



Characteristics of Fasting in Ramadan in Type 2 Diabetes Patients on Empagliflozin in the DAR Global Surveys of 2020 and 2022

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Abstract

Background The safety of Ramadan fasting in individuals is determined by an interplay between Ramadan, patients, and medication factors.

Objective To analyze the challenges associated with Ramadan fasting among patients with diabetes treated with Empagliflozin and other antiglycemic agents who participated in the Diabetes and Ramadan (DAR) global surveys of 2020 and 2022.

Methods Building on data from the DAR Global surveys, a sub-analysis was performed on patients treated with Empagliflozin ($n = 1,464$) to reflect on the patients' experience and to analyze the challenges associated with Ramadan fasting.

The observational survey was conducted in five geographic regions (Gulf countries, Maghreb countries, Middle East [Egypt, Türkiye, and Iraq], Indian subcontinent, and Southeast Asia) in Muslim type 2 diabetes patients post-Ramadan 2020 and 2022. The patients were divided into four groups: Those treated with (1) Empagliflozin without sulphonylureas or insulins, (2) Empagliflozin plus sulphonylureas, (3) Empagliflozin plus insulins, and (4) Empagliflozin plus sulphonylureas and insulins. Descriptive statistics on medical data and baseline demographics were generated, and odds ratios regarding symptomatic hyper- and hypoglycemic events were calculated. The fasting behavior as well as diabetes management of the patients were evaluated.

Results Despite having diabetes, a large proportion of patients fasted during Ramadan. Patients treated with Empagliflozin without sulphonylureas or insulins showed significantly lower symptomatic hypo- and hyperglycemic complication rates during Ramadan fasting (6.9 and 8.4%, respectively). In patients on concomitant treatment with sulphonylureas, slightly higher rates of symptomatic hyper- and hypoglycemic events were observed. In patients who received insulins, significantly

Keywords

- Ramadan
- fasting
- type 2 diabetes
- Empagliflozin
- hypoglycemia
- hyperglycemia

higher rates of symptomatic hyper- and hypoglycemic events were observed. The highest rates of symptomatic hypo- and hyperglycemic events (19.7 and 22.2%, respectively) were observed in patients who were given concomitant treatment with sulphonylureas and insulins, with odds ratios up to 3.31 compared to Empagliflozin without sulphonylureas or insulins. Very low hospitalization rates (0.38%) due to symptomatic hyper- and hypoglycemic events were observed.

Conclusion Hypoglycemia rates were influenced by the type of therapies administered to the patients. Based on the results of this study, it may be concluded that Empagliflozin monotherapy or in combination with sulphonylureas may be relatively safe for Ramadan fasting, whereas caution is advised for patients taking additional insulin combinations.

Introduction

Muslims facing significant health challenges are generally exempt from fasting. Nevertheless, studies indicate that up to 94.8% of Muslims with type 2 diabetes (T2D) opt to fast.^{1–6} The act of fasting can increase the risk of various complications, including acute hypo- and hyperglycemia, diabetic ketoacidosis, thrombosis, and dehydration.³ Established guidelines recommend that health care professionals should conduct risk assessments for patients planning to fast during Ramadan, and patients categorized as high or very high risk for adverse events related to fasting should be counselled against participating in the fast.^{1,2,4}

The EPIDIAR study underscored the challenges faced by individuals with diabetes who fast during Ramadan and emphasized the necessity for enhanced diabetes management through structured patient education prior to Ramadan, along with tailored management guidelines for health care providers.³ Such guidelines and recommendations have been established for the management of diabetes during Ramadan, accompanied by educational initiatives^{2,7} and can empower individuals to optimally modify their lifestyle during this period to reduce the likelihood of complications.⁸

Previous studies have shown that sodium-glucose linked transporter 2 (SGLT2) inhibitors can be effectively and safely used in the treatment of T2D during Ramadan.^{9,10} The present sub-analysis focuses on T2D patients treated with Empagliflozin, a SGLT2 inhibitor, approved in 2014 and used in the management of T2D.^{11–13} It is commonly used alone or in combination with other antidiabetic agents to achieve optimal blood sugar regulation. The reason for focusing on Empagliflozin was that it has not been studied very well during Ramadan so far, and it was the most widely used SGLT2 inhibitor in the surveys. In this study, Ramadan fasting-associated challenges and risks of patients treated with four different therapeutic combinations were analyzed. The first group received Empagliflozin without sulphonylureas. The second group was treated with Empagliflozin in combination with sulphonylureas. The third group received Empagliflozin alongside insulin therapy. The fourth group had a combination of Empagliflozin, sulphonylureas, and

insulins, representing an intensified treatment regimen for glycemic management. The findings of this sub-analysis of T2D patients treated with Empagliflozin will enhance our understanding of current fasting practices in this cohort across various regions.

Patients and Methods

Study Design

This study is a sub-analysis of the Diabetes and Ramadan (DAR) Global surveys for Muslims within five geographic regions: Gulf countries (Kingdom of Saudi Arabia, United Arab Emirates, and Qatar), Maghreb countries (Algeria, Morocco, and Tunisia), Middle East (Egypt, Türkiye, and Iraq), Indian subcontinent (India, Pakistan, and Bangladesh), and Southeast Asia (Brunei and Malaysia).^{14–16} Data collection started post Ramadan (between June and August 2020 and 2022), where investigators undertook the survey during routine clinic consultation. Since the surveys took place after Ramadan, recall bias might have affected the outcome. The analysis focuses on patients who were treated with Empagliflozin and other antiglycemic agents.

Data Collection

Physicians from both primary and specialist centers conducted the survey by asking their patients about various aspects of their Ramadan experience and/or reviewing the patients' files. The survey questions looked into (1) breaking of fast due to diabetic illness, (2) occurrence of complications of symptomatic hypo- and hyperglycemia during Ramadan fasting and requirement for hospitalization and emergency department care, and (3) level of Ramadan-focused diabetes education and self-monitoring blood glucose (SMBG) practices during Ramadan. Data were collected either directly through an online questionnaire or transcribed later from a paper-based questionnaire to the online platform.

Baseline characteristics and care patterns for people with T2D who were fasting during and after Ramadan 2020 and 2022 were evaluated. Symptomatic hypoglycemia was identified depending on the presence of typical symptoms such as headache, shakiness, sweating, fatigue, or nausea (not

confirmed by SMBG). Symptomatic hyperglycemia was determined as higher blood glucose levels (>300 mg/dL or 16.6 mmol/L). Details of physical activity and food habits were not included in the questionnaire. Disease duration, presence of diabetes-related complications, and comorbidities such as hyperlipidemia and hypertension, as well as the use of antidiabetic medications during Ramadan, were retrieved from the patient's records. As the survey was conducted post-Ramadan, the pre-Ramadan assessment of specific risk stratification for Ramadan fasting was not performed. Data were then subdivided on whether patients were treated with Empagliflozin or not. For those on Empagliflozin, data were then subdivided according to concomitant therapy with sulphonylureas, insulin, both, or neither of the two groups.

Statistical Analysis

Descriptive statistics were used to describe the patient demographics and other clinical characteristics. All continuous variables were represented as the mean $\pm$ standard deviation. Several variables, such as proportions of participants experiencing daytime symptomatic hypoglycemia and symptomatic hyperglycemia, or any categorical variable, were presented as frequencies and percentages. Descriptive statistics were calculated using SPSS software (IBM Corporation, Armonk, New York, United States). Data were stratified by the overall participants with T2D and geographical regions. Not all data were available for all measurements and, therefore, total numbers of patients (n) included in the calculation differ between measurements. Missing data were not imputed. Odds ratios, 95% confidence intervals, and p -values from two-tailed Fisher's exact tests for comparing treatment groups regarding the occurrence of symptomatic hyperglycemia and symptomatic hypoglycemia in fasting patients, or preexisting diabetes complications in all patients, were calculated using SAS 9.4 (SAS Institute Inc., Cary, North Carolina). Due to the explorative nature of the analysis and the small sample sizes, no adjustment for multiple comparison was made.

Results

Population Demographics

A total of 1,462 patients, 668 female (45.7%) and 794 male (54.3%), met the inclusion criteria for the sub-analysis. The countries with the highest number of participants were from the Indian subcontinent (788, 54.6%), followed by the Gulf countries (293, 20.3%), Southeast Asia (243, 16.8%), the Middle East (Egypt, Türkiye, and Iraq) (117, 8.1%), and the Maghreb countries (3, 0.2%) (see ►Table 1).

The participants were divided into four treatment groups, (1) patients treated with Empagliflozin, but no insulin or sulphonylureas (440 patients, 30.1%), (2) patients treated with Empagliflozin and sulphonylureas, but no insulin (320 patients, 21.9%), (3) patients treated with Empagliflozin and an insulin but no sulphonylureas (612 patients, 41.9%), and (4) patients treated with Empagliflozin, an insulin, and sulphonylureas (92 patients, 6.3%). On average, the patients in Group

1 were the youngest and also had the shortest duration of diabetes (for further demographic data, see ►Table 1).

Baseline Characteristics

The HbA1c values were highest in patients treated with Empagliflozin combined with an insulin or both an insulin and sulphonylureas. Body mass index (BMI) values in all groups were above World Health Organization recommendations of a BMI ranging between 18.5 and 25.0 for a healthy body weight,¹⁷ but comparable across groups. Systolic blood pressures ranged from 124.8 to 132.5 mmHg across groups. In regard to low-density lipoprotein values, an increase was observed from Group 1 to Group 4. Most patients in all groups were nonsmokers. The diabetes complications surveyed were on average most frequent in Group 4, with a visible increase from Group 1 to Group 4. For further details, see ►Table 2.

The comparisons between treatment groups for the occurrence of diabetes complications showed differences and revealed several significant odds ratios as per ►Fig. 1. Patients were treated with a variety of medications. Metformin use varied from 86.6% (381) in Group 1 to 93.5% (86) in Group 4. Similarly, use of DPP4 inhibitors varied slightly from 52.3% of patients (230) in Group 1 to 50.0% (46) in Group 4. Variations in GLP-1 agonist use were more obvious among the groups, as it was administered to 1.8% of patients (8) in Group 1, 5.9% (19) in Group 2, 7.0% (43) in Group 3, and 7.6% of patients (7) in Group 4.

Intentions and Abilities to Fast/Duration of Fasting

The rate of patients with an intention to fast was very high in all four treatment groups. In Group 1, 92.3% of patients (405) had an intention to fast. In Group 2, it was 92.5% (296), in Group 3, it was 85.6% (524), and in Group 4, 88.0% (81).

Fasting for 30 days was reported for 66.4% of patients (269) in Group 1, 67.2% of patients (199) in Group 2, 53.3% of patients (279) in Group 3, and 63% of patients (51) in Group 4. The mean duration of fasting (and standard deviation) was 28 days (± 5.6) in Group 1, 28.5 days (± 3.8) in Group 2, 27.6 days (± 5.4) in Group 3, and 27.4 days (± 5.2) in Group 4.

Symptomatic Hypoglycemia during Ramadan Fasting

In regard to the overall occurrence of symptomatic hypoglycemia (identified based on symptoms, not SMBG-confirmed), an increase in rates from Group 1 to Group 4 was observed. In total, in Group 1, 28 of 405 patients who fasted (6.9%) experienced symptomatic hypoglycemia. In Group 2, it was 29 of the 296 patients who fasted (9.8%); in Group 3, 91 of the 524 patients who fasted (17.4%), and in Group 4, it was 16 of the 81 patients who fasted (19.7%) who experienced symptomatic hypoglycemia.

The comparisons between treatment groups for the occurrence of symptomatic hypoglycemia showed several significant odds ratios, as shown in ►Fig. 2. Frequent hypoglycemia for more than 8 days varied among the groups, as in Group 1, it was 3.4% (1), in Group 2, it was 3.6% (1), in Group 3, it was 5.6% (5), and in Group 4, it was 6.2% of patients (1) who experienced hypoglycemia.

Table 1 Baseline demographic data of patients

Characteristics		GROUP 1 Empagliflozin (N=440)		GROUP 2 Empagliflozin + sulphonylur- eas (N=320)		GROUP 3 Empagliflozin + insulins (N=612)		GROUP 4 Empagliflozin + sulphony- lureas + insu- lins (N=92)	
		n	%	n	%	n	%	n	%
Gender	Female	186	42.4	142	44.4	289	47.3	51	55.4
	Male	253	57.6	178	55.6	322	52.7	41	44.6
Region	Gulf countries	87	20.2	93	29.6	86	14.1	27	30.3
	Maghreb countries	2	0.5	0	0	1	0.2	0	0
	Middle East	31	7.2	25	8	59	9.7	2	2.2
	Indian subcontinent	278	64.6	150	47.8	318	52.1	42	47.2
	Southeast Asia	34	7.9	46	14.6	145	23.8	18	20.2
Age (y)	<40	54	12.3	27	8.5	57	9.3	7	7.6
	40–49	149	33.9	77	24.1	140	22.9	22	23.9
	50–59	135	30.8	102	32	187	30.6	33	35.9
	60+	101	23	113	35.4	227	37.2	30	32.6
	Mean ± SD	50.8 ± 10.4		53.9 ± 10		54.6 ± 10.7		54.3 ± 9.5	
Duration of diabetes (y)		n	%	n	%	n	%	n	%
	<10	303	69.2	180	56.3	197	32.3	34	37
	10–19	117	26.7	109	34	269	44.2	46	50
	≥20	18	4.1	31	9.7	143	23.5	12	13
	Mean ± SD	7.8 ± 5.8		9.3 ± 6.3		13.7 ± 7.8		11.9 ± 6	

Abbreviation: SD, standard deviation.

The comparisons between treatment groups regarding the occurrence of hypoglycemia for more than 8 days did not result in any significant odds ratios. Also, when comparing the treatment groups without insulins (groups 1 and 2) with the treatment groups receiving insulins (groups 3 and 4), no significant odds ratios were detected. Across all groups, only three patients were hospitalized due to symptomatic hypoglycemia during Ramadan fasting (two treated with Empagliflozin and sulphonylureas and one treated with Empagliflozin, sulphonylureas, and an insulin).

Symptomatic Hyperglycemia during Ramadan Fasting (Blood Glucose >16.6 mmol/L, or 300 mg/dL)

The overall occurrence of symptomatic hyperglycemia increased from Group 1 to Group 4. In Group 1, 8.4% (34) experienced symptomatic hyperglycemia, while in Group 4, it was 22.2% (18). The rates of symptomatic hyperglycemia and corresponding odds ratios are depicted in ►Fig. 3.

Frequent hyperglycemia for more than 8 days also varied among the groups. In Group 1, it was 9.1% of patients (3), in Group 2, it was 10.7% of patients (3), in Group 3, it was 25.0% of patients (17), and in Group 4, it was 16.7% of patients (3) who experienced hyperglycemia.

Across all groups, only two patients were hospitalized due to symptomatic hyperglycemia during Ramadan fasting (one treated with Empagliflozin and sulphonylureas, one treated with Empagliflozin and an insulin). Of the 152 symptomatic hyperglycemic events across all treatment groups, most

events occurred during eating hours (85, 56%), whereas it was 30% (45) during eating and fasting hours and 14% (22) during fasting hours.

Breaking of Fast Due to Diabetes-Related Illness

Small rates of patients stopped observing the fast due to symptomatic hyper- and hypoglycemic events. Among the patients who experienced symptomatic hypoglycemia, 28.6% (8) in Group 1, 13.8% (4) in Group 2, 12.1% (11) in Group 3, and 37.5% (6) in Group 4 stopped observing the fast. Among those patients who experienced symptomatic hyperglycemia, 8.8% (3) in Group 1, 13.8% (4) in Group 2, 13.2% (9) in Group 3, and no patient in Group 4 stopped observing the fast, as depicted in ►Fig. 4.

Self-Monitoring of Blood Glucose

SMBG was done more frequently during Ramadan than before by 7.9% of patients (34) in Group 1, 19.1% (59) in Group 2, 13.7% (80) in Group 3, and 39.1% (34) in Group 4. Less frequent SMBG was documented for 16.3% of patients (70) in Group 1, 16.2% (50) in Group 2, 17.3% (101) in Group 3, and 8% of patients (7) in Group 4. Furthermore, 63.5% of patients (273) in Group 1, 47.4% (146) in Group 2, 56.4% (328) in Group 3, and 37.9% (33) in Group 4 did SMBG at the same frequency as before during Ramadan. In total, 12.3% of patients (53) in Group 1, 17.2% (53) in Group 2, 12.5% (73) in Group 3, and 14.9% (13) of patients in Group 4 did not self-monitor their blood glucose levels.

Table 2 Baseline risk factors, comorbidities, and complications in the various subgroups

Characteristics		GROUP 1 Empagliflozin (N = 440)		GROUP 2 Empagliflozin + sulphonylur- eas (N = 320)		GROUP 3 Empagliflozin + insulins (N = 612)		GROUP 4 Empagliflozin + sulphony- lureas + insulins (N = 92)	
		n	%	n	%	n	%	n	%
HbA1c (%)	<7.5	190	45.5	93	31.2	136	23.8	15	17.6
	7.5–9.0	148	35.4	127	42.6	184	32.1	36	42.4
	>9	80	19.1	78	26.2	252	44.1	34	40
	Mean ± SD	7.9 ± 1.6		8.3 ± 1.6		9 ± 1.8		8.9 ± 1.6	
BMI (kg/m ²)	Mean ± SD	29 ± 5.9		28 ± 6.3		29 ± 7.1		29.6 ± 8.2	
SBP (mm Hg)	Mean ± SD	124.8 ± 19		126.1 ± 21		132.1 ± 21		132.5 ± 21.4	
DPB (mm Hg)	Mean ± SD	79 ± 12.3		78.3 ± 13.3		78.8 ± 11.9		80.9 ± 10.2	
LDL (mg/dL)	Mean ± SD	101.8 ± 38.7		104.5 ± 37.8		117.9 ± 44.3		118.6 ± 40.4	
Smoking status		n	%	n	%	n	%	n	%
	Current smoker	21	7.4	8	3.9	18	5.2	4	6.5
	Past smoker	11	3.9	24	11.8	45	13.1	6	9.7
	Non-smoker	251	88.7	171	84.2	280	81.6	52	83.9
Diabetes complications	Hypertension	114	25.9	152	47.5	272	44.4	74	80.4
	Hyperlipidemia	124	28.2	144	45.0	262	42.8	72	78.3
	Retinopathy	22	5.0	22	6.9	113	18.5	20	21.7
	Neuropathy	26	5.9	43	13.4	122	19.9	35	38.0
	Microalbuminuria	13	3.0	20	6.3	66	10.8	15	16.3
	Nephropathy/CKD	22	5.0	17	5.3	91	14.9	12	13.0
	Macrovascular disease	34	7.7	32	10.0	105	17.2	18	19.6
	Diabetic foot disease	12	2.7	5	1.6	32	5.2	6	6.5
	None	160	36.4	65	20.3	103	16.8	6	6.5

Abbreviations: BMI, body mass index; CKD, chronic kidney disease; DBP, diastolic blood pressure; LDL, low-density lipoprotein; SBP, systolic blood pressure; SD, standard deviation.

Ramadan-Focused Diabetes Education

A high proportion of patients in the study received Ramadan-focused diabetes education. In Group 1, 72.5% of patients (312) received education, in Group 2, it was 66.2% (204), in Group 3, it was 66.8% (388), and in Group 4, it was 80.5% of patients (70). Education was done in the clinic during routine consultation for 64.0 to 87.4% of the patients, in a group session for 1.6 to 7.6% of the patients, online or through an app for 1.7 to 4.5%, or via leaflet for 3.6 to 47.0% of the patients.

Discussion

The focus of the present survey-based study was to describe the experience of patients treated with Empagliflozin in combination with other antiglycemic agents and the associated concerns and challenges during Ramadan fasting. There were four treatment groups: Group 1: Empagliflozin without sulphonylureas or insulins, Group 2: Empagliflozin plus sulphonylureas, Group 3: Empagliflozin plus insulins, and Group 4: Empagliflozin plus sulphonylureas and insulins.

We observed that 89.2% of the patients fasted and the mean duration of fasting was similar amongst the four groups, ranging from 27.4 to 28.5 days, which aligns with recent studies on Ramadan fasting among patients with diabetes.^{5,6,14–16} Despite the elevated risk of diabetes-associated complications during fasting, these studies uniformly showed high rates of fasting among diabetes patients across different geographical regions.

One of the two major risks for diabetes patients during fasting is hypoglycemia. Depending on the study group, 6.9 to 19.7% of the participants from the present study experienced symptomatic hypoglycemia. The mean number of days on which patients experienced hypoglycemia was 2.5 to 4.1, and only a low proportion of patients (up to 6.2%) experienced hypoglycemia on more than 8 days, for which no significant differences were recognized between the groups. The findings are similar to what was reported in previous studies.^{3,5,14–16}

As expected, patients treated with Empagliflozin without sulphonylureas or insulin had a significantly lower rate of hypoglycemic events than patients treated with Empagliflozin plus insulins (odds ratio = 2.27) and patients treated with

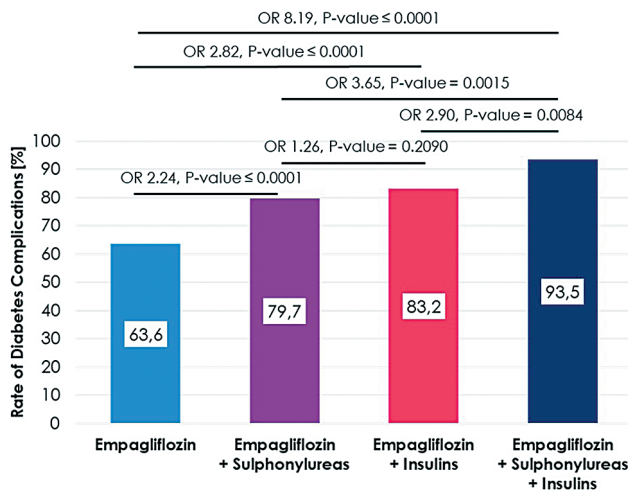


Fig. 1 Rates of type 2 diabetes complications with odds ratios across treatment groups. *p*-Values were calculated using the two-tailed Fisher's exact test. OR, odds ratio.

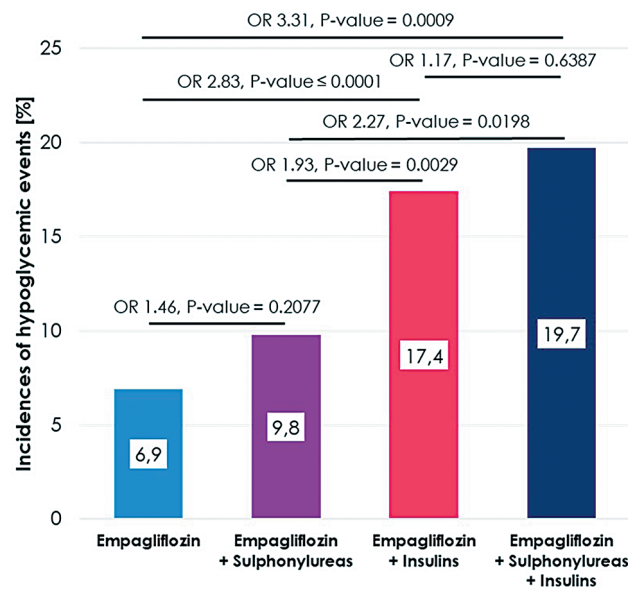


Fig. 2 Incidences of symptomatic hypoglycemia across treatment groups with odds ratios. Hypoglycemia was identified based on symptoms (not SMBG-confirmed). *p*-Values were calculated using the two-tailed Fisher's exact test. OR, odds ratio; SMBG, self-monitoring blood glucose.

Empagliflozin plus sulphonylureas and insulin (odds ratio = 3.31). This group had a shorter duration of diabetes and fewer diabetes-related complications. The mode of action of the SGLT2 inhibitor, when used alone, could have led to these lower rates of hypoglycemia compared to concomitant treatment with sulphonylureas and/or insulin. On the contrary, there was no significant difference in hypoglycemia rates between patients treated with Empagliflozin without or with sulphonylurea. This finding is quite reassuring that the combination of SGLT2 inhibitors and sulphonylureas does not significantly increase the risk of hypoglycemia in individuals who chose to fast in Ramadan. The severity of hypoglycemic events in Group 1 and Group 2 was so moderate that no hospital admissions were necessary. Only two patients from Group 3 and one patient from Group 4 needed to be hospitalized.

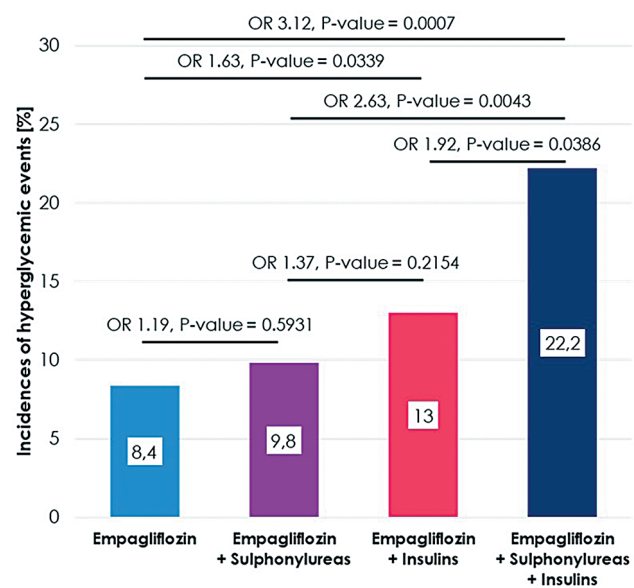


Fig. 3 Rates of symptomatic hyperglycemia with odds ratios across treatment groups. Hyperglycemia was defined as blood glucose >16.6 mmol/L, or 300 mg/dL. *p*-Values were calculated using the two-tailed Fisher's exact test. OR, odds ratio.

The other major risk for diabetes patients during fasting is hyperglycemia. The rate of patients who experienced hyperglycemia during fasting was 8.4 to 22.2% in this study. This is comparable to the previous studies reporting 16.3%^{14,15} and 11.6%.⁶ The mean number of days on which patients experienced hyperglycemia was 4.0 to 7.2. Patients treated with Empagliflozin without sulphonylureas or insulin had significantly lower rates of hyperglycemic events than patients treated with Empagliflozin plus insulin (odds ratio = 1.63) and Empagliflozin plus sulphonylureas and insulin (odds ratio = 3.12). Reassuringly, only two cases required hospitalization due to hyperglycemia, corresponding to a total hospitalization rate of 1.3%. As expected, most hyperglycemic events occurred during eating hours. A likely explanation for the rate of hyperglycemia being lower in the Empagliflozin-only group could be the lack of fear of hypoglycemia, which is sometimes associated with overeating as a self-defense mechanism. It could also be related to the fact that patients on additional sulphonylureas and/or insulin were more advance in their disease, which is frequently associated with higher blood glucose levels.

Surprisingly, more patients in Group 1, treated with Empagliflozin only, broke their fast during hypo- or hyperglycemia compared to those on more intensive therapies. It has to be noted that the risk of hypoglycemia for patients on Empagliflozin is comparably low, but some people during fasting do experience hypoglycemia even on diet only. However, this unexpected finding has to be further investigated in future studies with confirmed hypoglycemia and with better education for all groups.

Despite differences between the treatment groups, it has to be emphasized that in total, among 1,306 fasting patients, only 5 cases of hospitalization due to critical hypo- or hyperglycemic situations were reported (0.38%).

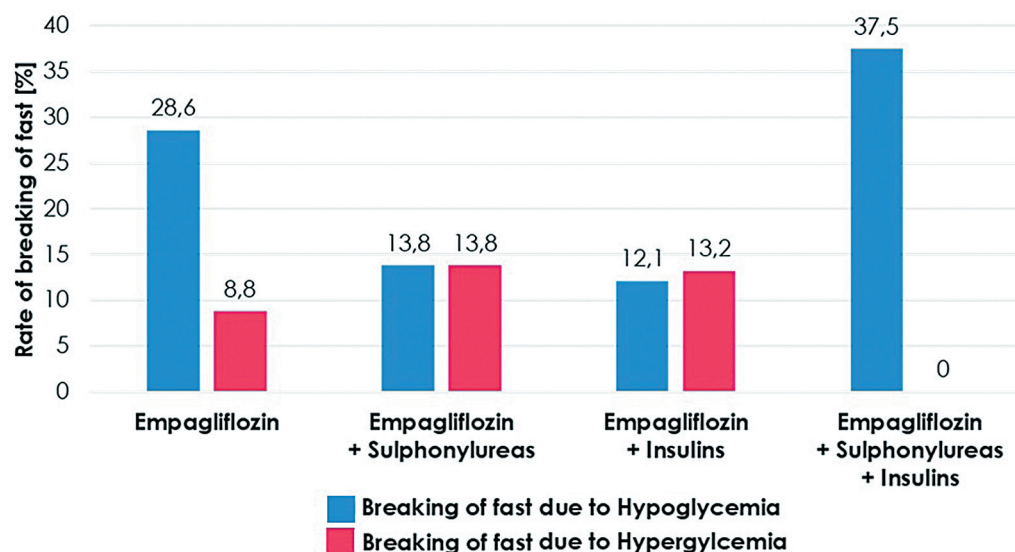


Fig. 4 Patients who stopped observing the fast due to symptomatic hypo- or hyperglycemic events. Hypoglycemia was identified based on symptoms (not SMBG-confirmed). Hyperglycemia was defined as blood glucose >16.6 mmol/L, or 300 mg/dL. SMBG, self-monitoring blood glucose.

Ramadan-focused education is an essential component of diabetes care to reduce diabetes-related complications. Education rates in this study were relatively high (66.2–80.5%) compared to previous studies.^{14,15} However, there was still a relevant proportion of up to one-third of patients who did not receive such an important intervention. Increasing this rate might further reduce diabetes-related complications during Ramadan fasting. It is noteworthy that most of the diabetes-related education is still based on personal contact in the clinical context during routine consultation. Only 1.7 to 4.5% of the patients received their education online or through an app. Using more digital health applications for this specific education in the future might be a valuable complement to the other educational techniques, since it would allow easy and on-demand access to relevant information and also could serve as a digital diabetes coach. The lack of education on diabetes self-management is reflected by low SMBG rates in all four groups.

There are some limitations associated with the present study. Several methodical aspects have to be considered. Unfortunately, no data on diet, physical activity, and medication adjustments were collected. In regard to several questions that the patients were asked, recall bias may be a concern, as patients might struggle to accurately remember their SMBG practices, dietary habits, or health outcomes, especially if the consultation occurs weeks after Ramadan. However, as is usually the case, Muslims have to compensate for days when they broke their fast, recall is usually strong. Also, selection bias could arise if only patients who regularly visit clinics or those with specific health conditions are included in the study, potentially excluding healthier individuals who do not seek frequent medical care. Another aspect is that hypoglycemia was not confirmed by SMBG but reported based on symptoms. This might explain the differences in hypoglycemia rates with regard to other studies. This method may lead to overestimation of hypoglycemic

events. Although the inclusion of participants from different geographical regions allows a broader picture of Ramadan practices, it also can introduce additional confounders, such as varying medical and social structures and especially Ramadan-focused medical strategies.

Conclusion

Patients with diabetes on SGLT2 inhibitor Empagliflozin without concomitant insulin and/or sulphonylureas therapy showed a significantly lower rate of symptomatic hypo- and hyperglycemia during Ramadan fasting. Patients who needed additional sulphonylurea therapy experienced such complications slightly more frequently, while patients who needed insulin alongside Empagliflozin therapy showed a significantly higher rate of symptomatic hypo- and hyperglycemia complications.

This underscores that hypoglycemia rates are influenced by the types of therapies administered to the patients. Based on these results, it may be concluded that Empagliflozin monotherapy or in combination with sulphonylureas may be relatively safe for Ramadan fasting, whereas caution is advised for patients taking additional insulin combinations.

Author Confirmation

All the authors contributed to the conduct of the study and preparation of the manuscript. It is hereby confirmed that the manuscript has been read and approved by all named authors and that no other persons have satisfied the criteria for authorship.

Compliance with Ethical Principles

The surveys, which were the basis for the present sub-analysis, had the approval of the local research and ethics authorities in each participating country, according to local regulations.

Data Availability Statement

The original data supporting this study can be obtained by reasonable request to the corresponding author.

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Conflict of Interest

None declared.

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