: total mass, total fat mass, total lean mass (sum of all muscle and soft organ tissue), total fat free mass, total tissue mass, total tissue % fat, estimated total visceral adipose tissue mass and volume, and total bone mineral content (sum of all skeletal tissue within the body).

2.5. Statistical methods

Demographic characteristics and outcome data were summarized with frequencies and percentages for categorical variables and medians (interquartile ranges) or mean $\pm$ standard error for continuous variables. Repeated measures ANOVA using a linear mixed model was used to compare the changes in CGM indicators and body composition outcomes at various time-points, taking account of within-subject variability over time. The normality of residuals was assessed by examining a histogram and a quantile-quantile normal plot after the linear mixed model was constructed. The residuals were normal for all variables, only the $AUC_{above140}$ required natural log-transformation using ln ($AUC_{above140}$ + 1). Post hoc pairwise comparisons were performed as necessary with Bonferroni adjustment. Bivariate analyses (non-parametric Spearman's correlation and regression analyses) were utilized to examine relationships between CGM outcomes and their potential predictors. Findings were considered to be statistically significant at the 5% level. Statistical analyses were performed using Stata Special Edition Version 13.1 (StataCorp LP, College Station, TX).

3. Results

A total of 21 non-diabetic adults who met eligibility criteria were recruited and underwent CGM. Three out of 6 subjects who underwent only pre-Ramadan CGM had inaccurate results due to the sensor's low intrinsic signal and/or missing valid calibration glucose readings, and were excluded from analyses. Out of the 18 subjects with accurate CGM results, 12 successfully completed CGM at all three time-points (before, during and after Ramadan) and 15 during the two time-points (during and after Ramadan). Out of the 18 subjects with accurate CGM results, 14 underwent DEXA scans at all three time-points and 1 at two time-points (before and after Ramadan).

The baseline characteristics of study participants (N = 18) are presented in Table 1. The baseline BMI of study participants ranged from 19.0 to 24.7 kg/m^2 in men and from 17.3 to 33.7 kg/m^2 in women. All participants were normotensive (mean arterial pressure 72.0 to 100.3 mmHg). The duration of the daily daytime fast during

Table 1
Baseline characteristics of study participants (N = 18).

Sex	
● Female	13 (72%)
● Male	5 (28%)
Ethnic origin	
● Non-white	12 (67%)
● White	2 (11%)
● Unknown[a]	4 (22%)
Age (years)	24 (21–27)
Baseline BMI (kg/m^2)	23.9 (20.6–28.9)
Systolic blood pressure (mmHg)	118 (113–126)
Diastolic blood pressure (mmHg)	69 (61–71)
Mean arterial blood pressure (mmHg)	84 (80–89)

Data expressed as N (%) or median (interquartile range).
BMI, body mass index.
[a] 4 subjects were labelled as "Unknown" because the subjects declined to disclose their ethnic origin.

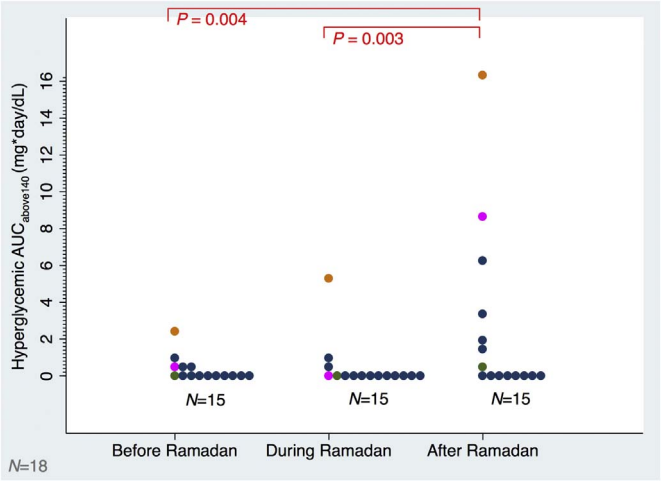

Fig. 1. Hyperglycemic AUC at the three time-points.
A significantly increased hyperglycemic exposure indicated by the hyperglycemic area under the continuously monitored interstitial glucose concentration curve (above 140 mg/dL) after Ramadan compared to both before and during Ramadan.
$AUC_{above140}$, the hyperglycemic area under the interstitial glucose concentration curve (above 140 mg/dL) normalized for a 24-hour period. *Green dots* - Case 1, *Orange dots* - Case 2, *Magenta dots* - Case 3. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Ramadan was 15 h on average.

A total of 34,182 accurate CGM sensor readings (median duration 66 h) and 438 capillary blood glucose values [mean absolute difference median (interquartile range) 8.5 (6.9–11.1) %] were obtained from the 18 subjects. Since blood glucose meter reading ranges were < 100 mg/dL, the correlation (one of the optimal accuracy criteria) was reported as N/A and was not evaluated.

The CGM indicators of glucose exposure and glucose variability at the three time-points are presented in Table 2. The CGM profiles showed a significant increase in the hyperglycemic $AUC_{above140}$ after Ramadan compared to both before (P = 0.004) and during Ramadan (P = 0.003; Fig. 1). The results showed the subjects were, on average, 2.54 mg/dL above the upper-level glucose threshold for the entire day after Ramadan. Besides the greater hyperglycemic exposure after Ramadan, the CGM results also uncovered an increased glucose variability after Ramadan than before Ramadan as indicated by SD (P = 0.014). Changes in two mean-dependent outcomes (CV% and J-index) across the three time-points did not reach statistical significance (P = 0.053 and P = 0.052, respectively). There were no significant differences in the highest-, lowest-, average sensor readings, LAGE, total AUC, and $AUC_{below70}$ across the three time-points. No statistically significant changes in body weight, BMI, and all body composition outcomes were detected (Tables 2 and 3).

Bivariate analyses were performed to explore associations between the spectrum of BMI and various CGM outcomes. The analyses showed that both the total AUC and the average glucose were positively associated with the BMI during (P = 0.004 and P = 0.005, respectively) and after Ramadan (P = 0.013 and P = 0.01, respectively). No significant correlation was found between BMI and CGM outcomes before Ramadan.

Interestingly, three individuals (*Cases 1–3*) had total AUC after Ramadan increased above 2421 mg * day/dL, which has previously been reported as the mean total AUC for adults with normal glucose tolerance [7]. *Case 1* (32-year-old female, BMI 26.7 kg/m^2, $AUC_{above140}$

Table 2
Glycemic control across the three time-points (N = 18).

CGM indicators	Pre-Ramadan	During Ramadan	Post-Ramadan	P
Glucose exposure and variability				
CGM duration (hours)	64 (54.8–68.4)	70 (67.3–70.8)	64 (56.3–67.7)	0.279
Total sensor readings (N per subject)	768 (658–821)	834 (808–849)	768 (675–812)	0.279
Highest sensor reading (mg/dL)	128 (124–149)	133 (120–140)	134 (124–163)	0.177
Lowest sensor reading (mg/dL)	66 (62–74)	62 (57–68)	65 (58–69)	0.173
Average sensor reading (mg/dL)	95 (90–97)	92 (90–95)	95 (86–99)	0.111
LAGE (mg/dL)	62 (48–86)	66 (55–84)	66 (57–102)	0.231
J-index	11 (9.8–12.5)	11 (10–11.7)	12 (9.4–12.6)	0.052
SD (mg/dL)	10 (9–14.1)	13 (10–14)	13 (11–19)	**0.042**
CV%	11 (9.4–14.8)	14 (10.9–17.7)	13 (12.9–17.3)	0.053
Total AUC (mg * day/dL)	2268 (2167–2329)	2198 (2149–2272)	2284 (2052–2366)	0.113
$AUC_{below70}$ (mg * day/dL)	0.3 (0–2.19)	1.9 (0.07–3.8)	0.6 (0.08–3.79)	0.227
$\ln(AUC_{above140} + 1)$[a]	0.21 ± 0.094	0.18 ± 0.125	0.72 ± 0.255	**0.003**
CGM Sensor Optimal Accuracy				
Mean absolute difference (%)	7.4 (5.1–10.5)	9.1 (7.3–14.2)	9.6 (8.1–11.8)	0.059
Valid calibrations (N per subject)	10 (8–12)	10 (8–11)	10 (8–11)	0.687
Anthropometrics				
Body weight (kg)	64.6 (56.7–71.6)	62.2 (56.2–70)	64 (56.5–70.2)	0.290
BMI (kg/m^2)	23.9 (20.6–28.9)	22.8 (20–25.7)	23.6 (20.2–28.8)	0.274

Data expressed as median (interquartile range) unless otherwise stated.
$AUC_{above140}$, the hyperglycemic area under the interstitial glucose concentration curve (above 140 mg/dL) normalized for a 24-hour period; $AUC_{below70}$, the hypoglycemic area under the interstitial glucose concentration curve (below 70 mg/dL) normalized for a 24-hour period; *BMI*, body mass index; *CGM*, continuous glucose monitoring; *CV*, coefficient of variation; *LAGE*, largest amplitude of glycemic excursion; *SD*, standard deviation; *total AUC*, the area under the interstitial glucose concentration curve for the entire day.
The P values in bold are statistically significant at the 5% level.
[a] Mean ± standard error.

Table 3
Body composition across the three time-points (N = 15).

	Pre-Ramadan (N = 15)	During Ramadan (N = 14)	Post-Ramadan (N = 15)	P
Body mass index (kg/m^2)	23.2 (20.3–28.9)	22.8 (20–25.7)	23.6 (20.2–28.8)	0.276
Total mass (kg)	64.6 (56.7–71.6)	62.2 (56.2–70)	64 (56.5–70.2)	0.290
Total fat mass (g)	20,391 (11762–34,065)	20,543 (12117–26,772)	20,525 (12641–34,935)	0.550
Total lean mass (g)	37,452 (32269–45,690)	36,971 (32212–45,269)	37,424 (31814–45,031)	0.610
Total bone mineral content (g)	2292 (2134–2531)	2291 (2135–2397)	2288 (2137–2555)	0.199
Total fat-free mass (g)	39,767 (33886–46,148)	39,179 (34100–44,775)	39,737 (34108–46,690)	0.637
Total tissue (g)	61,786 (53347–68,034)	59,628 (53785–66,290)	61,238 (53930–67,362)	0.758
Total tissue fat (%)	36 (18.7–46.6)	34.7 (18.8–44.4)	35.8 (18.8–48.5)	0.622
Total estimated visceral adipose tissue volume (cm^3)	260 (150–514)	235 (124–581)	261 (108–634)	0.115
Total estimated visceral adipose tissue mass (g)	246 (142–485)	222 (117–548)	246 (102–598)	0.117

Data expressed as median (interquartile range).
Outcomes measured using a dual energy X-ray absorptiometry scan.

shown by *green dots* in Fig. 1) had other CGM indicators within normal ranges suggesting normal glucose exposure and glucose variability at all three time-points. *Case 2* (24-year-old female, BMI 28.9 kg/m^2, $AUC_{above140}$ shown by *orange dots* in Fig. 1) demonstrated a pattern with a normal glucose exposure before Ramadan (total AUC 2388 mg * day/dL, average glucose 100 mg/dL, $AUC_{above140}$ 2.57 mg * day/dL, J-index 14.4), greater glucose exposure during Ramadan (total AUC 2478 mg * day/dL, average glucose 103 mg/dL, $AUC_{above140}$ 5.31 mg * day/dL, J-index 15.1), continuing after Ramadan (total AUC 2597 mg * day/dL, average glucose 108 mg/dL, $AUC_{above140}$ 16.5 mg * day/dL, J-index 17.4). *Case 3* (30-year-old female, BMI 33.7 kg/m^2, $AUC_{above140}$ shown by *magenta dots* in Fig. 1) showed the highest glucose exposure before Ramadan (total AUC 2771 mg * day/dL, average glucose 115 mg/dL, $AUC_{above140}$ 0.39 mg * day/dL, J-index 15.6), followed by overall improvement during Ramadan (total AUC 2278 mg * day/dL, average glucose 95 mg/dL, $AUC_{above140}$ 0.0 mg * day/dL, J-index 11.7) and return back to deteriorated glucose control after Ramadan (total AUC 2653 mg * day/dL, average glucose 111 mg/dL, $AUC_{above140}$ 8.47 mg * day/dL, J-index 16.9).

The CGM pattern of 12 participants whose total glucose exposure (total AUC) after Ramadan was in the normal range (ranging from 1943 to 2366 mg * day/dL) was distinguished by wider glucose variability during Ramadan, reaching its maximum after Ramadan (SD ranging from 8 to 20 mg/dL, CV% ranging from 9.9 to 19.8%, LAGE ranging from 43 to 107 mg/dL).

Incomplete food and activity data from the most of the study participants precluded any assessments of preprandial-, postprandial-, or activity-related glucose outcomes. However, no changes in body composition were noted.

4. Discussion

The primary findings of this study were dynamic changes in glucose control after Ramadan in healthy non-diabetic young adults. The changes were characterized by an increased duration and severity of hyperglycemia after Ramadan, accompanied by an increased variability in continuously monitored glucose levels in the entire cohort.

The most striking secondary observations were two types of glucose patterns (typical and atypical) discerned from the comprehensive CGM analysis. The patterns, characterized by dynamic glucose changes, may reflect some of the mechanisms underlying glucose regulation and early alterations in glucose metabolism healthy young adults. The majority of our study participants had *a typical CGM pattern* characterized by both normal glucose exposure and variability that did not exceed clinically significant thresholds [7–10], or change across the three time-points. *The atypical CGM pattern* was recognized in 2 out of 18 (11%) subjects. It was distinguished by the prolonged increased glucose exposure, particularly in response to a meal (mild postprandial hyperglycemia, followed by late postprandial hyperglycemia). Remarkably, the fasting CGM glucose levels at the three time-points remained normal, suggesting that sufficient insulin action was present to counterbalance the glucagon-mediated hepatic glucose output. The atypical CGM pattern in non-diabetic individuals might suggest early impairment of the acute insulin release following a glucose load. The impairment of the first phase insulin release is a key initial defect early in the pathogenesis of type 2 diabetes, and can precede the development of clinical hyperglycemia by years or even decades [11].

Several studies have already investigated the impact of Ramadan fasting on health-related outcomes in healthy individuals [12–16] and in those with various diseases, including diabetes [17–23]. The studies investigating effects of Ramadan fasting on fasting blood glucose in non-diabetic adults with normal body weight (16 studies with a total of 776 participants) were meta-analyzed [14] and showed a reduction in fasting glucose levels during Ramadan with the overall pooled standardized weighted mean difference of − 1.10 mg/dL (95% confidence interval/CI = − 1.62 to − 0.58 mg/dL, P = 0.001) [14]. In our study, we did not separately evaluate morning fasting glucose at the three time-points. The major drawback to evaluating morning “fasting” glucose during Ramadan is the nocturnal eating period followed by a postprandial state after the last food intake, usually at dawn (Suhur). Therefore, the interpretation of morning “fasting” glucose during Ramadan can be difficult to interpret as many individuals are still in the postprandial or early post-absorptive state at the time of the test. Aware of this pitfall, Gnanou et al. [24] assessed Ramadan effects on glucose homeostasis in 20 young healthy Malaysian men with normal body weight. They reported decreases in body weight, BMI, plasma glucose, insulin and adiponectin as well as increases in insulin sensitivity (P < 0.01 for all) measured at 1 pm, after 8 h of daylight fasting during Ramadan [24]. Despite its limitations, the study [24] demonstrates a beneficial acute effect of Ramadan fasting on glucose homeostasis in young non-diabetic adults. Future research should establish whether increases in insulin sensitivity during Ramadan are also present in overweight and obese individuals and if so, to what extent and duration.

To date, several Ramadan studies utilized CGM technology in various diabetes populations [25–29]. Only one diabetes study [28] also enrolled non-diabetic controls (N = 7; aged 36.2 ± 13.4 years; BMI 26.6 ± 2.6 kg/m^2). The authors did not find any differences in evaluated CGM indicators between Ramadan and non-Ramadan (either before or after Ramadan) periods [28]. Of note, the conclusions [28] were based on comparisons of selected CGM indicators at non-standardized two time-points only, with a cut-off for hyperglycemia of ≥ 150 mg/dL that was much higher than in our study. The cut-offs deployed in our study were based on previously published normative ranges for tissue glucose derived from CGM for subjects without diabetes [7–10]. The current study supports and extends previously reported results [28] by providing more comprehensive evaluation of glucose exposure and glucose variability that were increased after Ramadan.

Limited data exist on continuously monitored glucose exposure and

glucose variability in healthy adults outside of Ramadan/other types of religious fasting [7–9,30–34]. Our results are in agreement with a previous A1C-Derived Average Glucose observational study [30] that identified pre-diabetic continuously monitored glucose levels in 10% of non-diabetic subjects. In our study, 2 (~11%) non-diabetic young adults showed atypical glucose profiles resulting in estimated glycated hemoglobin/HbA1c (calculated from CGM sensor glucose data) in the pre-diabetic range. These CGM findings add substantially to our understanding of what constitutes a normal glucose profile. It is possible that more in depth investigation into the course of continuously monitored glucose levels (over 72–144 h) will provide novel avenues for effective screening and early detection of pre-diabetes.

Several possible factors and mechanisms could help explain the observed changes in glucose profiles. These include, but are not limited to altered dietary behaviors with a shift in the timing, decreased frequency and increased quantity of meals, disrupted sleep patterns and sleep restriction [2] that reduced insulin sensitivity in otherwise healthy subjects [35], disruption of endocrine circadian rhythms (cortisol, thyrotrophin, melatonin, growth hormone) [3], disruption of a balance between circulating levels of insulin and glucose counter-regulatory hormones during extended periods of fasting and unlimited energy intake [36], and changes in hormones regulating energy intake (e.g., ghrelin involved in hunger/control of meal size) and early- (e.g. glucagon-like peptide 1, peptide tyrosine tyrosine, cholecystokinin, insulin, amylin, etc.) and late- (e.g. leptin) post-ingestive control of satiety (control of inter-meal interval) [37].

With respect to dietary patterns, Ramadan fasting consists of alternate fasting and feasting periods - “the feast period” from sunrise to sunset, when food abstainers may consume food ad libitum, and “the fast period” during the daylight hours with absolute food-, fluid-, smoking, medications, and other restrictions. Besides the variability in daily fasting time and the seasonal shift, cultural differences with respect to habits and diet can influence the peri-Ramadan health-related outcomes [4]. Increased energy intake has been reported in Moroccan men [38] and in Saudi [39] and Tunisian [40] healthy men and women, whereas unchanged intake in healthy Tunisian [41] and Jordanian women [42] and in men and women in United Arab Emirates [43].

Finally, significant dysglycemia and deranged CGM profiles have been reported in obese first-degree relatives of type 2 diabetes patients [34]. Although we did not collect the family history of diabetes, our findings support the previous observations of non-diabetic dysglycemia [34].

Whilst our study is the first to examine the physiological acute and chronic effects of Ramadan fasting upon continuous monitoring of glucose in healthy adults across three time-points, several potential limitations need to be considered. The study needs to be replicated in a larger sample. Unfortunately, we could not obtain sufficient food intake and activity data records from the participants, which precluded assessments of preprandial-, postprandial-, and activity-related glucose outcomes. As expected, the sensor's low intrinsic signal and/or missing calibrations in some of the participants resulted in missing or inaccurate CGM data that were excluded. Other limitations of the iPro2 device used include the physiological gap between the interstitial and blood glucose readings (10–15 min) and the dependence on the accuracy of the glucose meter used [44]. Barriers to adoption, adherence, and effectiveness of iPro2 in the present study consisted of the procedure to apply the sensor, subject's level of numeracy and literacy, and lack of adherence to calibration and food/activity diary completion. Furthermore, the present study was limited by formal testing for glucose intolerant states. Finally, the study has only investigated glucose responses to Ramadan fasting in the state of Qatar. Consequently, the findings might not be representative of and generalized to other Muslim populations.

In summary, our work has outlined the physiological acute and chronic effects of Ramadan fasting on continuously monitored glucose levels and circadian glucose profiles in young adults without diabetes. The findings suggest that greater glucose exposure and wider glucose variability 4–6 weeks after Ramadan may occur as part of physiological responses to unlimited energy intake after extended periods of restricted feeding. Future study needs to examine the durability of the observed glucose changes and their clinical implications. Furthermore, it needs to be examined whether specific diet and lifestyle advice during Ramadan will prevent the subsequent greater glucose exposure after Ramadan. Further research and improved understanding of the continuously monitored glucose patterns can provide novel avenues for early detection of prediabetes and facilitate timely prevention efforts.

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Disclosure of interest

MP, HZ, TA, SMC, OO and OC declare that they have no conflicts of interest concerning this article. ST has served on an advisory board for Novo Nordisk.

Author contributions

MP substantially contributed to the conception of the CGM aspects of the study, participated in analysis and interpretation of data, and prepared the first draft. HZ, TA, SMC and OC participated in acquisition of data and conduct of the study and helped to draft the manuscript. OO performed the statistical analysis and helped to draft the manuscript. ST conceived the study and participated in the design, coordination, and conduct of the study, and helped to draft the manuscript. All authors revised the article critically for important intellectual content and approved the final version.

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