Ramadan in Egyptian people with type 2 diabetes: effect on cardiometabolic parameters

HANAN M AMER,[1] YARA M EID,[1] MARAM MM ABOROMIA,[1] YOMNA KABANY[2]

Abstract

Background: Most Muslims with diabetes have a strong desire to fast during the month of Ramadan but some cannot perform it because of the risk of complications such as hypoglycemia, hyperglycemia, diabetic ketoacidosis, dehydration and thrombosis. During Ramadan, the meal pattern and fluid intake are markedly altered and there are delayed and shortened periods of sleep. These changes in meal and sleep rhythm could lead to undesirable changes in metabolism and increased risk of complications.

Aims: To study the effect of Ramadan fasting on metabolic parameters and cardiovascular disease risk in patients with type 2 diabetes mellitus (T2D).

Methods: This cohort study was conducted on 80 people with T2D who were intending to fast during Ramadan in the year 2014; the average number of fasting hours was 15 hours. They were subjected to clinical, anthropometric and laboratory evaluation before and after Ramadan.

Results: There were significant increases between pre- and post-Ramadan total cholesterol levels (3.77±1.19 mmol/l vs 5.24±1.03 mmol/l, p< 0.001), triglycerides (1.7±0.95 mmol/l vs 2.22±1.51 mmol/l, p< 0.004), LDL-C (2.03±1.08 mmol/l vs 3.04±1.19 mmol/l, p< 0.001), fasting insulin (6.1±3.7 mu/l vs 12.6±8.2 mu/l, p<0.001), HOMA IR (2.42±1.6 IU vs 7.02±8.9 IU, p< 0.001), creatinine (71.62±17.68 umol/l vs 83.11±26.53 umol/l , p< 0.001), systolic blood pressure (SBP) (134.9±10.8 mmHg vs 141.2±11.9 mmHg , p< 0.001) and diastolic blood pressure (DBP) (94.7±10.7 mmHg vs 101.8±11.3 mmHg, p < 0.001). The 10-year cardiovascular disease risk increased from 5.18±7.8 to 7.6±9.9 (p< 0.001). There was no significant change in body mass index.

Conclusion: Ramadan fasting in Egyptian people with T2D appears to have a significant effect on lipid profiles and blood pressure that could adversely impact cardiovascular risk. Current guidance is more focused on glycemic control, with adjustments to oral hypoglycemic agents and insulin dose. Cardiovascular disease risk assessment and guidance prior to Ramadan fasting should not be overlooked.

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Key words: Ramadan, cardiometabolic parameters, type 2 diabetes mellitus

[1] Ain-Shams University Hospitals Internal Medicine department, Cairo, Egypt
[2] National Diabetes Institute, Cairo, Egypt.

Address for correspondence: Professor Dr Yara M Eid
Internal Medicine, Ain Shams University, El-Demerdash street, El Weili, Cairo Governorate 4390042
E-mail: dryara_eid@med.asu.edu.eg

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Background

More than one billion Muslims worldwide fast during Ramadan, which is a month during which they abstain from eating, drinking and smoking from dawn to sunset. During Ramadan there are changes in the quality of food, eating and sleep patterns, physical activity and hydration which might have an impact on the risk of cardiovascular diseases.[1] These changes may include the consumption of more carbohydrates and sweet food, mainly in the form of two large meals at dawn and sunset. It has been established that a given nutrient ingested at an unusual time can induce different metabolic effects but the physiological changes in Ramadan are not well known.[2]

The shifting of the eating pattern toward a nocturnal one impacts the cardiometabolic milieu profoundly.[3] These changes are accompanied by neurohormonal alterations induced through activation of the hypothalamic-pituitary axis which results in increased secretion of catecholamines and cortisol, and they consequently could affect endothelial function, atherosclerotic heart disease and stroke risk.[4]

The most common risk factors associated with increased risk of atherosclerotic heart disease or stroke are abnormalities in plasma lipids and some coagulation and haemostatic factors, hypertension and smoking. Lipid profiles are affected by factors such as changes in dietary habits including consuming different dietary fats and increased consumption of refined sugar, and by reduced physical activity.[1] Though studies in healthy subjects have shown a beneficial effect on lipid profiles, there are few studies concerning lipid profile changes and its impact on cardiovascular risk in people with T2D during Ramadan fasting.[3]

Similarly, studies on the effect of Ramadan fasting on non-traditional cardiovascular risk factors are few, with six studies to date reporting conflicting results on HOMA-IR.[1,4-9]

Aim of the study

To study the impact of Ramadan fasting on metabolic parameters,

cardiovascular risk and anthropometry in a sample of the Egyptian population with T2D.

Design

This cohort study was conducted on 80 people with T2D who were intending to fast during Ramadan in 2014, with an average of 15 fasting hours and an average temperature of 39/23°C. The study was approved by the local faculty ethical committee and was conducted at the Ain-Shams University Hospitals diabetes outpatient clinic. People with T2D were invited for full clinical and anthropometric examination and laboratory evaluation a few days before and after Ramadan.

Subjects who joined the study were examined clinically for anthropometric measurements including weight, height, BMI and waist-hip ratio. Before and after Ramadan fasting, laboratory evaluation included fasting blood sugar, 2hr post-prandial blood sugar, HbA_{1C}, lipid profile (TC, LDL-C, HDL-C and TG), serum creatinine, urine albumin/creatinine ratio, high-sensitivity C-reactive protein (hsCRP) and fasting insulin for calculation of HOMA-IR. A Framingham risk score was calculated to determine cardiovascular risk score before and after Ramadan. People with type 1 diabetes, chronic kidney disease > stage 3, hepatic disease CHILD B and C classification and pregnant patients were excluded from the study and provided with appropriate medical advice. Changes in the lipid profile, hsCRP, HOMA-IR and 10-year cardiovascular risk at the end of Ramadan fasting were the primary outcomes of this study.

All people recruited in the study completed the pre- and post-Ramadan visits at their regular monthly visits for dispensing medications.

All data were collected in an Excel sheet at clinic visits. At the end of the study data were exported to SPSS version 21 and adjustment to normal distribution was tested by the Kolmogorov-Smirnov test. Quantitative variables were expressed as mean ± standard deviation (SD) for normally distributed data and as median (interquartile range) for non-parametric data. Qualitative variables were expressed as frequency and percentage. A paired t test was used for comparing between two related means, Mann Whitney was applied for non-parametric variables and Chi-squared (X2) test of significance was used in order to compare proportions between qualitative parameters.

Results

All recruited patients completed the study visits before and after Ramadan, with a total number of 80 subjects. The mean age of the study population was 49.91±10 years with a gender distribution of 19 (23.75%) males and 61 (76.25%) females. Smokers constituted 22.5% of the study population and 67.5% of the patients were hypertensive (table 1).

Anthropometric parameters

The BMI and WHR showed no significant change after Ramadan fasting (p value 0.62; 0.65) respectively (table 1).

Laboratory parameters and cardiovascular risk assessment

The lipid profile changed significantly after Ramadan. Increases occurred in TC from 3.77±1.19 mmol/l to 5.24±1.03 mmol/l (p <0.001); in TG from 1.7±0.95 mmol/l to 2.22±1.51 mmol/l (p=0.004); in LDL-C from 2.03±1.08 mmol/l to 3.04±1.19 mmol/l) (p<0.001); and in HDL-C from 1.08±0.38 mmol/l to 1.18±0.17 mmol/l (p= 0.014)

Table 1 Comparison of study variables using paired t test

Variable	Before Ramadan	After Ramadan	Mean Difference	T	P value
FBS mmol/l	9.1 ± 2.4	11.8±10.6	2.7	-0.23	0.8
PPBS mmol/l	15.6 ±4.7	16±4.8	0.4	-0.88	0.38
HbA_{1C} mmol/mol	65 ± 6.06	64 ± 6.39	-1	0.554	0.6
TC mmol/l	3.77±1.19	5.24±1.03	1.47	-10.7	<0.001
TG mmol/l	1.7±0.95	2.22±1.51	0.52	-2.92	0.004
HDL-C mmol/l	1.08±0.38	1.18±0.17	0.1	-2.5	0.014
LDL-C mmol/l	2.03±1.08	3.04±1.19	1.01	-7.17	<0.001
Fasting insulin U/L	6.1 ± 3.7	12.6 ± 8.2	6.537	2.3	<0.001
HOMA-IR	2.42±1.6	7.02±8.9	4.56	-4.5	<0.001
BMI kg/m^2	36.1±5.9	36±5.6	0.1	0.5	0.62
Waist hip ratio	0.906±0.11	0.907±0.11	0.0005	-0.45	0.65
Ser.creat. µmol/l	71.62±17.68	83.11±26.53	11.49	-5.1	<0.001
Urine alb/creat.ratio	21.2 ± 6.5	21.4 ± 6.2	0.291	-1.84	0.07
SBP mmHg	134.9 ± 10.8	141.2 ± 11.9	6.28	14.32	<0.001
DBP mmHg	94.7 ± 10.7	101.8 ± 11.3	7.13	-9.97	<0.001
10 years CVD risk	5.18± 7.8	7.6±9.9	2.38	-4.09	<0.001

Glycemic parameters including FBS, PPBS and HbA_{1C} showed no significant changes after Ramadan; FBS was 9.1 ± 2.4 mmol/l before vs 11.8±10.6 mmol/l after (p=0.8); PPBS 15.6±4.7 mmol/l before vs 16±4.8 mmol/l after (p=0.38); HbA_{1C} 65±6.06 mmol/mol before vs 64±6.39 mmol/mol after (p=0.6). HOMA-IR, however, increased significantly from 2.42±1.6 IU to 7.02 ±8.9 IU, p< 0.001 (table 1).

Cardiovascular risk parameters including SBP, DBP and 10-year cardiovascular risk increased significantly after Ramadan (134.9±10.8 mmHg vs 141.2±11.9 mmHg, p < 0.001 for SBP; 94.7± 10.7 mmHg vs 101.8±11.3 mmHg, p value < 0.001 for DBP; 5.18 ± 7.8 vs 7.6±9.9 for 10-year CVD risk p < 0.001) (table 1). The proportion of people testing positive on hsCRP qualitative testing increased from 51% before Ramadan to 61% afterwards (figures 1 and 2).

Assessment of renal function showed a significant increase of mean serum creatinine by 11.49 µmol/l while ACR showed no significant change after Ramadan (table 1).

Discussion

Studies focusing on Ramadan and cardiovascular risk in people with T2D are lacking: studies have been either conducted in people without diabetes who had cardiovascular disease or high cardiovascular risk, or have included only a small subpopulation of people with diabetes.[10]

The current study focused on the impact of Ramadan on lipid profile, cardiovascular risk (represented by hsCRP and 10-year cardiovascular risk) and anthropometry. Ramadan was associated with

Figure 1. HsCRP qualitative before Ramadan

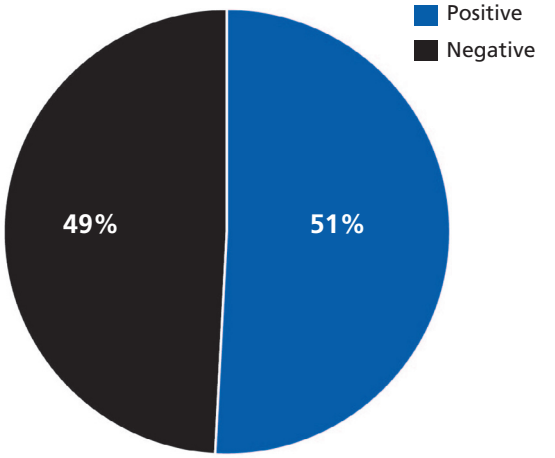
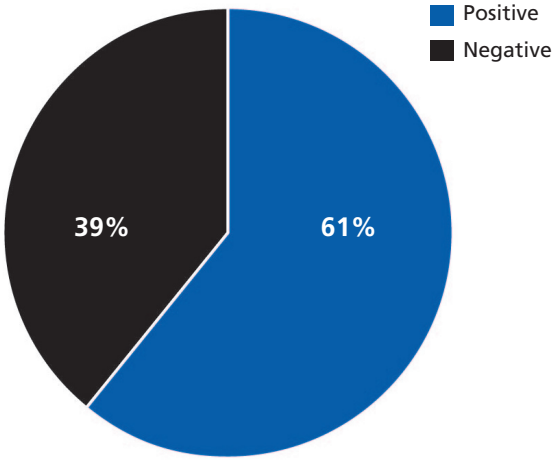


Figure 2. HsCRP after Ramadan



significant elevations of TC, LDL-C, HDL-C and TG. Framingham 10-year cardiovascular risk increased significantly while there was no significant impact on BMI. In the current study all elements of the lipid profile, including HDL-C, significantly increased after Ramadan. Similar findings have been reported by Sfar *et al*,[11] who documented an increase in all parameters of the lipid profile except for LDL-C in people with T2D after Ramadan, associated with a non-significant rise in total calorie intake, a fall in carbohydrate intake, and a rise in fat intake with an increased ratio of animal to vegetable protein. Earlier studies in people with T2D by Khaled and Belbraouet[12] and Bagheri *et al* showed a significant increase of TC by the end of Ramadan in the first study and a significant increase of TG in the second study; only one lipid parameter was tested in each of these studies.[13]

Contrary to our results, Al-Kirwi in his study on 28 people with T2D demonstrated a significant decrease of total cholesterol and LDL-C while HDL-C increased significantly and TG increased non-significantly.[14] The author attributed these results to the quality and quantity of food intake during Ramadan, although food recall was not reported in this study. Another study conducted in Algeria demonstrated no change in TC, TG or LDL-C by the end of Ramadan while HDL-C decreased significantly.[15]

Baccouche *et al* in a study conducted in elderly people with cardiovascular risk factors showed a significant increase in HDL-C, a significant decrease in TG and no change in TC and LDL-C by the end of Ramadan. It is worth noting that in this study only 50% of the people had T2D.[16]

The studies reporting the effect of Ramadan fasting/intermittent fasting on lipid parameters yielded conflicting results which might be attributed to inclusion of populations with mixed risk factors in some of these studies, small sample size in others, and to differences in dietary habits and physical activities across studies.[4]

The significant rise of lipid parameters in our study could be attributed to the nature of dietary habits among Egyptians during Ramadan. There is a tendency to consume more sweets, sweetened beverages and fried food.[4]

Several mechanisms have been proposed for the rise in HDL-C over Ramadan, including increased expression of PPAR-α which is preferentially activated during states of energy deprivation and fasting. On activation of PPAR-α the plasma HDL-C rises as a result of induction of hepatic apolipoprotein A-I and apolipoprotein A-II expression. Fasting also causes decreased expression of the CETP enzyme (cholesterol ester transfer protein) which is responsible for transfer of cholesterol esters from HDL-C to VLDL-C, an action that reduces HDL-C concentration.[17,18]

T2D confers a significant cardiovascular risk, reflected as a 2 to 4-fold rise in the risk for coronary artery disease, stroke and heart failure. In our study SBP and DBP and 10-year Framingham cardiovascular risk showed a significant rise after Ramadan fasting. The non-traditional cardiovascular risk factors of hyperinsulinemia, insulin resistance and microalbuminuria were also examined in our study.[19] HOMA-IR, which was measured as a surrogate of insulin resistance, showed a significant rise after Ramadan whereas ACR and hsCRP showed no change.

Our data were similar to those from a pilot study conducted by Aranson *et al*[5] in that hsCRP showed no change, yet contrary to our finding of a rise of HOMA-IR after Ramadan Aranson *et al* found no change during and after fasting. That study followed a fasting pattern of 3-4 weeks with a set goal of 18-20 fasting hours rather than Ramadan fasting and was conducted on people with T2D on metformin therapy. Similarly, Nematy *et al*, reporting on a cohort of people with cardiovascular disease and metabolic syndrome, reported no change in HOMA-IR and hsCRP yet there was an improvement in 10-year coronary artery disease risk.[1] Another study on 56 patients with established cardiovascular disease that included 20 people with T2D also showed no change in hsCRP after Ramadan[20] and a study that focused on 19 participants with metabolic syndrome showed no change in fasting insulin, HOMA-IR and hsCRP after Ramadan fasting.[7] A recently published study conducted on 160 healthy subjects showed a significant increase in HOMA-IR at the end of Ramadan.[6] Studies of changes in hsCRP during Ramadan in a healthy population reported no significant changes.[1,6] HOMA-

IR showed no change in one of these studies1 but in another study) Metin et al reported a significant rise.[8]

The rise in HOMA-IR could be attributed to the impact of fasting on different hormones such as leptin, adiponectin and cortisol which might impact on insulin resistance and also to the shift of metabolism during fasting hours toward glycogenolysis and lipolysis which increases free fatty acids and eventually influences peripheral insulin resistance.[6] In addition, the combination of a reverse feeding schedule characterized by a nocturnal feeding pattern and a reversed and interrupted sleep pattern could lead to hormonal alterations notably involving growth hormone and cortisol, leading to decreased glucose tolerance and increased insulin resistance.[9] Studies in healthy individuals showed an increase of insulin resistance during Ramadan fasting,[3] and an earlier study showed that acute starvation in healthy individuals induces an insulin-resistant state.[21] Thus, insulin resistance might reflect an adaptive metabolic response aiming for energy conservation,[22] so Ramadan fasting leads to an insulin-resistant state.[3]

In the current study SBP and DBP increased significantly after Ramadan fasting. A recent meta-analysis that included 33 studies and a simultaneous observational study on the effect of Ramadan fasting on blood pressure reported a significant reduction of SBP and DBP after Ramadan fasting in most studies. In this meta-analysis and observational study subgrouping of pooled data showed SBP and DBP reduction among healthy, hypertensive and diabetic subgroups but not in the CKD subgroup.[23]

Many factors may theoretically influence the blood pressure (BP) during Ramadan. These include feeding patterns, sleep changes and changes in the timing of intake of medication.[24] Additionally, in our study in which 67% of the study population were hypertensive, other traditional and cultural factors could contribute to the rise of blood pressure during Ramadan, like liquorice ingestion which is very popular among Egyptians during the month of Ramadan to quench thirst.[25] Another factor is an increased salt intake during Ramadan.[26] It has been reported that consumption of high sodium content food is rising in developing countries,[27] with the Middle East countries having higher levels of sodium consumption compared to other areas.[28]

The current study showed non-significant differences in WHR and BMI before and after Ramadan (0.9±0.1 and 0.9±0.1 for WHR, p = 0.652 and 36.1±5.9 and 36±5.6 for BMI, p=0.62). Numerous studies using small groups of people with diabetes have shown few changes in anthropometric measurements during Ramadan.

Our findings were similar to those of Ghania *et al*,[29] with the mean body weight and BMI of the cohort showing no change despite the marked changes in food habits. Sfar H *et al* noted that weight and BMI decreased in the group with T2D but were similar to that in a non-diabetic control group, with no statistical differences between the groups.[11] Also, Sahin *et al* found that weight and waist circumference were not different before and after Ramadan (p > 0.05) as most people with diabetes deliberately reduced their daily activities during Ramadan to avoid hypoglycemia.[30]

Malekmakan *et al* found that BMI, waist circumference, hip circumference, and systolic and diastolic blood pressure all reduced significantly during Ramadan with the reduction being significantly greater in men for body mass and weight.[31] The population studied was highly selected however, comprising staff from Shiraz University of Medical Sciences.

Fernando *et al* analyzed weight and body composition changes during Ramadan and found a significant reduction in fat percentage specifically in overweight and obese subjects but not in normal weight subjects.[32] This reduction was lost with the gradual return to pre-Ramadan weight at 2-5 weeks post Ramadan.

The current study showed a non-significant increase in FBG level, PPBG and HbA_{1c} after Ramadan, with no reported severe hypoglycemic episodes or hyperglycemic emergencies. Some studies show no significant change in the serum levels of glucose while others report higher or lower FBG after Ramadan. A recent meta-analysis reviewing the impact of Ramadan fasting on the metabolic profile among people with T2D concluded that fasting resulted in slight improvement in FBS and HbA_{1c} in the 11 studies included in this meta-analysis, with moderate to considerable heterogeneity.[33] It is worth nothing that our study did not include specific Ramadan-focused education which, as suggested by other studies, could have impacted our results.[34]

Lastly, in our study serum creatinine was significantly elevated at the end of Ramadan fasting, with no change noted in the urine albumin/creatinine ratio. Similarly, a meta-analysis examining the effect of time-restricted feeding during Ramadan on body composition and metabolic parameters showed a significant decline of kidney function and estimated GFR within the normal range in healthy individuals, and in one study in people with type 2 diabetes.[35] Conversely, a study conducted in people with T2D with and without CKD found a significant rise of serum creatinine at the end of Ramadan fasting in those without CKD, while no difference was noted in those with CKD.[36] This finding reflects the effect of restricted fluid intake during the hours of fasting on the kidneys, the function of which becomes directed toward water conservation and maintaining fluid balance, especially when Ramadan coincides with summer thus prolonging fasting hours.[35]

Limitations

Our study lacked dietary food recall, which could be of value in correlating with the results and evaluating the impact of Ramadan dietary habits on lipid profile. Also, this study reflects a short-term impact of Ramadan fasting on cardiometabolic risk. Some Muslims habitually fast two days per week and mid lunar month over the year beside Ramadan fasting, which could have a longer-term impact.

Interpretation and generalisation

The interpretation of the study results should be viewed within the context of when Ramadan occurs during the year, which affects the duration of fasting hours. The place where the study was conducted reflects cultural differences in food patterns and social activities in Egypt, which differ from Muslim cultures in other parts of the world.

Conclusion

Ramadan fasting in Egyptian people with T2D appears to have

Key messages

- Ramadan fasting in Egyptian people with type 2 diabetes appears to have a significant effect on lipid profiles and blood pressure that could adversely impact cardiovascular risk
- Current guidance is more focused on glycemic control with adjustments to oral hypoglycemic agents and insulin dose
- Cardiovascular disease risk assessment and guidance prior to Ramadan fasting should not be overlooked

significant effects on lipid profiles and blood pressure that could adversely impact cardiovascular risk. Current guidance is more focused on glycemic control and oral hypoglycemic agents and insulin dose adjustments. Cardiovascular disease risk assessment and guidance prior to Ramadan fasting should not be overlooked.

Conflict of interest The authors have no conflicts of interest to declare.
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