Original article

The frequency of major complications among fasting people with diabetes according to risk categories of IDF-DAR guidelines 2016

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ABSTRACT

Aim/background: To determine the frequency of major complications among fasting people with diabetes according to risk categories of IDF-DAR guidelines 2016.

Methods: This prospective observational study was conducted around Ramadan of 2017, at Baqai Institute of Diabetology and Endocrinology, Karachi, Pakistan. People with diabetes having intention to fast during Ramadan were recruited. Demographic data collection along with risk categorization was done during pre-Ramadan visit. Structured education was given on one to one basis to each of the study participants. Assessment of complications was made during post Ramadan visit.

Results: There were 131 participants in this study. Mean age was 53.77 ± 12.67 years. Sixty three percent were males. 4.58% were of type 1 diabetes while 95.41 were of type 2 diabetes. Mean duration of diabetes was 9.92 ± 7.752 years and mean HbA1c was 8.711 ± 1.878 . Major hypoglycemia occurred in 31.2% of very high-risk category only. None of the high risk and moderate/low risk categories had major hypoglycemia. There was no major hyperglycemia noted in any of the categories of patients. 50% of very high risk and 3.3% of high-risk category required breaking of fast. None of the participants required hospitalization.

Conclusion: In this prospective study, majority of fasting people with diabetes fall into high risk category and did not develop major complications. Very high-risk category had highest number of complications while low to moderate category develop none. Further large-scale studies are needed to validate our finding.

1. Introduction

Ramadan fasting is an essential pillar of Islam. It is mandatory for all adult healthy Muslim to fast during the Holy month of Ramadan. Nevertheless, children and patients on health risks are comforted from fasting.¹ During fasting, adult Muslims are not permitted to take food-stuff, water, smoking, oral drugs and sexual intercourse from dawn till dusk. Duration of a fast can be as lengthy as 18–20 h per day and can be as short as 11 h per day, depending on geographical place of the country and season of the year.

Many of the Muslims with diabetes insist on fasting against physician's advice and it is the challenge to manage this group of patients during Ramadan. During fasting diminished fluid intake and alteration of meal and medication schedule can render patients with diabetes vulnerable to glycemic instabilities and dehydration especially during the day time. Major complications which can happen in fasting individuals with diabetes are hypoglycemia, hyperglycemia, diabetic ketoacidosis and hyperosmolar hyperglycemic state.²

A prospective cohort study determined that fasting rises the

frequency of symptomatic hypoglycemia about 1.6-fold in patients with type 2 diabetes during Ramadan.³ In the same way EPIDIAR study observed that fasting during Ramadan increased the risk of severe hypoglycaemia by 4.7 and 7.5-fold in patients with Type 1 diabetes and Type 2 diabetes respectively.⁴

Recent study from UAE concluded that hypoglycemia in adolescents with type 1 diabetes is encountered significantly in the last few hours of fasting. The incidence of hypoglycemia was 0% from 19:00 to 23:00 and 69% from 11:00 to 19:00.⁵ On the other end a retrospective study in 2007–2008 on incidence of diabetic ketoacidosis during Ramadan fasting concluded that there was no increase in the incidence and mortality from DKA during Ramadan which might specify that Ramadan fasting is not a major risk factor for diabetic ketoacidosis.⁶ Few studies have reported worsening in glycemic control and some have shown no adverse effect during fasting in Ramadan.^{7–9}

Consensus guidelines by IDF-DAR 2016 classified fasting individuals with diabetes into three risk categories i.e. very high-risk category, high risk category and moderate/low risk category.¹⁰ However, these risk categories are assumptive and not evidence based. This study was

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therefore designed to observe the frequency of major complications among peoples with diabetes of different risk categories who fasted during the month of Ramadan 2017.

2. Methodology

This was the prospective cohort study which was conducted at Baqai Institute of Diabetology and Endocrinology, a tertiary care diabetes centre in Karachi, Pakistan. People with diabetes regardless of age, gender, type, duration of diabetes and co-morbidities who intended to fast in the month of Ramadan of 2017, were recruited through non-probability convenient sampling. Patients who were not willing to fast or critically ill patients were excluded. Duration of study was 3 months (from May 2017 (1438 A.D) till August 2017 (1438 A.D)). Ethical approval was taken from Institution review board. Informed consent was taken from all study participants.

Pre-designed close ended questionnaire was used which comprised of two sections. Section A included pre-Ramadan information of patient's demographic profile, type of diabetes, duration of diabetes and questions regarding risk stratification according to IDF DAR risk categories, 2016. Structured educational counselling was done on one-to-one basis. These people with diabetes were called for post Ramadan follow up to assess the frequency of complications including major hypoglycemia and major hyperglycemia, need of fast discontinuation and hospitalization by using section B of questionnaire. The data analysis was done on Statistical Package for Social Sciences (SPSS) version 20 to compute mean, standard deviation and percentages.

3. Operational definitions

Minor hypoglycemia: Blood Sugar level equal to or less than 70 mg/dl by capillary glucometer (irrespective of symptoms).

Minor hyperglycemia: Blood Sugar level equal to or greater than 200 mg/dl by capillary glucometer.

Major hypoglycemia: Blood Sugar level equal to or less than 40 mg/dl by capillary glucometer (irrespective of symptoms) or hypoglycemia that required third person assistance irrespective of blood sugar level.

Major Hyperglycemia: Diabetic ketoacidosis, Hyperosmolar hyperglycemic state.

4. Results

Total 131 people with diabetes participated in this study. Their demographic properties are shown in Table 1. Patients are categorized into very high risk (n = 16), high risk (n = 91) and moderate/low risk (n = 24) and the detailed characteristics of study participants according to IDF-DAR risk categories are revealed in Table 2.

Major complications are outlined in Table 3. Major hypoglycemia occurred in 31.2% of very high-risk category only (p-value < 0.0001). None of the high risk and moderate/low risk categories had major hypoglycemia. There was no major hyperglycemia including diabetic ketoacidosis, hyperosmolar hyperglycemic state in any of the categories

Table 2

Characteristics of study participants according to IDF-DAR risk categories.

Characteristics of very high risk category (n = 16)	Percentage
History of recurrent hypoglycemia and recent Admission with severe hypoglycemia (n = 7)	43.75%
Hypoglycemia unawareness (n = 2)	12.5%
Poorly control type 1 DM (n = 5)	31.25%
Advance macrovascular complications (n = 2)	12.50%
Characteristics of high risk category (n = 91)	
Type 2 DM with sustained poor glycemic control (n = 65)	71.60%
With stable macrovascular disease (n = 21)	22.70%
Without stable macrovascular disease (n = 44)	48.90%
Well controlled type 1 DM (n = 2)	2.15%
CKD stage 3 (n = 1)	1.05%
With multiple dose of insulin or mixed insulin therapy (n = 23)	25.20%
Characteristics of moderate/low risk category (n = 24)	
Biguanide only (n = 2)	8.33%
Second generation sulfonylureas only (n = 1)	4.16%
Biguanide and Incretin based therapy (n = 7)	29.16%
Biguanide and second generation sulfonylureas (n = 5)	20.83%
Biguanide, Incretin based therapy and second generation sulfonylureas (n = 9)	37.5%

of patients. 50% of very high risk (n = 5 due to major hypoglycemia, n = 2 due to minor hypoglycemia and n = 1 due to minor hyperglycemia) and 3.3% of high-risk category (due to minor hyperglycemia) required breaking of fast (p-value < 0.0001). None of the patients required hospitalization. Minor hypoglycemia developed in 12.5% (n = 2) and minor hyperglycemia noted in 6.25% (n = 1) people of very high risk category respectively. In high risk category 3.3% (n = 3) of people developed minor hyperglycemia.

Fig. 1 compared the episodes of major hypoglycemia among all three categories (very high risk, high risk and moderate/low risk category) of fasting people with diabetes. There were 7 participants with type 1 DM, n = 5 were in very high risk (poorly controlled T1DM) and n = 2 were in high risk (well controlled T1DM). Major hypoglycemia occurred in 3 out of 7 (42.8%) people with T1DM as compared to T2DM where only 2 out of 124 (1.6%) developed major hypoglycemia (p-value < 0.0001) as shown in Table 4.

5. Discussion

In this prospective study among fasting people with diabetes of different risk categories, major hypoglycemia was reported only in very high-risk category. High risk category with maximum number of patients did not develop any of the major complications including severe hypoglycemia, diabetic ketoacidosis or hyperglycemic hyperosmolar state. None of the patient required hospitalization from any of the risk category.

IDF-DAR in 2016 defined fasting risk categories of people with diabetes into three risk categories very high risk, high risk and moderate/low risk according to their co morbid conditions and medications.¹⁰

Table 1

Patient's demographic profile.

Variable	Very high-risk category	High-risk category	Moderate/low risk category	Overall
N	16/131 12.2%	91/131 69.47%	24/131 18.32%	131
Mean Age (years)	43.13 ± 17.78	55.29 ± 10.59	55.13 ± 13.13	53.77 ± 12.67
Gender				
Male	7 (43.75%)	63 (68.8%)	13 (54.2%)	83 (63.35%)
female	9 (57.1%)	28 (31.18%)	11 (45.8%)	48 (36.64%)
Type of diabetes				
Type 1	5 (28.57%)	2 (2.15%)	0 (0%)	6 (4.58%)
Type 2	11 (71.4%)	89 (97.8%)	24 (100%)	125 (95.41%)
Mean Duration of diabetes (years)				9.92 ± 7.752
Mean HbA1c				8.711 ± 1.878

Table 3
Episodes of major complications among IDF-DAR risk categories.

IDF-DAR risk category	Major hypoglycemia		P-value
	Yes	No	
Very high risk	5 (31.2%)	11 (68.8%)	< 0.0001
High risk	0 (0%)	91 (100%)	
Moderate/low risk	0 (0%)	24 (100%)	
Overall	5 (3.8%)	126 (96.2%)	
	Major hyperglycemia		P-value
	Yes	No	
Very high risk	0 (0%)	16 (100%)	N/A
High risk	0 (0%)	91 (100%)	
Moderate/low risk	0 (0%)	24 (100%)	
Overall	0 (0%)	131 (100%)	
	Hospitalization		P-value
	Yes	No	
Very high risk	0 (0%)	16 (100%)	N/A
High risk	0 (0%)	91 (100%)	
Moderate/low risk	0 (0%)	24 (100%)	
Overall	0 (0%)	131 (100%)	
	Breaking the fast		P-value
	Yes	No	
Very high risk	8 (50%)	8 (50%)	< 0.0001
High risk	3 (3.3%)	88 (96.7%)	
Moderate/low risk	0 (0%)	24 (100%)	
Overall	11 (8.4%)	120 (91.6%)	

Data presented as n(%).

P-value < 0.05 considered to be statistically significant.

According to IDF- DAR guidelines very high-risk category patients must not fast. There were 12.2% patients in very high-risk category that experienced most of the complications in this study. This finding is consistent with other studies.^{2,4,12} Almost 70% study participants of this category developed major hypoglycemia and half of them broke the fast. Similarly, minor hyperglycemia/hypoglycemia observed more in very high-risk category patients but no episode of major hyperglycemia, DKA, HHS occurs and none required hospital admission.

Patients in this category need to be seen at least 2–3 months before Ramadan and must be stabilized before Ramadan if they want to fast. Even after medical supervision if patients are not stable before Ramadan then they should be advised not to fast seems to be a better option.

Nearly 70% participants of our study were in IDF –DAR high risk category. According to IDF –DAR guidelines this high-risk category

Table 4
Proportion of patients with major hypoglycemia among people with type 1 and type 2 DM.

	Overall	Type 1	Type 2	P-value
Total no. Of patients	131 (96.3%)	7 (5.34%)	124 (94.6%)	< 0.0001
Major hypoglycemia	5 (3.9%)	3 (42.8%)	2 (1.6%)	

Data presented as n(%).

P-value < 0.05 considered to be statistically significant.

patient should not fast¹⁰ but these patients opted to fast and no serious complication including major hypoglycemia, diabetic ketoacidosis or hyperosmolar hyperglycemic state were reported in this study. However, episodes of minor hypoglycemia and hyperglycemia did occur. Very small number of high-risk category patients broke the fast due to minor hyperglycemia but none of them required hospitalization. This finding is compatible to our previous research during which none of the fasting patients with Type 1 or Type 2 diabetes required hospitalization.¹¹

Looking further into high risk category, it was observed that 1/3rd of patients were of type 2 diabetes with sustained poor glycemic control, and 1/4th of these patients had stable macrovascular disease additionally. Although these comorbidities may put these people with diabetes on high risk of getting complications during fast. Our group in this category did not develop major complication and it has already been reported by several earlier studies. Salim I et al. showed that majority of cardiac patients fasted safely.¹² Others noted that under medical supervision fasting was possible for most patients with stable cardiovascular disease without any significant harmful effects.^{13,14} Another systemic review and metanalysis revealed that the incidence of cardiac events during fasting was found to be similar to the non-fasting period and Ramadan fast was not related to any increase in the incidence of acute cardiac disease.¹⁵ Similarly, study reported that fasting has no effect on stroke occurrence¹⁶ as well as on number of hospitalization needed for people with cerebrovascular accidents.¹⁷

Although very small number of our study participants were with well controlled type 1 diabetes, and none of them had any major complication. This finding is comparable to Al-Khawari et al.,¹⁸ Bin Abbas et al.,¹⁹ AlAlwan et al.²⁰ and Alvi SF et al.²¹ studies that patients with type 1 diabetes fasted safely during Ramadan. Similarly, a minor number of our patients were with diabetes who were in CKD stage 3, also did not develop any major complication. This finding is consistent with previous reports by Bragazzi et al.²² and Bernieh et al.,²³ One fourth of our study participants in this category were on multiple doses of insulin or mixed insulin therapy and fasted safely. Although limited data is available in this regard, studies have reported safe fasting among insulin taking people during Ramadan.^{24–26}

Fig. 1. Episode of major hypoglycemia during fasting.

Contrary to IDF-DAR recommendations not to fast for high risk category, people in this group opted to fast and did not develop any major serious complication. This study again has shown like previous studies that people with poor glycemic control can fast without major complications if given prior education and advice.^{27–29} However risk assessment and management must be individualized and not merely on categorization.

Around one fourth study participants were in low/moderate risk category. These included people with diabetes who were using biguanide, 2nd generation SU and/or incretin based therapy either alone or in several combinations. No major hypoglycemia, major hyperglycemia and minor hypoglycemia/hyperglycemia noted in this category. None of them broke the fast and no one required hospitalization and these people with diabetes fasted safely during Ramadan. This finding is similar to previous many studies that biguanides, second generation SU and incretin based therapy can be safely and effectively used in people with T2DM during Ramadan fasting.^{30,31} Pooled analysis of three randomized trial revealed that treatment with either DPP-4 inhibitors or glimepiride during Ramadan fasting have equally low risks of experiencing significant hypoglycemia.³² Likewise a double blind, randomized trial STEADFAST study concluded that DPP4 inhibitors is safe and effective treatment for people with diabetes during Ramadan fasting.³³

6. Conclusion

In this prospective study, majority of fasting people with diabetes fall into high risk category and did not develop major complications. Very high-risk category had highest number of complications while low to moderate category develop none. Risk assessment and advice to fast or not to fast should be make on individual basis and not merely on risk categorization. Further large prospectively designed multi-centered studies are required to validate our findings.

7. Limitations

Single centered study with relatively small sample size and there is a chance of recall bias are major limitations of this study.

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None.

Author's contribution

YA: Concept and design, interpretation of data, edit and review the manuscript.

DI: Data collection, writing, edit and review the manuscript.

SA: Data collection, writing, edit and review the manuscript.

Declaration of competing interest

None.

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