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Attitude and safety of patients with diabetes observing the Ramadan fast

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ABSTRACT

Aims: To describe the attitude of type 2 diabetes patients toward Ramadan fasting. A Secondary purpose was to describe rates of hypoglycemia during Ramadan according to type of treatment.

Methods: A prospective, non-randomized study for 2 years. Participants with type 2 diabetes attending Dammam Diabetes Center, Saudi Arabia were stratified for fasting according to ADA recommendations. Results are presented using mean, standard deviation and percentages.

Results: Total of 360 participants with type 2 diabetes. Mean ± SD glycosylated hemoglobin was 8.9 ± 2.1. More than 80% of individuals were in the ADA higher risk group however, they all fasted Ramadan. The mean non-fasting days was 2.6 days and overall rate of hypoglycaemia was 24.7%. Both parameters were directly proportionate to the risk stratification level (P-value <0.05). Despite hypoglycaemia, 29.3% continued fasting.

Hypoglycemia was highest in patients treated with insulin (P-value <0.05) followed by those treated with oral agents including sulphonylurea as compared to oral agents excluding sulfonylurea (P-value = 0.002). Those who experienced hypoglycemia prior to Ramadan had the highest rate of hypoglycemia during Ramadan (53.3%) (P-value = 0.0065).

Conclusions: Despite medical advice, the vast majority of type 2 diabetes participants categorized as high risk, fasted Ramadan. Approximately one quarter of people with type 2 diabetes in our cohort experience hypoglycaemia and this was directly related to their fasting risk level. A sizeable proportion continued the fast despite hypoglycemic. Insulin therapy with or without oral agents and previous episodes of hypoglycemia before Ramadan predicted hypoglycemia risk during Ramadan. HbA1c and weight showed some clinical improvements post Ramadan fasting. This is a single center study of mostly high risk fasting patients and hence, these results should not be generalized.

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1. Introduction

Many Muslims with a medical condition that potentially exempt them from fasting Ramadan insist on fasting despite the advice provided by healthcare professionals not to fast [1,2]. These patients represent a challenge not only for themselves but also for healthcare professionals [2,3]. Epidemiological studies of Muslims with diabetes showed that the majority of patients with diabetes mellitus (DM) fasted during Ramadan [4,5]. Indeed, clinical practice shows that some individuals with diabetes in the higher risk groups who insist on fasting, are able to do so with no major hypoglycemia. New era in the treatment of diabetes with drugs that have improved pharmacokinetics and reduced risk for hypoglycemia are currently available. Few studies have investigated best treatment regimens during Ramadan in individuals with diabetes [2,3]. Furthermore, Ramadan-focused patient education programs may play a role in safer fasting during Ramadan [2,3,6]. Full collaboration between the patient and diabetes care team that is based on mutual understanding of the religious obligations and medical aspects of fasting is essential [7,8].

This study investigated the attitude of patients with diabetes who undertake the fast of Ramadan in the Eastern province, Dammam, Saudi Arabia, to understand their practice and attitude, Ramadan-related awareness and health-related needs. A secondary purpose of this study was to determine the safety and effect in relation to use of diabetes medication on the glycemic control during Ramadan fasting and the risk for hypoglycemia and to find some predictors associated with increased risk for hypoglycemia during fasting.

2. Materials and methods

2.1. Study design and participants

This is a prospective, non-randomized study conducted in an outpatient setting of a secondary/tertiary referral hospital at the Endocrinology and Diabetes Centre of Dammam Medical Complex, Eastern Province, Saudi Arabia. The total duration of the study corresponded to the period of the month preceding Ramadan, during, and one month after the end of Ramadan for 2 consecutive years (2015, 2016). Prior to their inclusion, all adult eligible individuals who declared the interest in fasting consented to participate in the study after approval of hospital ethical committee. The eligibility criteria for inclusion were all individuals >14 years with the diagnosis of type 2 DM who had decided to fast Ramadan. Exclusion criteria were those below 14 years of age and those who did not intend to fast the month of Ramadan. All subjects included in the study received Ramadan focused diabetes education which included educational dietary counseling sessions addressing meal planning, exercise, self-monitoring of blood glucose (SMBG), recognizing and managing acute complications, and guidance about management of medication during Ramadan. Participants were stratified by their physician according to American Diabetes Association (ADA) Ramadan recommendations [2].

2.2. Data collection

384 subjects with diabetes (172 males, and 212 females) were selected and interviewed during the study period. Patients were asked to answer a questionnaire and responses were recorded by the trained staff. Questionnaire data included demographic details, diabetes related characteristics; history of diabetes related complications as well as biometric and biochemical measurements before and up to 1 month after Ramadan. Self-monitoring of blood glucose (SMBG) and its frequency, and types of antidiabetic agents used were recorded. Data also included number of broken fast days and reasons for not fasting if applicable. The frequency of hypoglycemia with either symptoms or blood glucose level below 70 mg/dl (3.9 mmol/l) during Ramadan and the prior month as well as action taken when hypoglycemia occurred were also recorded. Major hypoglycemia was defined as any subject with hypoglycemia that requires medical assistance.

2.3. Statistical analysis

Responses to questions about knowledge and practices are presented in the form of numbers and percentages. The data was tabulated on Microsoft Excel. Values were expressed mainly as mean, standard deviation (SD) and percentages. Comparisons were performed using analysis of variance for variables and chi-square, Fisher exact test or students paired 't' test and odds ratio (OR) wherever appropriate. P value <0.05 was considered statistically significant.

3. Results

Total of 384 subjects were interviewed, (n = 24) patients were excluded as they did not intend to fast following health care providers advise. Reasons for not fasting were; new onset diabetes, unstable blood glucose, recurrent hypoglycemia, renal failure and other medical reasons not related to diabetes.

3.1. Demographic characteristics of the study population

The overall demographic features of the study population are shown in Table 1. Total of n = 360; the mean age was 53.8 years, with a mean duration of diabetes of 12.5 years. Mean body mass index (BMI) at baseline was 33.9 kg/m^2 and HbA1c at baseline was 8.9%.

3.2. Diabetes-related complications and associated risk factors

Data on the presence of any diabetes-related complications and associated risk factors was available in 160 subjects and are shown in Table 1. The overall frequency of diabetes complications and comorbidities was relatively high which reflects the selection bias since these are patients who attend clinic in secondary/tertiary care hospital.

Table 1 – Demographic and clinical characteristics of the study population.

	Number (%)	Mean ± SD
Number of patients	360 (90%)	
SEX		
Female	197 (54.7)	
Male	163 (45.3)	
AGE	Range 23–82 yrs.	53.8 yrs. ± 9.3
Duration of DM (Years)	Range 1–40 yrs.	12.5 yrs. ± 8.3
Overall Weight BMI (baseline)	Range 24–64	33.9 ± 7.0
Obesity + overweight	(96.7)	–
BMI ≥ 25–29.9	(26.7)	
BMI ≥ 30	(70.0)	
Overall HbA1c (baseline)	Range 4.6–17.4	8.9 ± 2.1
Hypertension	(63.8)	–
Dyslipidemia	(72.5)	–
Coronary artery disease	(16.9)	–
Stroke/TIA	(3.8)	–
Peripheral vascular disease	(0.6)	–
Retinopathy	(26.9)	–
Nephropathy	(8.8)	–
Neuropathy	(43.8)	–
Diabetic foot	(6.9)	–

3.3. *Metabolic control and clinical changes after Ramadan*

Weight: after Ramadan 20.1% of participants experienced weight loss, 9.0% experienced weight gain, and 70.9% had no change in weight. BMI after Ramadan decreased from a mean ± SD of 32.49 kg ± 7.35 to 32.26 ± 7.49P Value (0.012).

HbA1c: HbA1c was 8.79% ± 2.02 before Ramadan and 8.59% ± 1.87 after Ramadan with a mean ± SD change of 0.2 ± 0.15, P Value (0.022).

3.4. *Fasting by ADA risk stratification and patients attitudes and behavior*

Table 2 includes the different fasting risk stratification of our patients. Overall >80% of patients were in the higher risk groups (P < 0.05). High risk and very high risk category were routinely advised not to fast. The number of broken fast days ranged from 0 to 20 days with a mean ± SD of 2.6 days ± 3.4. This was 0 days for low risk, 1 day for moderate risk, 2.2 days for high risk and 2.7 days for very high risk group. Of those who had hypoglycaemia during fasting hours, (29.3%) of them continued the fast.

Self-monitoring of blood glucose (SMBG): all people with diabetes followed in our diabetes center receive glucometers and blood glucose strips free of charge irrespective of the type of treatment. However, only 83% reported monitoring blood glucose during fasting. This ranged from 1 to 7 times/day (mean 2.1 ± 1.2) and 22.7% monitored blood glucose only when symptomatic.

3.5. *Incidence of hypoglycemia*

Hypoglycemia during fasting (Table 2) occurred in 3.3% in low risk group and was 27.8% in very high-risk category (P value = 0.0004). The overall hypoglycemia rate was 24.7%, (n = 89); with one single episode of major hypoglycemia requiring medical assistance. Hypoglycemia occurred at non-fasting hours in 7.9% (n = 7), and during fasting hours in 92.1% (n = 82) (see Table 3).

Frequency of hypoglycemia was highest within 2 h of iftar time (Chart 1) and this corresponded with highest rate of resistance to break fasting (43%).

Table 2 – Hypoglycemia during fasting by ADA risk stratification status.

ADA risk Stratification	Total n (%)	Hypoglycemia n (%)	No Hypoglycemia n (%)	Continued fasting when hypoglycemic
Low	30 (8.3)	1(3.3)	29 (96.7)	0 (0)
Moderate	15 (4.2)	1(6.7)	14 (93.3)	0 (0)
High	190 (52.8)	57 (30.0)	133 (70.0)	15 (28.8)
Very high	108 (30.0)	30 (27.8)	78 (72.3)	9 (32.1)
*Unknown	17 (4.7)	0 (0.0)	17 (100.0)	–

* 17 participants did not have adequate information to complete ADA risk stratification.

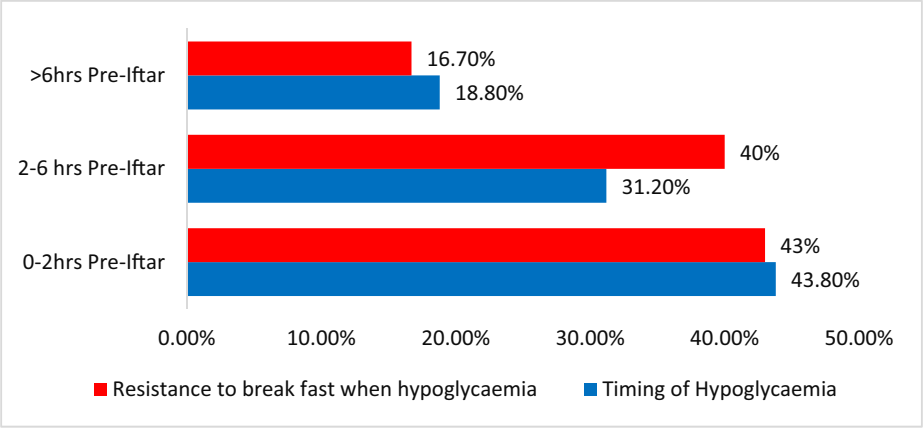

Chart 1 – Timing of hypoglycaemia during fasting hours and resistance to break fasting in relation to time.

Table 3 – Hypoglycemia during fasting.

	n (%)
Over all Hypoglycemia	89 (24.7)
Hypoglycemia during fasting hours	82 (92.1)
Hypoglycemia during non-fasting hours	7 (7. 9)
*Major hypoglycemia	1 (1.1)
Minor hypoglycemia	88 (98.9)
Continued fasting when hypo	24 (29.3)
Broken fast days (mean ± SD) due to diabetes related issues	2.6 days ± 3.4
Range of broken fast days	1–20 days

* Major hypoglycemia defined as any symptomatic hypoglycemia required emergency department visit or hospital admission.

3.6. *Treatment and hypoglycemia*

Table 4 Summarize the medications and Risk of hypoglycemia.

Repeated hypoglycemic events was classified as 1–4 times or >4 times. Hypoglycemia was highest in insulin only users (46.9%) and Insulin + oral agents (35.2%) as compared to oral agents only (14.0%) with P value <0.00001. Oral agents only including SU had significantly higher rate of hypoglycemia (20.2%) as compared to oral agents excluding SU (4.9%) (P value = 0.002).

3.7. *Relationship between previous episodes of hypoglycemia and hypoglycemia during Ramadan*

Chart 2 show that (53.3%) of those with hypoglycemia before Ramadan had hypoglycemia during Ramadan, Odds ratio (OR) 2.7, and P value = 0.0065. Frequent hypoglycemic episodes (>4 times) during Ramadan occurred in 25% of those with hypoglycemia before the month of fasting. All subjects who had pre-Ramadan hypoglycemia and during the month of fasting were on insulin based therapy (50% were on insulin therapy alone, 37.5% MDDI ± Non-SU-OHA and 12.5% on basal insulin + SU-OHA).

Table 4 – Hypoglycemia and repeated rate of hypoglycemia in relation to medications.

Treatment	Total on regimen n (%)	n (%) with hypoglycemia on regimen	Repeat rate	
			1–4 times n (%)	>4 times n (%)
Insulin only	49 (13.6)	23 (46.9)	20 (87)	3 (13)
Insulin + OHA	108 (30.0)	38 (35.2)	36 (94.7)	2 (5.3)
Basal Insulin + SU-OHA	47 (13.1)	14 (29.8)	13 (92.9)	1 (7.1)
Basal Insulin + Non-SU-OHA	12 (3.3)	0 (0)	0 (0)	0 (0)
MDDI ± Non-SU-OHA	49 (13.6)	24 (49)	23 (95.8)	1 (4.2)
Oral agents only	200 (55.6)	28 (14.0)	23 (82.1)	5 (17.9)
Oral agents (including SU)	119 (33.1)	24 (20.2)	19 (79.2)	5 (20.8)
Oral agents (excluding SU)	81 (22.5)	4 (4.9)	4 (100)	–
Lifestyle only	3 (0.8)	0 (0)	–	–

Multiple daily dose of insulin (MDDI); Basal-Bolus, basal-plus, or premixed insulin twice daily.

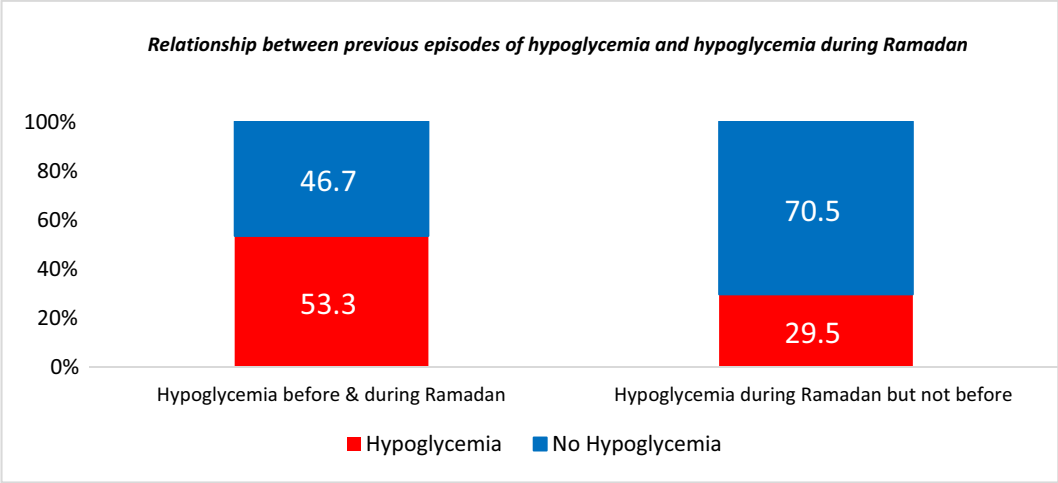

Chart 2 – Relationship between previous episodes of hypoglycemia and hypoglycemia during Ramadan.

4. Discussion

In our study, only 24 persons out of 384 opted not to fast despite the fact that the vast majority of our cohort were in the high risk category. This is consistent with what has been reported in the CREED study [5]. Indeed, this is comparable to what was reported by Mustafa et al. [6] where more than 60% of patients with diabetes who fasted during Ramadan were in the higher risk groups (very high-risk category 33.8%, high-risk category 29.6%).

While our study population had high level of comorbidities and high risk of fasting, severe hypoglycemia was rare during fasting (1%). In a retrospective study of glycemic trends during Ramadan in fasting diabetic subject's frequency of hypoglycemia was 21.7% whereas 4% patients had major hypoglycemic episodes [9] which is in line with what was observed in CREED and contrary to what was reported in EPIDIAR study [4].

The attitude of 29.3% of study cohort who continued fasting when hypoglycemic is of concern. The resistance to break the fast was higher the closer the hypoglycemic event to the time of iftar. All diabetes and Ramadan guidelines emphasis the importance of education about the need to break fasting when it occurs at any time during fasting hours even if happened close to the time of iftar [2,3]. A number of reasons for fasting against medical advice among patients with diabetes are reported in the literature. They include the psychological impact of non-fasting in the form of the feeling of exclusion associated with the denial of the disease and the feeling of medical opposition to divine power and spiritual imperatives [10]. Ramadan-focused education was shown to be beneficial in empowering those living with diabetes to change their lifestyles during Ramadan [11].

The incidence of hypoglycemia during Ramadan was observed to be highest for those treated with insulin alone and those on combination of Insulin + OHA. These results were similar with what has been reported by Abdul Jabbar et al in CREED study where the incidence of hypoglycemia during Ramadan for participants treated with a combination of oral anti-diabetic medication and insulin (13.5%) was similar for those treated with insulin alone (16.8%) [5].

But when looking at the details of our data for those treated with insulin in combination with oral agents the risk was lower if basal insulin is used with non-SU oral agents as compared to other more intensive insulin regimens. This observation may support the reported lower risk of hypoglycemia with basal insulin analogs as compared to the use of premixed insulin formulations for type 2 diabetes [12]. Indeed, the IDF-DAR guidelines has placed basal insulin as moderate/low risk and this data supports this risk categorization [3].

Sulphonylurea and other insulin secretagogue still represent one of the main treatment modalities, however, diabetes and Ramadan guidelines highlight that some SU such as Glyburide (glibenclamide) are associated with higher risk of hypoglycemia, compared to gliclazide, glimepiride, and glipizide [2,3,13,14]. This was also observed in our study. Both Gliclazide and Glibenclamide were used equally in this study and we are unable to compare the rates of hypoglycaemia to the individual drug.

It was noticed in this study that hypoglycemic events before Ramadan increases the risk and frequency of hypoglycemia during Ramadan especially for those on insulin based therapy. This result is consistent with what has been reported by the CREED study that hypoglycemic episodes before Ramadan increases an individual's risk of having an episode during Ramadan [5]. Indeed, this re-enforces the importance including the previous history of hypoglycaemia in risk assessment [2,3].

In this study, a significant reduction of 0.2% in mean HbA1c was observed during Ramadan fasting. This result is similar to what has been reported by Melanie Yee Lee Siaw in Singapore with 0.3% reduction of HbA1c in Ramadan [15] and it highlights that Ramadan fasting could be a tool for better glycaemic control. However, this observation cannot be generalized.

The Limitation of the study; this study was conducted in a secondary/tertiary care center, so it may be subjected to some bias in term of the rate of complications, the number of type 2

DM participants on more complex regimens and insulin therapy. Also the high baseline HbA1c reflects the barriers of tight glycemic control in the region that may underestimate and bias the hypoglycemia risk and results.

The present study provided an overview of characteristics and attitudes of people with type 2 diabetes attending 2ry/3ry care service in Saudi Arabia who fast Ramadan and some of the predictors of the hypoglycemia risk. Despite medical advice, the majority of participants fasted, and continued the fast when hypoglycemic regardless of their ADA risk status category which emphasizes the need for pre-Ramadan patient education. Fasting was associated with significant reduction in BMI and HbA1c. Insulin therapy with or without oral agents as well as previous episodes of hypoglycemia before Ramadan predicted risk of hypoglycemia during Ramadan. Due to the nature of the study cohort, these results could not be generalized to all people with diabetes.

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The authors declared that there is no financial support and sponsorship.

Conflicts of interest

There are no conflicts of interest.

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