

ORIGINAL ARTICLE

Fasting in Ramadan is safe for Individuals Suffering from Type 2 Diabetes Mellitus in Pakistan

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ABSTRACT

Background: Whether diabetics should fast or not in Ramadan has been a controversial idea since long and the answer even more debatable. It confers safety measures to be known by the diabetics thoroughly, such as when to break the fast and what the hypoglycemic cut offs are. We aimed to determine hypoglycemic events and safety of Ramadan fasting among individuals with Type 2 Diabetes Mellitus (DM).

Methods: This was an observational study enrolling diabetics who decided to fast in Ramadan, were aged >18 years, visited the primary health care center in Sikanderabad and Clifton clinic and gave consent to participate in the study. The exclusion criteria was Type 1 Diabetes Mellitus, Gestational diabetes, drug induced Diabetes and Maturity Onset Diabetes of the Young. A total of 103 participants were included in the study. Data was captured pre-Ramadan, during Ramadan and post-Ramadan in the year 2019. Multivariate Logistic regression was computed and chi-square taken for association of risk factors with hypoglycemia. p -value <0.05 was considered significant.

Results: Mean HbA1c before Ramadan was $9.2\% \pm 2.1$ and after Ramadan $7.7\% \pm 1.4$ (p -value <0.05) showing a reduction of 1.5%. Mean weight of the patients before Ramadan was $68.3\text{kg} \pm 1.6$ and during Ramadan $64.8\text{kg} \pm 1.4$ (p -value <0.00) showing a dip of 3.5 kg however mean weight 1 month after Ramadan was $66.5\text{kg} \pm 1.9$ depicting a rise again of 1.8kgs. Higher the risk category of American Heart Association, those who had hypoglycemic events before Ramadan and those on basal-bolus combination insulin had more hypoglycemic events (p -value <0.05).

Conclusion: Fasting in Ramadan shows a major reduction in weight (3.5kg) as well as corrects hyperglycemia (1.5%). However, hypoglycemia was attributed to high risk patients only hence Ramadan fasting proved to be quite safe in individuals with Type 2 DM.

Keywords: Glucose; Ketoacidosis; Diabetes; Gestational Diabetes Mellitus.

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INTRODUCTION

Out of the 1.5 billion Muslims around the world¹, millions fast in the month of Ramadan every year. Fasting requires abstinence of eating and drinking from dawn until dusk with only two meals usually: one after sunset (iftar) and one just before dawn (suhur). As personal and religious beliefs influence adherence to treatment and health behavior, all diabetics should be adequately counseled before fasting to ensure they fast safely².

Type 2 Diabetes is a chronic disease; affecting people of all ages, genders and nationalities, globally. In 2016, prevalence of type 2 diabetics in Pakistan was 11.7%³. In these patients, periodic fasting and calorie restriction decreases insulin resistance⁴, improves various metabolic pathways⁵ and reduces the risk of cardiovascular diseases⁶, apart from being an effective way of weight loss⁷.

Nonetheless, diabetics are at risk of various complications due to fasting, namely hypoglycemia, hypergly-

cemia, Diabetic ketoacidosis, dehydration, and thrombosis⁸. Hypoglycemia can be triggered after fasting a long duration, missing Suhur or using antidiabetic medications, particularly insulin and sulfonylureas⁷. Therefore, patients must be properly advised regarding features of hypoglycemia and when to break the fast to avoid serious outcomes⁸. Our study aimed to identify factors associated with complications during fasting amongst type 2 diabetics. This will help develop Ramadan-focused interventions to make fasting a safe and fruitful experience for diabetics.

METHODS

This observational study was done in Ramadan 2019 including a total of 103 Type 2 Diabetics, aged >18 years, visiting the primary health care center in Sikanerabad and Clifton general practice clinic and who gave consent to participate. The exclusion criteria included Type 1 DM, GDM, drug induced Diabetes and MODY approved by ZU ERC ref 2080420FJFM.

Pre-collected patient data of 5 months (3 months preceding Ramadan, 1 month of Ramadan and 1-month post-Ramadan) was extracted at the index date (study enrolment). Last HbA1c, number of hypoglycemic episodes (blood glucose <70mg/dl) in Ramadan, treatment taken and pre-Ramadan counseling was recorded. Baseline factors included hypoglycemic episodes before Ramadan, age, region, HbA1c before Ramadan, American Diabetes Association (ADA) risk category, gender, physical activity, anti-diabetic medication before Ramadan and its dosage form.

Data was analyzed using SPSS version 20. Mean and standard deviation was taken for numeric data such as age and HbA1c and weight before and after Ramadan. Frequency and proportion were assessed for categorical variables such as gender, ethnicity, ADA risk category, hypoglycemic events before and during Ramadan, hyperglycemic episodes, incidence of DKA, use of oral or injectable anti-diabetics, types of insulin and Self-Monitoring. Pre-Ramadan counseling and side effects of drugs were mentioned. Multivariate Logistic regression was computed and chi-square taken for association of risk factors with hypoglycemia. p -value <0.05 was considered significant.

RESULTS

Mean age of patients was 44.6+10.15. There were 66%(68) males and 34%(35) females. Mean HbA1c before Ramadan was 9.2%+2.1 and after Ramadan 7.7%+1.4 (p -value<0.00) showing a reduction of 1.5% (Figure 1). Mean weight before Ramadan was 68.3kg+1.6 and during Ramadan 64.8kg+1.4(p -value <0.00), depicting a dip of 3.5kg however, it became 66.5kg+14.9 1 month after Ramadan showing a rise of 1.8kgs. Majority of people were Urdu speaking 44 (42.7%) followed by Pushtun 25(24.3%), Punjabi 15(14.6%), Sindhi 12(11.7%) and Balochi 7(6.8%). There was no incidence of Diabetes Ketoacidosis (DKA) during the study. Since, 34% of the participants broke their fast due to hypoglycemia (<70mg/dl) or hyperglycemia (>300mg/dl).

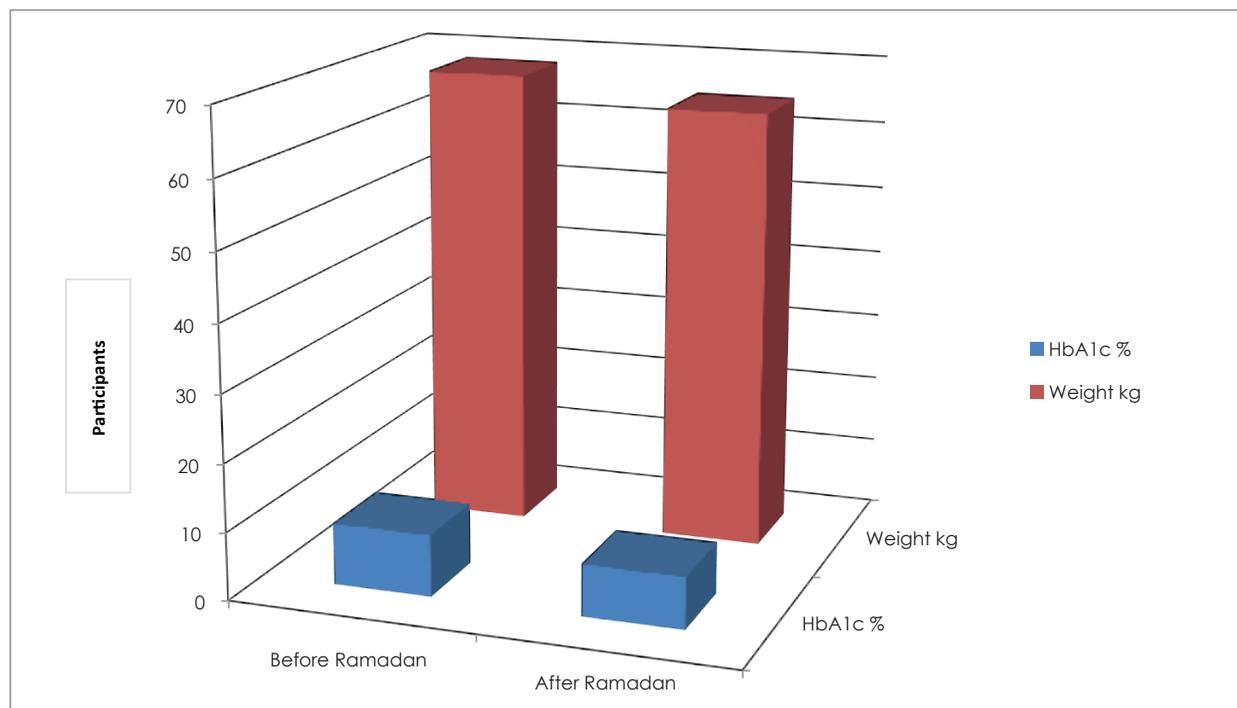


Figure 1: Difference in glycemic control and weight before and after Ramadan.

21(100%) of those who had hypoglycemic events at ADA very high risk followed by 14(60%) high risk, 7(58.3%) moderate risk and 0% low risk (p-value 0.00). Hence, higher the risk the more the chances to have hypoglycemia (Table 1). 15(75%) of those

with hypoglycemia did heavy physical activity (>20min 1-2 times per week) followed by 2(40%) who did extensive exercise (>20min ≥3 times per week) then 25(32.1%) who only did light physical activity (p-value 0.002).

Table 1: Analyzing safety of Ramadan fasting by determining association of risk factors causing hypoglycemic events.

Risk Factors	Hypoglycemic Events n(%)	Chi-square Values	p-Value
ADA* risk category			
Low Risk	0(0)	68.2	0.000
Moderate Risk	7(58.3)		
High Risk	14(60.9)		
Very High Risk	21(100)		
Exercise/wk			
Only light physical activity	25(32.1)	12.1	0.002
Heavy physical activity	15(75)		
Extensive physical activity	2(40)		
Hypoglycemic events before Ramadan			
Positive	40(93)	83.4	0.000
Negative	2(3.3)		
Types of insulin			
Basal only	0(0)	51.1	0.000
Basal bolus	19(100)		
Pre-mixed	15(62.5)		
Oral anti diabetic agents			
Metformin	4(10.3)	31.5	0.000
SU	4(80)		
Metformin+SU	8(88.9)		
Metformin+DPP 4 inhibitor	15(48.4)		
Metformin+SGLT2 inhibitor	9(52.9)		
Metformin+TZDs	2(40.8)		
GLP1**-receptor agonist			
Positive	4(33.3)	0.312	0.409
Positive	38(41.8)		
Pre-Ramadan counseling			
Done	19(37.3)	0.52	0.586
Not done	23(44.2)		

SMBGs***			
None	4(19)	11.5	0.009
1-2times	25(40.3)		
3-4times	9(56.2)		
>5times	4(100)		

* ADA (American Diabetic Association), **GLP1 (Glucagon like polypeptide 1), *** SMBGs (Self-Measurement of Blood Glucose).

Those who had hypoglycemic episodes in Ramadan also reported them before Ramadan 40(93%) (p-value 0.00). Patients with the most hypoglycemic events were on basal-bolus insulin 19(100%) requiring multiple daily injections followed by premixed insulin users 15(62.5%) whereas, basal insulin users did not report any hypoglycemia (p-value 0.00) (Figure 2a).

Majority of the patients with hypoglycemic events used Metformin plus sulfonylurea 8(88.9%) as OADs followed by sulfonylurea only 4(80%) then metformin plus SGLT2 inhibitors 9(52.9%) followed by metformin plus DPP4 inhibitors 15(48.4%) and metformin plus TZDs 2(40.8%). Metformin used alone caused least hypoglycemia; 4(10.3%). All results are

statistically significant (p-value 0.00). Thus, 38(41.8%) of those who had hypoglycemia, did not use GLP-1 receptor agonist while 4(33.3%) did, but the results were not statistically significant (p-value 0.409). Since, 23(44.2%) of those who had hypoglycemia while fasting, were not guided about fasting safely while 19(37.3%) underwent pre-Ramadan counseling. Pre-Ramadan education was inversely proportional to hypoglycemic events but this was not statistically significant (p-value 0.586). 25(40.3%) of those who had hypoglycemia, checked their sugars 1-2 times per day followed by 9(56.2%) who checked sugars 3-4 times per day followed by 4 who checked their blood glucose >5 times a day and those who did not check their sugars (p-value 0.009) (Figure 2b).

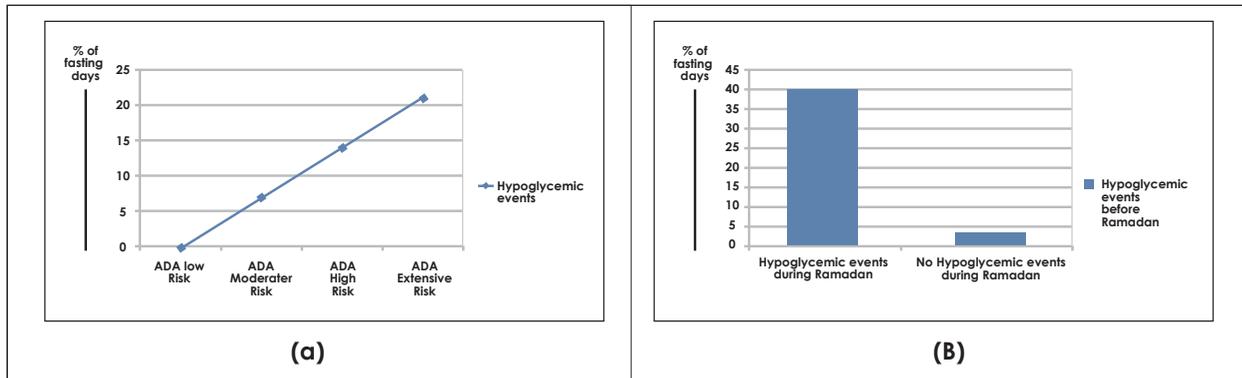


Figure 2: (a) Graph comparing hypoglycemic events during Ramadan with American diabetic association risk categories (b) graph showing association of hypoglycemic events before and after Ramadan.

DISCUSSION

Several parameters can contribute to evaluate safety of fasting. Type 2 diabetes is usually diagnosed in late forties; suggested by our findings as well. Likewise, a study conducted in Abha also reported a mean age of 45 in type 2 diabetics⁷. In contrast, a study in Karachi showed a mean age of 49 and 51 at a PHC and tertiary setup respectively¹⁰. However, Bangladesh had a mean age of 54.7¹¹ whereas Tunisia reported it being 58.3¹². However, 43 centers from Egypt, Israel, Jordan, Lebanon, KSA and UAE, had a mean age of 55, which gives a more holistic picture¹³. Furthermore, Pakistanis are affected by risk factors different to those of others, which could explain these variations.

Although our study had majority males, another study covering all 4 provinces of Pakistan depicted more female diabetics (52.20%)¹⁴. Likewise, Egypt, Iran, Jordan and Saudi Arabia India, Indonesia, Malaysia, France, Germany, UK, Turkey, Saudi Arabia, Kuwait and UAE, all reported more females^{13,15}. Contrastingly, Tunisia had 61.5% malediabetics¹⁶. The ethnic distribution of type 2 diabetes in Karachi highlighted an Urdu speaking majority. However, there are no studies to date affirming this.

For diabetics, the higher the ADA risk category, the more the chances are of hypoglycemia during fasting. A multi-country study including India, Indonesia, Malaysia, France, Germany, UK, Turkey, Saudi Arabia, Kuwait, and UAE also showed very high-risk

category patients fasting the least number of days mostly because of hypoglycemic events¹⁵. However, Pakistan lacks data establishing the relationship between ADA categories and hypoglycemia.

Hypoglycemia was mostly associated with heavy physical activity. However, hypoglycemia during Ramadan has been suggested with decreased physical activity¹⁶. Whereas another study in Karachi also concluded it being more frequent with heavy exercise¹⁴. There was an overall reduction in HbA1c levels before and after Ramadan. However, a study in Bangladesh concluded no significant change in pre and post levels¹¹. Likewise, there was significant weight reduction in Ramadan, which was reverted within a month and could be attributed to patients returning to their old eating habits. Although many studies reported similar trends in patients during fasting¹⁷, a few also reported no significant change¹⁸.

A survey on diabetics in Tunisia noted no ketoacidosis¹², as comparable to our study. However, we observed 40.8% hypoglycemic events, whereas KSA reported 52% cases during Ramadan⁹. Contrastingly, another study found a 25.5% risk of hypoglycemia in diabetics¹⁹. In addition, a study from Pakistan also found lower incidences of hypoglycemia (23.18%)¹⁴. 34% broke their fast in our study due to hypo or hyperglycemia. In a study from Pakistan, about 47% patients discontinued fasting following hypoglycemia¹⁴. Another study, reported lower figures (28.5%)¹². Interestingly, those who had hypoglycemia during Ramadan also reported episodes before Ramadan. However, these episodes can increase during Ramadan in diabetics¹² whereas some studies suggested the contrary²⁰.

According to a meta-analysis, fasting diabetics with basal-bolus regimes are at risk and should modify their dose;²¹ we found most hypoglycemia with basal-bolus insulin. In Singapore, 43.6% of those who had hypoglycemia, were on OHA and insulin¹⁹. Drugs like metformin, alpha-glucosidase inhibitors, thiazolidinediones and GLP-1 receptor agonists are associated with lower risk of hypoglycemia and can be used safely during fasting without dose modification. We found hypoglycemia least with Metformin. Whereas incidence of hypoglycemia increases with sulfonylureas;²² however, short-acting ones cause less hypoglycemia²³. Metformin and Thiagliazides may be continued like before for their additional benefits along with reducing hypoglycemia²³. GLP-1 Receptor Analogues are probably safest, being glucose-dependent²³ and cardio-protective, especially with MI²⁴. Furthermore, some patients prefer not using injectable drugs due to religious concerns²⁵.

Therefore, pre-Ramadan counseling can educate diabetics about risks associated with fasting and how to minimize them. We found an inverse

relationship between hypoglycemia and pre-Ramadan counseling. Patients receiving individual Pre-Ramadan education are more likely to self-monitor blood glucose, have better weight and HbA1c control and less likely to have hypoglycemia¹³. Contrastingly, a trial on diabetics indicated no significant impact of pre-Ramadan counseling on biochemical parameters. Although, Ramadan-focused education proved beneficial in observational studies, it did little in RCTs²⁶. However, lack of adequate counseling prevented diabetics from breaking their fast even during hypoglycemia²⁷.

Self-monitoring enables diabetics to maintain normal HbA1c and blood glucose while also predicting hypoglycemia. Most patients self-monitor blood glucose 1-2 times a day²⁸; as highlighted by our study. Self-monitoring and counseling helps lower HbA1c levels²⁸. However, a study in England concluded the contrary²⁹. Nonetheless, type 2 diabetics using OAD agents or a combination are more likely to benefit from self-monitoring³⁰.

CONCLUSION

Ramadan fasting in our study proves to drop the weight by 3.5kg as well as helps achieving euglycemia by a decline in 1.5% HbA1C. Hypoglycemia was only seen in ADA very high risk category (100%, p-value 0.00), those with basal bolus regime of insulin and taking Metformin plus Sulfonylurea (88.9% p-value 0.00) group of anti diabetic agents as well as those who failed to do frequent SMBGs hence Ramadan fasting proves to be quite safe in individuals with Type 2 DM. It is recommended that a pre Ramadan consultation must be done with one's physician so that appropriate changes in medical regime can be made in order to minimize the risk of hypoglycemia.

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CONFLICT OF INTEREST

Authors have no conflict of interest among them.

ETHICS APPROVAL

ZU ERC has approved study with the reference code (ref code 2080420FJFM).

PATIENT CONSENT

Informed consent was taken from all participants. Anyone wishing to discontinue being part of study was respected and done so.

AUTHORS' CONTRIBUTION

FJ was involved in the conception, data acquisition, analysis and interpretation as well as manuscript writing and proof reading. TK was involved in manuscript writing and proof reading. ZA and AG participated in manuscript writing.

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