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The characteristics and pattern of care for the type 2 diabetes mellitus population in the MENA region during Ramadan: An international prospective study (DAR-MENA T2DM)

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ABSTRACT

Aims: We aimed to describe the characteristics and care of participants with diabetes during Ramadan in the Middle East and North Africa (MENA).

Methods: In this prospective, observational study, we analysed the number of fasted days, number of participants fasting, glycemic control, rate of hypoglycemic events, and lifestyle patterns for participants with T2DM during Ramadan 2016.

Results: The population included 1749 participants with T2DM. The mean (SD) duration of fasting was 27.7 (5.0) days, and 57.3% of participants fasted for the full duration of Ramadan. Following Ramadan, a significant improvement in HbA1c, FPG, and PPG was observed ($p < 0.0001$). Confirmed hypoglycemia increased significantly from before to during Ramadan (incidence: 4.9% vs. 10.4%, $p < 0.001$; adverse events: 0.11 vs. 0.22 events/month/participant, $p < 0.001$) and was dependent on the treatment regimen. Severe hypoglycemia incidence was 0.2% before versus 0.9% during Ramadan ($p = 0.031$), whereas adverse events

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remained comparable (0.01 events/month/participant; p = 0.154). Most participants (97.4%) reported lifestyle changes during Ramadan.

Conclusions: This prospective study is the first to describe the characteristics and care of participants with T2DM during Ramadan in MENA, and can be utilized in the development of evidence-based care to ensure the safety of participants who fast.

1. Introduction

There are 40 million adults with diabetes in the Middle East and North Africa (MENA) region, and approximately 93% are Muslim [1,2]. Even though fasting is not required for Muslims with serious health issues, including some people with diabetes, a high proportion of Muslims with type 2 diabetes mellitus (T2DM) do fast during Ramadan. For example, the CREED study noted that 63.6% fasted every day, and 94.2% fasted for at least 15 days during Ramadan 2010 [3].

Daily length of fasting is dependent on the timing of Ramadan for a given year as well as the geographic location. In the MENA region, fasting during Ramadan in 2016 started at dawn on June 6 and finished on the evening of July 5, where the daylight hours ranged between 13 h and 36 min to 14 h and 25 min, and included the longest daylight hours of the year for the MENA region. The previous multiregional studies, CREED and EPIDIAR, included shorter daylight hours as they were conducted in countries primarily in the Northern hemisphere during the Ramadan periods of August to September and November to December, respectively [3–5].

Little is known about the effect of long-term fasting during Ramadan on diabetic control. Fasting may result in the deterioration of glycemic control and increase the risk of dyslipidemia, hypoglycemia, hyperglycemia, diabetic ketoacidosis, dehydration, and thrombosis [5–11]. Hypoglycemia is of particular concern during fasting. For example, the overall incidence of documented hypoglycemia during Ramadan across several regions in the CREED study was 7.1%, with 4.1% reported for the Middle East and 13% reported for North Africa [5].

During Ramadan, lifestyle may be temporarily altered, and the degree and type of change varies by region. The EPIDIAR study reported that approximately 50% of participants with diabetes experienced a change in lifestyle, with the proportion of participants with T2DM experiencing a change ranging from 25.2% to 54.4% for oral antidiabetic drug (OAD), insulin dose, weight, physical activity, sugar intake, food intake, fluid intake, and sleep duration [4]. Ramadan-focused education can enable individuals to adjust their lifestyle during Ramadan, minimize the risk of hypoglycemic events and weight gain, and be tempered to the local practices and seasonal time of year when Ramadan occurs [7,10,12–16]. A recent prospective study found that pre-Ramadan education reduced acute complications, including hypoglycemia risk and low-density lipoprotein (LDL) cholesterol and improved high-density lipoprotein (HDL) cholesterol [17].

There are few real-world studies investigating epidemiological outcomes of fasting during Ramadan; they are also limited by the data they report. The majority investigating real-life glycemic control practices during Ramadan fasting lack pre-Ramadan baseline data and adequate patient numbers. Therefore, the learnings that can be used for the development of evidence-based care guidelines specific to Ramadan fasting are limited [3,4]. By the nature of their study design, retrospective studies often lack baseline data either due to a lack of recording or as a result of being dependent on patient recall. Although some prospective studies have been performed, they generally lack pre-Ramadan data for some or all parameters and are relatively small-scale [18–20]. Large-scale, prospective studies with detailed collection and analysis of fasting parameters as well as glycemic, biochemical and biometric measures during and prior to Ramadan are, therefore, required in order to provide greater understanding of treatment requirements for individuals who choose to fast during Ramadan.

This prospective, observational study aimed to provide an epidemiological analysis to fully describe the characteristics and pattern of care of people with T2DM during Ramadan living in the MENA region. We sought to provide unique insights into daily fasting during Ramadan by capturing concerns specific to before and during the month of fasting, including pattern of care, glycemic control, hypoglycemia risk, lifestyle changes, and patient education on diabetes management.

2. Participants, materials and methods

2.1. Study design

This international, multicenter, prospective, observational study (Diabetes and Ramadan - Middle East and North Africa [DAR-MENA]) recruited adult people with type 1 diabetes mellitus (DAR-MENA T1DM) and T2DM (DAR-MENA T2DM) from private or public hospitals/clinic sites in MENA countries participating in Ramadan: Egypt, Iraq, Israel, Jordan, the Kingdom of Saudi Arabia, Kuwait, Lebanon, Morocco, Pakistan, and the United Arab Emirates. Algeria and Iran were initially included but did not have active sites.

The study used data reported to the Ramadan registry from April 21 to October 13, 2016. The dates of fasting during Ramadan in 2016 were dawn of June 6 to evening of July 5 and included the longest seasonal daylight hours of the year.

Participants who were aged ≥18 years with T1DM or T2DM, and who were Muslim and did or did not intend to fast, were eligible for study participation. Participants were also required to provide written informed consent forms (ICFs) for study inclusion. Women who were pregnant, had gestational diabetes, or were breastfeeding were excluded, as were those who were participating in another clinical trial.

Investigators were selected randomly from a master list (50% excess) created independently in each country based on a feasibility assessment. Investigators consecutively selected one participant per consulting session who met the eligibility requirements; consecutive selection was performed to limit participant selection bias.

The study aimed to enroll 2000 people from the MENA region, distributed according to the total population of people with diabetes for each participating country [21]. The required sample size was estimated based on the assumption that the changes in the pattern of care would impact almost 40% of people [3], and that the non-evaluability rate would be 26%. The inclusion of 2000 people per region was, therefore, estimated to provide a 95% confidence interval with a precision between ± 2.19%. The large representative sample size from a range of countries in the MENA region also decreased potential bias.

The manuscript was prepared in line with the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines [22]. This study was also conducted in accordance with the ethical principles laid down in the Declaration of Helsinki, and complied with all international guidelines, and national laws and regulations of each country in which the registry was performed. It should be noted that protocol deviations of participants without signed ICFs were detected during monitoring visits. Sites either gathered signed ICFs retrospectively or the participants were not included in the study database. All participants included in the study provided informed consent.

2.2. Measurements

Characteristics and adjustments to the pattern of care for the DAR-MENA T2DM population before and during Ramadan were recorded (Supplementary Fig. 1).

Measurements included the mean number of days fasted, number of participants who fasted for ≥1 day, ≥15 days, and 30 days, and reasons for fasting and not fasting as well as diabetes treatment among participants who fasted (including any modifications in antidiabetes medication or doses of medication).

The mean change during Ramadan compared with before Ramadan was calculated for glycemic profile (glycated hemoglobin [HbA1c], fasting plasma glucose [FPG], and postprandial plasma glucose [PPG]), lipid profiles (total cholesterol, triglycerides, HDL, and LDL), and biometric measures (weight, systolic/diastolic blood pressure [SBP/DBP], waist circumference, and heart rate).

The mean change of symptomatic confirmed/severe hypoglycemia and symptomatic confirmed/severe hyperglycemia incidence and adverse events (AEs) during Ramadan were compared with incidence and AEs within 1 month before Ramadan. Symptomatic confirmed hypoglycemia was defined as an event with clinical symptoms that are considered to result from hypoglycemia and confirmed by a self-measured plasma glucose (SMPG) measurement <70 mg/dL. Severe hypoglycemia was defined as a hypoglycemia event requiring assistance due to acute neurological impairment directly resulting from hypoglycemia. Symptomatic confirmed hyperglycemia was defined as an event with clinical symptoms that are considered to result from hyperglycemia and confirmed by an SMPG of ≥200 mg/dL.

Changes in co-morbidities, lifestyle, and access to education on diabetes management were also recorded.

For baseline data on glycemic and lipid profiles, values up to 6 months before baseline were used. The number and timing of hypoglycemia events within 4 weeks before visit 1 were recorded. Follow-up visits were performed at 1–2 months after Ramadan.

Study groups included the T2DM population and subgroups including participants on OADs only with sulfonylurea (SU), OADs only without SU, and insulin with or without OADs in order to determine treatment differences.

2.3. Statistical analysis

Study groups were compared using the Student *t*-test for numerical variables. Mean change during Ramadan or 1 month after compared with before Ramadan among each study subgroup using a paired *t*-test and Student's *t*-test for subgroup comparisons was determined for glycemic profiles (HbA1c, FPG, and PPG), lipid profiles (total cholesterol, triglycerides, and HDL/LDL), body weight, hypoglycemic incidence and AEs (symptomatic confirmed/severe), and hyperglycemic AEs (symptomatic confirmed/severe). Data were stratified by the population with T2DM and study subgroups: OADs only with SU, OADs only without SU, and insulin with or without OADs.

Descriptive quantitative variables were summarized with mean and standard deviation (SD), and descriptive categorical data were summarized by number and percentage of the population.

Not all data were available for all measurements and, therefore, total n values differ between measurements. Missing data were not imputed.

3. Results

3.1. Population demographics and baseline clinical characteristics

Of the 1894 participants enrolled, 1885 people with T1DM and T2DM from 113 sites were evaluable (DAR-MENA population) in the MENA region. The largest proportion of the enrolled DAR-MENA population was 1749 (92.3%) participants with T2DM, of which 1746 (92.6%) were evaluable (Fig. 1). In order to provide T2DM disease-specific analysis, the findings from the 1749 participants with T2DM (DAR-MENA T2DM) are the focus of this manuscript. Due to the high proportion of participants with T2DM in the DAR-MENA population, the results presented here are generally similar to those of the overall population (T1DM + T2DM; data not shown). The results of the DAR-MENA T1DM population will be published separately.

Of the participants with T2DM, the mean age was 55.2 years, 55.6% were male, and the mean diabetes duration was 10.2 years (Table 1). Almost two-thirds of the participants had inactive (22.2%) or low (41.7%) physical activity, while a little over a third had moderate (31.6%) or high (4.4%) physical activity. Few participants (11.7%) were smokers. The mean working hours were 6.5 h/day, and mean sleeping hours were

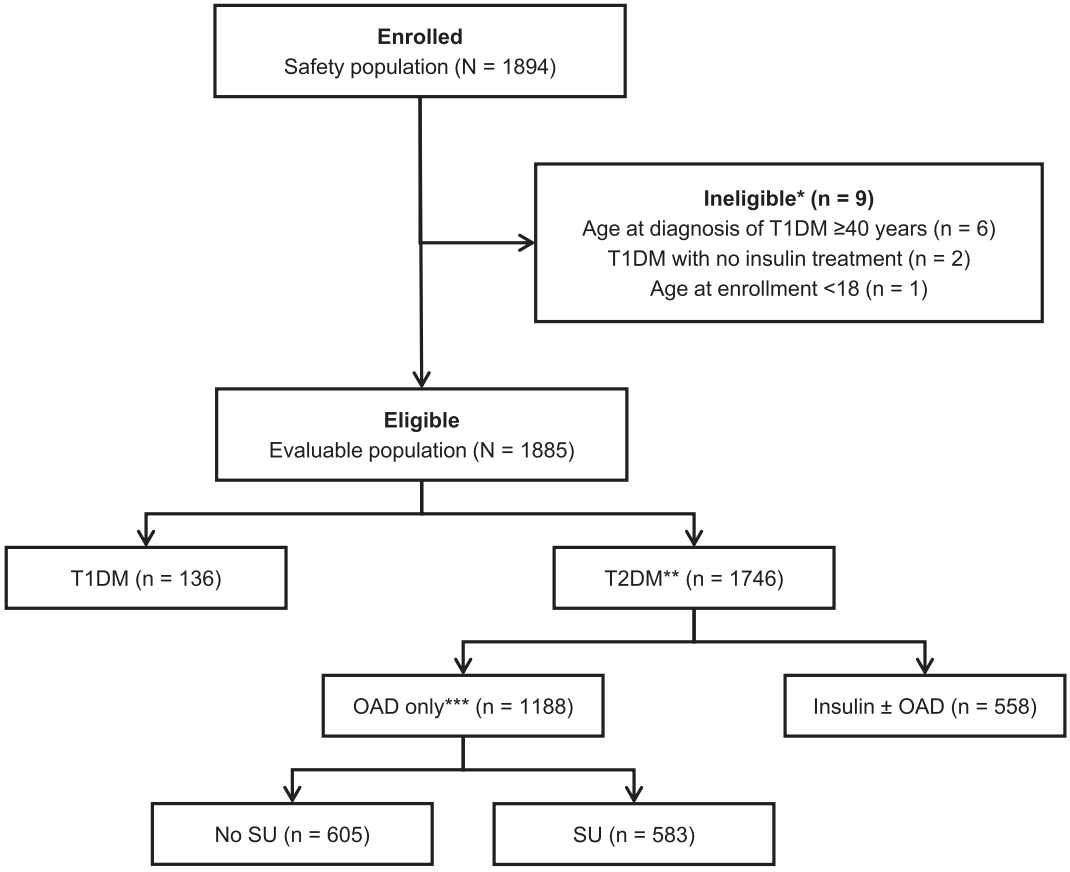

Fig. 1 – Flow diagram of participants' disposition. GLP-1 RA: glucagon-like peptide-1 receptor agonist, OAD: oral antidiabetic drug, SU: sulfonylurea, T1DM: type 1 diabetes mellitus, T2DM: type 2 diabetes mellitus. * Nine patients were excluded after being reviewed and approved by the sponsor; one patient was excluded per protocol exclusion criteria (age < 18 years), and eight patients were excluded due to illogical reported data (T1DM diagnosis ≥ 40 years and patients with T1DM without insulin treatment). ** Three participants were not taking any type of diabetic medication. * OAD includes participants taking an OAD ± GLP-1 RA.**

7.4 h/day. Before Ramadan, 28.6% (500/1749) of patients with T2DM were on an injectable + OAD.

At baseline, DAR-MENA T2DM participants had a mean HbA1c of 8.0% (64 mmol/mol), FPG of 151.2 mg/dL, and PPG of 203.8 mg/dL.

The most common co-morbidities included hypertension (27.5%) and dyslipidemia (13.7%; Supplementary Table 1). Antidiabetes therapies before Ramadan are presented in Supplementary Table 2.

3.2. *Fasting practice and pattern of care before and during Ramadan*

The mean (SD) duration of fasting for the DAR-MENA T2DM population was 27.7 (5.0) days during Ramadan 2016 (n = 1474). Fasting daily hours averaged 15.8 (1.0) h (n = 1473).

The number of days fasted differed slightly with treatment (Supplementary Table 3). Overall, out of a total of 1645 participants with T2DM, 89.7% fasted for ≥1 day, 86.3% fasted for ≥15 days, and 57.3% fasted for the full duration of Ramadan (30 days). The percentage of participants who fasted was highest in the OAD alone groups (no SU: 94.6%; with SU: 92.4%) and lowest in the insulin with or without OAD group (81.4%).

The majority of the DAR-MENA T2DM population who fasted listed personal decision (80.4%) as their motivating factor (Supplementary Table 4). For the 10.3% of participants who did not fast, the most common reasons for not fasting were fear of diabetic complications (48.8%), non-diabetes-related health issues (24.1%), previous experience of acute diabetic complications with fasting (22.9%), healthcare professional (HCP) advice (21.2%), and working conditions (4.1%; Supplementary Table 4).

Overall, 89.0% of the DAR-MENA T2DM population previously prescribed diabetic medication changed their medication, and 46.9% had a change in medication dose (Fig. 2). Of those previously prescribed therapy, 31.7% of participants on OADs without SU, 48.2% of participants on OADs with SU, and 62.0% of participants on insulin with or without OADs had a dose change.

Table 1 – Baseline demographics, participant characteristics, lifestyle, and medical history in participants with T2DM.

Participant characteristics	All (n = 1749)		
	Total n	n or mean	% or ± SD
Men	1749	973	55.6
Age, years	1749	55.2	± 11.1
Weight, kg	1745	84.7	± 16.0
Waist, cm	1477	100.3	± 14.3
BMI, mean (SD) kg/m^2	1739	30.8	± 5.8
Vital signs			
SBP, mmHg	1743	131.9	± 14.6
DBP, mmHg	1743	79.3	± 9.9
Heart rate, beats/min	1657	80.2	± 9.9
Lifestyle			
Physical activity			
Inactive	1744	388	22.2
Low	1744	728	41.7
Moderate	1744	551	31.6
High	1744	77	4.4
Smoking status (yes)	1746	205	11.7
Daily working and sleeping hours			
Working, h/day	1628	6.5	± 3.3
Sleeping, h/day	1681	7.4	± 1.3
Clinical characteristics			
HbA1c, %	1659	8.0	± 1.6
HbA1c, mmol/mol	1659	64	± 17
FPG, mg/dL	1512	151.2	± 51.1
PPG, mg/dL	1065	203.8	± 73.1
LDL, mg/dL	1156	104.5	± 36.9
HDL, mg/dL	1121	43.9	± 11.3
Triglycerides, mg/dL	1273	159.3	± 85.1
Total cholesterol, mg/dL	454	180.0	± 44.6
Serum creatinine, mg/dL	1298	1.2	± 1.4
Medical and surgical history (yes)	1749	993	56.8
Concomitant medications (yes)	1606	1325	82.5
Duration of diabetes, years	1749	10.2	± 8.0
Family history of diabetes (yes)	1730	1287	74.4
Late diabetes complications (yes)	1749	744	42.5
Most common diabetes complications			
Diabetic neuropathy	1749	573	32.8
Diabetic retinopathy	1749	161	9.2
Diabetic nephropathy	1749	156	8.9
Diabetes management before Ramadan, n (%)			
Physical activity only	1749	5	0.3
OADs	1749	1645	94.1
1 OAD	1645	361	21.9
2 OADs	1645	685	41.6
3 OADs	1645	433	26.3
>3 OADs	1645	166	10.1
OAD alone	1749	1145	65.5
Injectable therapy	1749	598	34.2
Insulin	1749	549	31.4
GLP-1 RA	1749	92	5.3
Injectable alone	1749	98	5.6
Study subgroups, n (%)			
OAD only*	1746**	1188	68.0
OAD without SU	1746**	605	34.7
OAD with SU	1746**	583	33.4
Insulin ± OAD*	1746**	558	32.0

BMI: body mass index, DBP: diastolic blood pressure, FPG: fasting plasma glucose, GLP-1 RA: glucagon-like peptide-1 receptor agonist, HbA1c: glycated hemoglobin, HDL: high-density lipoprotein, LDL: low-density lipoprotein, OAD: oral antidiabetic drug, PPG: postprandial plasma glucose, SBP: systolic blood pressure, SD: standard deviation, SU: sulfonylurea, T2DM: type 2 diabetes mellitus.

N.B. Co-morbidities are presented as supplementary information (Supplementary Table 1).

* OAD only includes participants taking an OAD ± GLP-1 RA.

** Three participants were not taking any type of diabetic medication and were excluded.

Table 2 – Comparison between before and after Ramadan for biochemical and biometric measures in participants with T2DM.

Characteristics	All n = 1749							
	Before Ramadan			After Ramadan			Change	p value
	Total n	Count/mean	%/± SD	Total n	Count/mean	%/± SD		
Weight, kg	1745	84.7	± 16.0	1643	84.0	± 14.4	–0.6 ± 4.1	<0.0001*
Waist circumference, cm	1477	100.3	± 14.3	1344	99.2	± 14.4	–0.6 ± 6.6	0.001*
SBP, mmHg	1743	131.9	± 14.6	1645	128.9	± 12.1	–3.1 ± 11.7	<0.0001*
DBP, mmHg	1743	79.3	± 9.9	1645	79.0	± 19.9	–0.3 ± 19.7	0.525*
Heart rate, beats/min	1657	80.2	± 9.9	1572	79.4	± 8.8	–0.9 ± 9.2	<0.0001*
Working, h/day	1628	6.5	± 3.3	1609	5.2	± 2.8	–1.2 ± 2.2	<0.0001*
Sleeping, h/day	1681	7.4	± 1.3	1633	7.6	± 1.6	0.1 ± 1.6	0.002*
Physical activity								
Inactive	1746	388	22.2	1641	399	24.3	–	0.146**
Low		728	41.7		668	40.7		
Moderate		551	31.6		518	31.6		
High		77	4.4		56	3.4		
Smoker								
Yes	1746	205	11.7	1724	178	10.3	–	0.754***
No		1541	88.3		1546	89.7		
HbA1c, %	1659	8.0	± 1.6	1377	7.5	± 1.2	–0.5 ± 1.2	<0.0001*
HbA1c, mmol/mol	1659	64	± 17	1377	59	± 13	–5 ± 13	<0.0001*
FPG, mg/dL	1512	151.2	± 51.1	1383	134.4	± 37.9	–16.4 ± 48.4	<0.0001*
PPG, mg/dL	1065	203.8	± 73.1	987	181.5	± 49.7	–25.0 ± 65.1	<0.0001*
LDL, mg/dL	1156	104.5	± 36.9	688	98.1	± 32.4	–5.2 ± 30.2	<0.0001*
HDL, mg/dL	1121	43.9	± 11.3	679	45.4	± 14.7	1.0 ± 12.6	0.059*
Triglycerides, mg/dL	1273	159.3	± 85.1	787	154.2	± 73.9	–2.6 ± 66.9	0.306*
Total cholesterol, mg/dL	1295	180.0	± 44.6	803	175.6	± 40.1	–4.9 ± 37.7	0.001*

DBP: diastolic blood pressure, FPG: fasting plasma glucose, HbA1c: glycated hemoglobin, HDL: high-density lipoprotein, LDL: low-density lipoprotein, PPG: postprandial plasma glucose, SBP: systolic blood pressure, SD: standard deviation, T2DM: type 2 diabetes mellitus.

* Paired *t*-test used to compare between metric variables before and after Ramadan.

** McNemar–Bowker test used to compare between physical activity before and after Ramadan.

*** McNemar test used to compare between categorical variables before and after Ramadan.

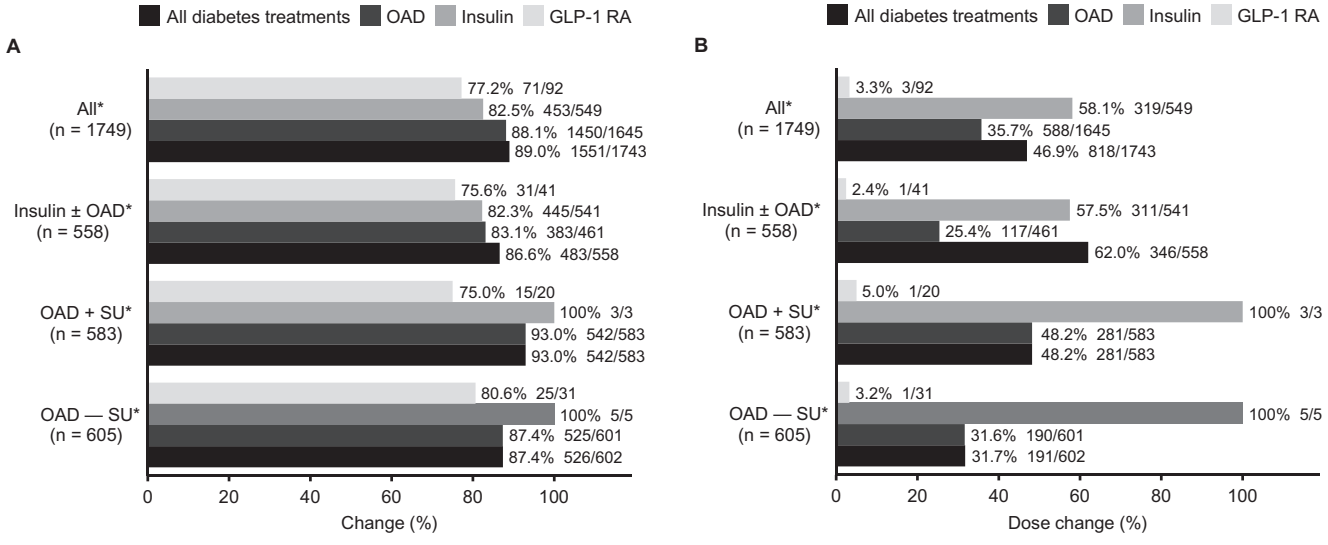

Fig. 2 – Modifications in diabetes treatment in participants with T2DM. GLP-1 RA: glucagon-like peptide-1 receptor agonist, OAD: oral antidiabetic drug, SU: sulfonylurea, T2DM: type 2 diabetes mellitus. * Out of 1749 patients with T2DM, three did not receive any type of diabetic medication.

3.3. Biochemical and biometric measures before and during Ramadan

Before and after fasting during Ramadan, there were significant changes in HbA1c, FPG, PPG, LDL, total cholesterol, weight, SBP, waist circumference, heart rate, and working and sleeping hours per day for the DAR-MENA T2DM population (Table 2). Notably, for the DAR-MENA T2DM population, there was a significant improvement ($p < 0.0001$) in mean (SD) HbA1c levels after Ramadan (7.5 [1.2]%; 59 [13] mmol/mol) compared with that before Ramadan (8.0 [1.6]%; 64 [17] mmol/mol). Although there was a mean (SD) statistically significant weight difference of –0.6 (4.1) kg ($p < 0.0001$) from before to after Ramadan, the change is not considered clinically significant. There was a significant decrease in mean (SD) working hours of –1.2 (2.2) from before to during Ramadan ($p < 0.0001$). Significant reductions in other biochemical and biometric measures were noted after Ramadan, including SBP, LDL, and total cholesterol, but they were also not considered clinically significant.

3.4. Hypoglycemia before and during fasting

In the DAR-MENA T2DM population, the incidence of hypoglycemia increased significantly from 4 weeks before versus during Ramadan for both confirmed hypoglycemia (4.9% vs. 10.4%, $p < 0.001$) and severe hypoglycemia (0.2% vs. 0.9%, $p = 0.031$; Fig. 3). Confirmed hypoglycemia AEs were significantly higher during Ramadan, with 0.22 events/-month/participant, compared with 4 weeks before Ramadan, with 0.11 events/month/participant ($p < 0.001$), whereas the severe hypoglycemia AEs were comparable, with 0.01 events/month/participant both before and during Ramadan ($p = 0.154$; Fig. 3).

The change in confirmed hypoglycemia, and corresponding AEs, were dependent on the treatment regimen (Fig. 3). People prescribed OADs without SU fasted with no statistically significant increase in confirmed hypoglycemia incidences or AEs from 4 weeks before Ramadan to during Ramadan (incidence: 2.1% vs. 4.3%, $p = 0.080$; AEs: 0.06 vs. 0.10 events/month/participant, $p = 0.387$), while a significant increase occurred with those receiving OADs with SU (incidence: 2.6% vs. 9.2%, $p < 0.001$; AEs: 0.04 vs. 0.19 events/month/participant, $p < 0.001$) and insulin with or without OADs (incidence: 10.2% vs. 18.2%, $p < 0.001$; AEs: 0.24 vs. 0.40 events/month/participant, $p = 0.011$). There was no significant increase in severe hypoglycemia incidence or AEs for treatment regimen subgroups.

3.5. Hyperglycemia before and during fasting

For the DAR-MENA T2DM population, the incidence of confirmed and severe hyperglycemia decreased from

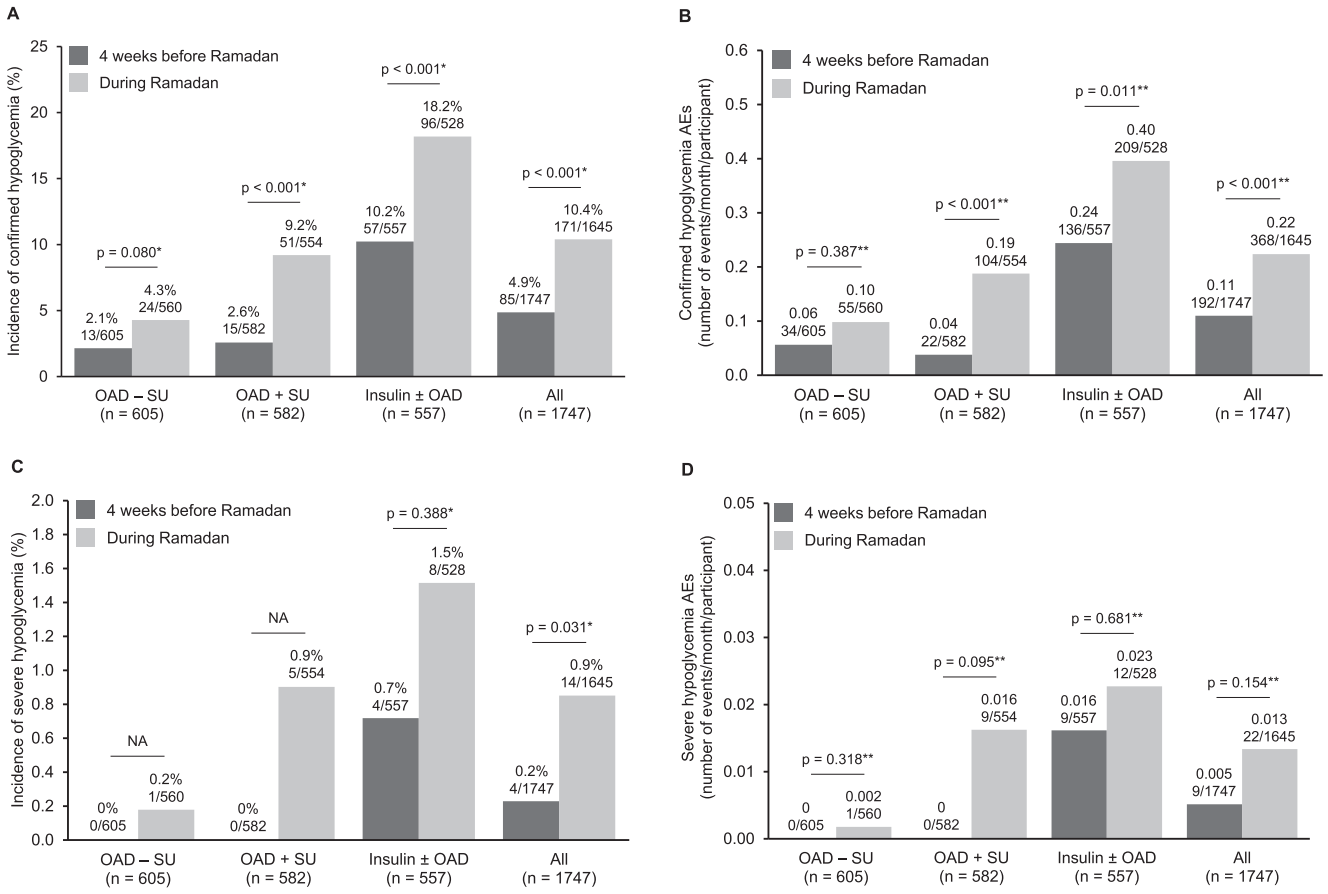

Fig. 3 – Confirmed and severe hypoglycemia before and during Ramadan by treatment in participants with T2DM. AE: adverse event, NA: not available, OAD: oral antidiabetic drug, SU: sulfonylurea, T2DM: type 2 diabetes mellitus. * McNemar test was used for paired categorical comparisons. ** Paired *t*-test was used for paired numerical comparisons.

4 weeks before Ramadan to during Ramadan (confirmed: 14.9% vs. 11.6%, p = 0.001; severe: 2.2% vs. 1.0%, p = 0.005; Supplementary Table 5). The decrease in hyperglycemia incidence was also observed by treatment regimen and was significant for OADs with SU for confirmed and severe hyperglycemia and with insulin with or without OADs for confirmed hyperglycemia.

The AEs for severe and confirmed hyperglycemia did not change significantly for the DAR-MENA T2DM population or by treatment regimen, except for the OADs with SU treatment regimen for severe hyperglycemia (Supplementary Table 5).

3.6. *Lifestyle changes and patient education on diabetes management*

In the DAR-MENA T2DM population, 97.4% of participants reported changes in their lifestyle during Ramadan fasting (Supplementary Table 6). Of those reporting a change, reductions were experienced by 83.7% for working hours, 46.8% for sleep duration, 89.9% for smoking, and 53.0% for physical activity. A change in food intake was reported for 65.5% of participants. Of those reporting a change in food intake, reductions were experienced by 41.6% in carbohydrates, 47.0% in sugars, 20.2% in proteins, 25.7% in vegetables, and 59.0% in fats. In participants reporting a change in fluid intake, 20.6% experienced a reduction.

More than half (60.6%) of the DAR-MENA T2DM population had access to education on diabetes management during Ramadan (Supplementary Table 7). The most common education format provided included diabetes educational sessions (55.3%), diabetes education programs (30.3%), and diabetes self-education (26.9%); 50.1% had access to educational material.

4. Discussion

DAR-MENA is the first prospective, large-scale, observational study of people with diabetes before and during Ramadan, to our knowledge. In this study, the findings relating to characteristics and pattern of care of people with T2DM describe what happens before and during Ramadan fasting in the months of the year with longer daylight hours.

DAR-MENA focuses on the MENA region, allowing for some homogeneity among fasting hours, ambient temperature, culture, and the attitude of physicians and patients. Main differentiators of the DAR-MENA T2DM population versus the previous retrospective studies, EPIDIAR and CREED, include the longer diabetes disease duration (10.2 years vs. 7.6–8.4 years), lower levels of hypertension (27.5% vs. 48.8–62.1%) and dyslipidemia (13.7% vs. 32.5–56.6%), and more patients on combined (injectable + OAD) therapies (28.6% vs. 7.3–18.3%) [3,4]. Additionally, the three studies cover different countries in different years and regions [3,4]. DAR-MENA also captured unique additional information, including baseline glycemic control, reasons for fasting and not fasting, and changes in lipid profile and blood pressure collected through two study visits, pre- and post-Ramadan.

In the DAR-MENA T2DM population, the majority fasted (89.7%) during Ramadan. Most (86.3%) participants fasted for over half of the days (≥15 days), and over half of the people studied (57.3%) fasted for the full 30 days of Ramadan. The EPIDIAR and CREED studies previously reported that 78.7% and 94.2%, respectively, of Muslim participants with T2DM fasted for at least 15 days during Ramadan [3,4].

In DAR-MENA T2DM, the majority of patients listed personal decision (80.4%) as their motivating factor for fasting. For patients who did not fast in DAR-MENA, the most common reason was fear of diabetic complications (48.8%).

Most participants with T2DM (89.0%) had a change to their medication from before to during Ramadan. A similar percentage of the DAR-MENA T2DM population modified their medication dose (46.9%) when compared with findings from the EPIDIAR study, in which it was also reported that <50% of the population modified their treatment dose [4]. The proportion of participants who had a dose change varied by treatment regimen, with 62.0% of participants on insulin with or without OADs, 48.2% of participants on OADs with SU, and 31.7% of participants on OADs without SU experiencing a dose change.

The glycemic profile of the DAR-MENA T2DM population improved following Ramadan fasting with a significant improvement ($p < 0.0001$) in HbA1c levels after Ramadan (7.5% [59 mmol/mol]) compared with before Ramadan (8.0% [64 mmol/mol]). Similar improvements were found for FPG and PPG, with significant reductions in mean levels ($p < 0.0001$) after Ramadan. In DAR-MENA T2DM, significant reductions in other biochemical and biometric measures were noted after Ramadan, including weight, SBP, LDL, and cholesterol, but they were not considered clinically relevant.

Hypoglycemia remains a risk for participants who fast during Ramadan. Confirmed hypoglycemia incidence and AEs increased significantly in DAR-MENA from before to during Ramadan, with both the incidence and the AEs doubling in participants with T2DM. Despite this significant increase, the incidence (10.4%) and adverse rates (0.22 events/month/participant) during Ramadan were still low; the AE rate equates to each person fasting for almost 5 months in order to experience a symptomatic confirmed hypoglycemia event. The observed increase in confirmed hypoglycemia was dependent on the treatment regimen, with a significant increase in incidence and AEs observed with those receiving OADs with SU ($p < 0.001$) or insulin with or without OADs ($p < 0.05$) but not with people prescribed OADs without SUs, and is likely a result of the known increased hypoglycemia risk with SU and insulin therapy. However, we wish to emphasize that the majority of people were able to fast without experiencing a symptomatic confirmed hypoglycemia event despite the observed differences between treatments. Severe hypoglycemia incidence (0.9%), despite a significant increase from before Ramadan, and AEs (0.01 events/month/participant), which did not significantly change, were low during Ramadan for the DAR-MENA T2DM populations; the severe hypoglycemia AE rate equates to each person fasting for about 100 months in order to experience a severe hypoglycemia event. A particular strength of the DAR-MENA study is that confirmed hypoglycemia was measured with SMPG with a cut-off level of 70 mg/dL. This is a well-defined criterion that is not subject to patient recall bias or missing data from medical notes.

Although it is generally understood that lifestyle changes occur during Ramadan, these changes can vary depending

on geographical region. For the MENA region, the vast majority of the DAR-MENA T2DM population reported changes to their lifestyle during fasting, including working hours, sleep duration, smoking, fluid and food intake, and physical activity.

The development and utilization of Ramadan-focused education programs to allow HCPs to provide better care and ensure the safety of people with diabetes who fast during Ramadan is still needed [7]. This cannot be achieved without a good understanding of peoples' characteristics and real-life practices to enhance evidence-based management of the disease during Ramadan fasting. In DAR-MENA T2DM, over half of the population indicated that they had access to education on diabetes management during Ramadan; however, the education methods used varied.

The results of this study are representative of the participating MENA countries and, therefore, caution should be exercised when interpreting these findings in relation to other geographic regions. Additionally, general rather than specific SUs and insulins were recorded as it is not possible to distinguish which particular ones were used in each individual country. It is also possible that participant care by the physician, such as the provision of diabetes education and adjustments of dose, may have been influenced by the participation in this study.

In conclusion, this first prospective study involving a relatively large population in the MENA region provides up-to-date data on the characteristics and pattern of care of people before and during Ramadan. It is reassuring that the DAR-MENA study did not find any major safety concerns. Although hypoglycemia remains a concern, confirmed and severe hypoglycemia risk were low both before and during Ramadan. Choice of therapy affected hypoglycemia risk, with an increase in confirmed hypoglycemia observed during Ramadan in study groups where patients with T2DM received OADs with SU or insulin with or without SU, but not for those receiving OADs without SU. The use of confirmed rather than just symptomatic hypoglycemia averts recall bias and issues with missing data from medical notes, thereby strengthening our findings. Our results indicate that further patient education is needed in the MENA region and support the International Diabetes Federation (IDF) and Diabetes and Ramadan (DAR) International Alliance Guideline recommendations, which suggest that for Muslims who choose to fast, treatment adjustments should be considered pre-Ramadan [18]. These findings are useful for the development of evidence-based care to ensure the safety of those who fast.

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Data availability statement

Qualified researchers may request access to patient-level data and related study documents, including the clinical study report, study protocol with any amendments, blank case report form, statistical analysis plan, and dataset specifications. Patient-level data will be anonymized, and study documents will be redacted to protect the privacy of trial participants. Further details on Sanofi's data sharing criteria, eligible studies, and process for requesting access can be found at: https://www.clinicalstudydatarequest.com.

Authors' contributions

M.H. developed the study concept and design. All authors contributed to the data analysis or interpretation of the results, and critically revised, provided final approvals of, and are accountable for the accuracy and integrity of the manuscript.

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Declaration of interest

F.A.A., S.S.A., F.A.K.K., M.O.A.-H., and A.A.S.: nothing to declare.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2019.02.020.

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