Clinical Characteristics and Outcomes of Diabetic Ketoacidosis in Patients With Type 2 Diabetes using SGLT2 Inhibitors

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ABSTRACT

BACKGROUND: Sodium glucose cotransporter 2 inhibitors (SGLT2i) use is associated with an increased risk of diabetic ketoacidosis (DKA).

OBJECTIVE: This study evaluated and compared the DKA characteristics and outcomes of users and non-users of SGLT2i.

METHODS: We retrospectively studied patients with type 2 diabetes mellitus (T2DM) admitted with DKA to Tawam Hospital, Al Ain City, UAE between January 2017 and March 2021. Demographic data, clinical, and laboratory findings were extracted from the electronic medical records.

RESULTS: A total of 55 patients with T2DM (62% UAE nationals, 50% women) were admitted with DKA. The average age was 54.0 ± 18.9 years and average diabetes duration of 15.7 ± 15.1 years. Seventeen patients (31%) were using SGLT2i. Infection was the main precipitating factor for DKA in (8 out of 17) SGLT2i users. Compared to non-users, SGLT2i users had lower systolic blood pressure (119.9 vs 140 mmHg; $P = .012$) and serum glucose levels (16.2 vs 24.9 mmol/L; $P < .001$) and higher Na level (137.5 vs 132.6 mmol/L; $P = .005$). Additionally, 56.3% of SGLT2i users had euglycemic DKA compared to 2.6% of nonusers ($P < .001$). Acute kidney injury (AKI) occurred more in SGLT2i users compared to non-users (94.1% vs 67.6%, $P = .043$). Further analysis revealed that SGLT2i users were about five times more likely to have prolonged hospital length of stay (⩾14 days) when compared with non-users (adjusted OR: 4.84; $P = .035$). Overall, there was no difference between the two groups with regards to DKA complications and mortality.

CONCLUSIONS: SGLT2i related DKA is associated with lower blood glucose levels, lower SBP, worse hypovolemia, increased risk of AKI, and longer hospital stay when compared to non SGLT2i related episodes. Since the benefits of SGLT2 inhibitors far outweigh potential risks, there is a need to raise healthcare professionals and patients' awareness about this potential association.

KEYWORDS: Ketoacidosis, diabetic ketoacidosis, Type 2 diabetes, SGLT2i, diabetic emergencies

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Introduction

Diabetic ketoacidosis (DKA) has been recognized as a serious and potentially life-threatening complication that mainly occurs in patients with type 1 diabetes (T1DM).[1] However, the incidence has been increasingly reported in patients with type 2 diabetes (T2DM). Factors associated with the increased risk of DKA in T2DM include infections, life threatening conditions, non-compliance to medications, new diagnosis of diabetes[2] and most recently the use of sodium glucose cotransporter 2 inhibitors (SGLT2i).[3,4] This is a novel class of hypoglycemic medications and is often prescribed as an add-on therapy in patients with uncontrolled diabetes.[4] However, new compelling indications for the use of SGLT2i include patients with atherosclerotic cardiovascular disease (CVD), and/or chronic kidney disease[5] as it has been shown to reduce the risk of heart failure, renal failure, myocardial infarction, and all-cause mortality.[6] Despite the approval of SGLT2i for use in diabetes management in 2013 by the Food and Drug Administration, a warning was issued by the same organization in 2015 following numerous case reports documenting SGLT2i induced DKA.[7]

Previous studies on SGLT2i produced conflicting results about the incidence of DKA as a complication. In one of the first observational studies, there was no increased risk of DKA noted between users and non-users of SGLT2i[8] while a doubling of the risk was reported in a study conducted in Sweden and Denmark.[9] Interestingly, a sevenfold increased risk of DKA in patients with T2DM on SGLT2i was reported after excluding T1DM[10] as well as almost threefold increase risk when compared with patients treated with dipeptidyl-peptidase-4 inhibitors.[11]

There is an upward trend in the occurrence of DKA among patients with diabetes in the United Arab Emirates (UAE).[12,13] To date, there are no published reports in the UAE on the incidence of adverse effects of SGLT2i treatment. This study

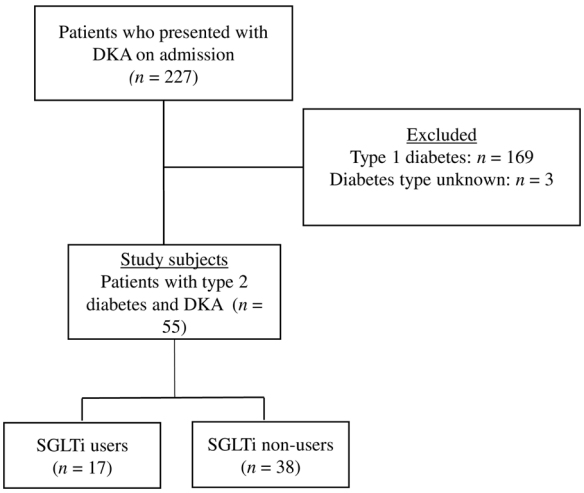

Figure 1. Flowchart of study cohort.

aimed to evaluate the characteristics, clinical features, biochemical values and outcomes of T2DM patients who developed DKA while using SGLT2i and compare that with the non-users of the drug.

Methods

The study included all patients aged 16 years and older who were admitted with DKA to Tawam Hospital, the main tertiary care hospital in Al Ain City, UAE from January 2017 to March 2021. Of 227 identified DKA cases, 55 cases (24%) were for patients with T2DM of which 17 cases were associated with SGLT2i use (Figure 1). SGLT2i is used only with T2DM in our hospital. The medical health records were identified using ICD 10 CM codes (E10.10, E10.11, E13.10, and E13.11). Local DKA diagnosis and management protocol is derived from international guidelines.[14,15] The DKA severity was classified based on the pH value as mild (pH 7.25-7.3), moderate (pH 7-7.24), or severe (pH < 7) using American Diabetes Association (ADA) criteria.[15] Glucose level above 13.9 nmol/L on admission was used to identify euglycemic from hyperglycemic DKA.[15]

Data that were extracted from the electronic medical records included demographic characteristics, baseline clinical, and chemical results upon admission as well as the DKA outcomes. Additionally, we collected information about the comorbidities and complications. Hemoglobin A1c (HbA1c) value on admission or within the preceding 3 months was recorded.

The type of diabetes was confirmed by studying patient's history and/or autoantibodies statuses when available. Acute kidney injury (AKI) was defined as increase in serum creatinine by ⩾26.5 µmol/L within 48 hours.[16] The Tawam Human Research Ethics Committee approved the study and waived the requirement for consent due to the retrospective nature of the study, the anonymity of the data collection, and the lack of interventions.

Data Analysis

Continuous variables are presented as means and standard deviation (SD), or medians and interquartile range (IQR), while categorical variables are presented as numbers and percentages. The student *t*-test, Mann-Whitney *U* test, and Fisher's exact test were used to compare continuous normally distributed variables, continuous non-normally distributed variables, and categorical variables, respectively. Multivariable penalized logistic regression model was used to analyze the association of SGLT2i use and prolonged hospital length of stay, adjusted for age, sex, and treatment regimen for diabetes.

Data were analyzed using SPSS version 28 (IBM Corp., Armonk, NY, USA) and R software, version 4.1.2 (The R Foundation, Vienna, Austria). All statistical tests with $P < .05$ were considered statistically significant.

Results

A total of 55 patients (62% UAE nationals) with T2DM were admitted with DKA. The mean age was 54.0 ± 18.9 years and approximately 50% were women (Table 1). The median diabetes duration was 11 (IQR 4-20) years. Approximately 31% (n = 17) of patients were receiving SGLT2i agents. Of those 52.9% (n = 9) were on empagliflozin, 41.2% (n = 7) were on dapagliflozin, and 5.9% (n = 1) canagliflozin. A greater proportion of SGLT2i users were also on metformin (82.4% vs 42.1%) and SU (47.1% vs 18.4%) compared to non-users, respectively (Table 1). There was no statistical difference in insulin use between the two groups. The main precipitating factor for DKA among the SGLT2i users was the coincidence of infection (8 out of 17). Interestingly, SGLT2i users had lower systolic blood pressure (SBP) (119.9 mmHg) and serum glucose levels (16.2 mmol/L (291.6 mg/dL)) compared to non-users (140.0 mmHg; $P = .012$) and (24.9 mmol/L (448.2 mg/dL)); $P < .001$), respectively. Applying the 13.9 mmol/L (250 mg/dL) cutoff for euglycemic DKA as defined by ADA,[15] 56.3% of SGLT2i users were euglycemic versus 2.6% of non-users ($P < .001$). SGLT2i users had higher Na levels (137.5 mmol/L) compared with non-users (132.6 mmol/L; $P = .005$) (Table 2). On admission, 20.0% of patients presented with severe DKA, 61.8% with moderate DKA, and 18.2% with mild DKA (Table 2). All SGLT2i users had urine Ketone +3 and more compared to 55.5% in non-users ($P = .007$). Despite no statistical difference, the pH (7.1 vs 7.2, $P = .067$) and HCO_3 levels (8.1 vs 9.5 mmol/L, $P = .267$) were numerically lower in patients with SGLT2i use compared to non-users. Additionally, more patients with SGLT2i use were admitted with severe DKA compared to non-users (29.4% vs 15.8%, $P = .455$) and time to DKA resolution was longer in patients using SGLT2i compared to non-users (23 vs 20.8 hours, $P = .541$).

While there was no difference between SGLT2i users and non-users in overall DKA complications and mortality, AKI occurred more in SGLT2i users compared to non-users (94.1% vs 67.6%, $P = .043$). The median length of hospital stay was 7 (IQR 4-16) days and the in-hospital mortality rate was 5.5%. The length of hospital stay was longer in SGLT2i users compared to non-users (11 vs 6.3 days, $P = .046$). According to the multivariable logistic model, SGLT2i users were almost five times more likely to have prolonged hospital length of stay (⩾14 days) when compared with non-users (adjusted OR = 4.84; 95% CI: 1.11, 26.78; $P = .035$) (Table 3).

Table 1. Sociodemographic and initial clinical presentation of DKA cases.

	TOTAL N = 55	T2DM (SGLT2I USERS) N = 17	T2DM (NON-SGLT2I USERS) N = 38	*P*-VALUE
Age (years) (SD)	54.0 (18.9)	57.5 (19.0)	52.4 (18.8)	.366
Sex, n (%)				
Female	27 (49.1)	10 (58.8)	17 (44.7)	.391
Male	28 (50.9)	7 (41.2)	21 (55.3)	
Nationality, n (%)				
Emirati	34 (61.8)	13 (76.5)	21 (55.3)	.395
Arab	10 (18.2)	3 (17.6)	7 (18.4)	
South Asian	8 (14.5)	1 (5.9)	7 (18.4)	
Other	3 (5.5)	0 (0.0)	3 (7.9)	
DM duration (years) (IQR) (n = 37)	11.0 (4.0, 20.0)	13.0 (10.0, 19.0)	9.5 (3.0, 26.0)	.339
Baseline medication, n (%)				
Metformin	30 (54.5)	14 (82.4)	16 (42.1)	.008
SU	15 (27.3)	8 (47.1)	7 (18.4)	.047
DDP4	18 (32.7)	8 (47.1)	10 (26.3)	.213
GLP1 agonist	6 (10.9)	2 (11.8)	4 (10.5)	1
Insulin	27 (49.1)	6 (35.3)	21 (55.3)	.245
Previous history of DKA, n (%) n = 54	8 (14.8)	1 (5.9)	7 (18.9)	.411
Comorbidities				
Microvascular complications, n (%)	21 (38.2)	8 (47.1)	13 (34.2)	.386
Macrovascular complications, n (%)	10 (18.2)	5 (29.4)	5 (13.2)	.255
CKD, n (%)	12 (21.8)	4 (23.5)	8 (21.1)	1
Active cancer, n (%)	6 (10.9)	4 (23.5)	2 (5.3)	.066
Presenting symptoms				
Nausea and vomiting, n (%)	35 (63.6)	13 (76.5)	22 (57.9)	.235
Abdominal pain, n (%)	24 (43.6)	8 (47.1)	16 (42.1)	.775
Shortness of breath, n (%)	11 (20.0)	3 (17.6)	8 (21.1)	1
Polyuria and polydipsia, n (%)	8 (14.5)	1 (5.9)	7 (18.4)	.411
Weight loss, n (%)	3 (5.5)	0 (0.0)	3 (7.9)	.544
Impaired LOC, n (%)	16 (29.1)	5 (29.4)	11 (28.9)	1
Fever, n (%)	13 (23.6)	5 (29.4)	8 (21.1)	.511
Newly diagnoses, n (%)	8 (14.5)	1 (5.9)	7 (18.4)	.411
Precipitating factors, n (%)				
Newly diagnosed alone	3 (5.5)	0 (0.0)	3 (7.9)	<.001
Insulin omission/noncompliance	7 (12.7)	0 (0.0)	7 (18.4)	
Infection alone	7 (12.7)	0 (0.0)	7 (18.4)	

(Continued)

Table 1. (Continued)

	TOTAL N = 55	T2DM (SGLT2I USERS) N = 17	T2DM (NON-SGLT2I USERS) N = 38	*P*-VALUE
Drug-induced alone	7 (12.7)	6 (35.3)	1 (2.6)	
Post-surgery	2 (3.6)	0 (0.0)	2 (5.3)	
Indeterminate	11 (20.0)	0 (0.0)	11 (28.9)	
Combination of above*	18 (32.7)	11 (64.7)	7 (18.4)	
Infection types (±Combination), n (%)				
Upper respiratory tract infection	3 (5.5)	1 (5.9)	2 (5.3)	.715
Urinary tract infection	8 (14.5)	4 (23.5)	4 (10.5)	
Pneumonia	4 (7.3)	1 (5.9)	3 (7.9)	
Skin and soft tissue	2 (3.6)	1 (5.9)	1 (2.6)	
Sepsis with bacteremia	3 (5.5)	1 (5.9)	2 (5.3)	

Abbreviations: CKD, chronic kidney disease; DDP4i, dipeptidyl peptidase-4 inhibitors; GLP-1, glucagon-like peptide-1; LOC, loss of coniousness; SD, standard deviation; SGL2i, sodium/glucose cotransporter-2 inhibitors.
*Among SGLT2i users combined precipitating causes include: 8 drug + infection, 1 drug + newly diagnosis, 1 drug + insulin omission, 1 drug + post-surgery state. Among non-SGLT2i users combined precipitating causes include: 2 newly diagnosed + infection, 2 infection + steroid, 1 newly diagnosed + steroid, 1 newly diagnosed + thyrotoxicosis, 1 infection + insulin omission.

Table 2. Biochemical findings and outcome of DKA.

	TOTAL N=	T2DM (SGLT2I USERS) N = 17	T2DM (NON-SGLT2I USERS) N = 38	*P*-VALUE
Vital signs at presentation				
Weight (kg) ±SD	74.6 (21.1)	75.9 (19.3)	73.9 (22.1)	.752
BMI (kg/m²) ±SD n = 53	28.1 (7.1)	29.0 (6.4)	27.7 (7.5)	.537
SBP (mmHg) ±SD	133.8 (27.7)	119.9 (16.1)	140.0 (29.7)	.012
Heart rate (beats/min) ±SD	109.2 (20.0)	110.9 (21.6)	108.4 (19.5)	.681
Respiratory rate (breaths/min) (IQR)	20.0 (19.0, 23.0)	20.0 (18.0, 22.0)	20.0 (20.0, 24.0)	.379
Initial venous blood gas results				
pH (unitless) (IQR)	7.2 (7.1, 7.2)	7.1 (7.0, 7.2)	7.2 (7.1, 7.2)	.067
HCO_3 (mmol/L) ±SD	9.6 (4.6)	8.4 (4.6)	10.1 (4.5)	.195
Glucose (mmol/L) ±SD	22.4 (8.1)	16.8 (8.4)	25.0 (6.6)	<.001
Initial blood test results				
Na (mmol/L) ±SD	134.1 (6.1)	137.5 (6.5)	132.6 (5.3)	.005
K (mmol/L) ±SD	4.4 (0.9)	4.5 (0.9)	4.4 (0.9)	.628
CL (mmol/L) ±SD	97.7 (7.7)	99.5 (8.7)	96.9 (7.2)	.243
Urea (mmol/L) (IQR)	7.1 (4.0, 11.3)	9.0 (4.2, 11.0)	6.7 (3.7, 11.5)	.512
HCO_3 (mmol/L) ±SD	9.1 (4.2)	8.1 (4.3)	9.5 (4.2)	.267
Creatinine (μmol/L) (IQR) n = 54	112.0 (89.8, 176.2)	111.0 (96.0, 129.0)	118.0 (81.0, 213.0)	.628
Creatinine at discharge (μmol/L) (IQR) n = 54	63.5 (45.0, 72.0)	54.0 (44.0, 66.0)	67.0 (49.0, 89.0)	.047

(Continued)

Table 2. (Continued)

	TOTAL N=	T2DM (SGLT2I USERS) N=17	T2DM (NON-SGLT2I USERS) N=38	*P*-VALUE
Lactic acid (mmol/L) (IQR) n=54	2.3 (1.4, 3.2)	2.3 (1.5, 3.7)	2.2 (1.4, 3.2)	.648
Anion gap (mmol/L) ±SD	27.3 (7.6)	29.8 (7.5)	26.2 (7.5)	.104
Serum glucose (mmol/L) ±SD n=54	22.3 (7.9)	16.2 (8.0)	24.9 (6.3)	<.001
HbA1C (%) ±SD n=51	10.2 (2.3)	9.9 (2.5)	10.4 (2.2)	.462
Urine ketones, n (%) (n=53)				
+1	6 (11.3)	0 (0.0)	6 (16.7)	.007
+2	10 (18.9)	0 (0.0)	10 (27.8)	
+3	25 (47.2)	10 (58.8)	15 (41.7)	
+4	10 (18.9)	6 (35.3)	4 (11.1)	
+5	2 (3.8)	1 (5.9)	1 (2.8)	
DKA severity, n (%)				
Mild	10 (18.2)	2 (11.8)	8 (21.1)	.455
Moderate	34 (61.8)	10 (58.8)	24 (63.2)	
Severe	11 (20.0)	5 (29.4)	6 (15.8)	
Outcomes of diabetes ketoacidosis				
ICU/HDU admission, n (%)	48 (87.3)	16 (94.1)	32 (84.2)	.416
Time to DKA resolution (h) (IQR)	21.0 (11.5, 27.0)	23.0 (13.0, 25.0)	20.8 (10.0, 27.0)	.541
Length of hospital stay (days) (IQR)	7.0 (4.0, 16.0)	11.0 (6.0, 17.0)	6.3 (4.0, 8.1)	.046
In-hospital mortality, n (%)	3 (5.5)	0 (0.0)	3 (7.9)	.544
Mechanical ventilation, n (%)	9 (16.4)	4 (23.5)	5 (13.2)	.435
AKI, n (%) n=54	41 (75.9)	16 (94.1)	25 (67.6)	.043
Need RRT, n (%) n=54	9 (16.7)	4 (23.5)	5 (13.5)	.439
Need inotropes, n (%) n=54	11 (20.4)	5 (29.4)	6 (16.2)	.293
Complications, n (%)				
None	28 (50.9)	7 (41.2)	21 (55.3)	.748
Pulmonary edema	2 (3.6)	1 (5.9)	1 (2.6)	
Hypokalemia	11 (20.0)	4 (23.5)	7 (18.4)	
DKA relapse	3 (5.5)	1 (5.9)	2 (5.3)	
MI/stroke	3 (5.5)	2 (11.8)	1 (2.6)	
Venous thrombosis	2 (3.6)	1 (5.9)	1 (2.6)	
Pancreatitis	2 (3.6)	0 (0.0)	2 (5.3)	
More than 1 complication (combo)	4 (7.3)	1 (5.9)	3 (7.9)	

Abbreviations: AKI, acute kidney injury; BMI, body mass index; DKA, diabetic ketoacidosis; GLP-1, glucagon-like peptide-1; HbA1C, hemoglobin A1c; HDU, high dependency unit; ICU, intensive care unit; IQR, interquartile range; MI, myocardial infarction; RRT, renal replacement therapy; SBP, systolic blood pressure; SD, standard deviation; SGL2i, sodium/glucose cotransporter-2 inhibitors.

Table 3. Association of SGLT2i use with prolonged hospital length of stay.

VARIABLE	AOR (95% CI)	*P*-VALUE
Age	2.36 (0.46, 41.99)	.332
Sex	2.42 (0.64, 10.13)	.197
SGLT2i	4.84 (1.11, 26.78)	.035
Metformin	0.26 (0.04, 1.30)	.103
SU	0.24 (0.03, 1.39)	.114
DDP4	3.32 (0.65, 24.68)	.154
GLP1 agonist	0.3 (0.00, 4.89)	.423
Insulin	1.08 (0.26, 4.45)	.917

Abbreviation: AOR: adjusted odds ratio for age, sex, and treatment regimen for diabetes.

Discussion

Limited reports have previously described the clinical and biochemical characteristics of DKA in patients with diabetes in the UAE.[12,13] This is the first study to specifically examine the clinical and biochemical characteristics of T2DM patients who were admitted with DKA and compare their outcomes based on the use of SGLT2i.

The risks and benefits of SGLT2i use have been extensively studied indicating reduced all-cause mortality with lower risk of cardiac events (heart failure, ischemic heart disease) and chronic kidney disease.[6] However, there is compelling evidence that SGLT2i increase the risk of DKA hospitalizations.[11,17,18] Of note that the average length of stay in our cohort matches the South Korean study of 9 (6-15) days[19] and corroborates our results, whereas fewer days were noted among Israeli patients (5.3 ± 1.9 days).[20] It is likely that most of the SGLT2i associated DKA can be successfully managed with standard DKA management protocol. However, differences in protocols on the use of glucose and/or ketone for insulin titration is worth exploring to clarify the variation in length of stay or DKA resolution time. In our center, insulin dose is titrated based on glucose readings. Several case reports have been published regarding the prolonged course of SGLT2i induced DKA requiring high doses of insulin to reverse ketonemia that persisted for several days.[21,22] In our study, all DKA cases associated with SGLT2i use had urine Ketone +3 and more compared to half of the cases in non-SGLT2i group. In a single arm study, reporting 20 cases of SGLT2i associated DKA, the median blood ketone was 5 (1.6-6.8) mmol/L.[23]

As might be expected, SGLT2i users had worse hypovolemia at presentation supported by the lower SBP readings and higher urea levels. While there was no difference in the need for renal replacement therapy, the incidence of acute kidney injury was more pronounced in patients with SGLT2i use. Additionally, hyponatremia, that is usually present in patients with hyperglycemia, was only observed mainly in non-SGLT2i users compared to euglycemic DKA associated with SGLT2i use. This is likely secondary to the lower glucose levels among SGLT2i users. While there was no difference in the outcomes and mortality, longer hospital stay for patients using SGLT2i in our cohort could probably be multifactorial in nature, relating to the delay of diagnosis due to relatively normal blood glucose, worse severity of DKA at presentation, hypovolemia and the higher incidence of AKI.

Furthermore, it is plausible to observe a wide range of international mortality rates among patients using SGLT2i when admitted with DKA related to their underlying cardiovascular conditions. Notwithstanding an increased rate in hospital admissions, the mortality rates from DKA has declined over the last 15 years in the some countries, chronicling a range from 1% to 3%.[24,25] Fortunately, all of our patients using SGLT2i survived despite severe onset and prolonged hospitalization in few cases.

Previous findings, also reported by the FDA Adverse Event Reporting System, suggest a female preponderance with a female-to-male ratio ranging from 1.21 to 3.0.[18,23] This was consistent with results in our study with a ratio female-to-male at 1.42. The explanation for this is not known. However, Fadini et al.[18] suggested a link for this outcome between SGLT2i-induced genitourinary tract infection and DKA; as this is physiologically more likely in females. In our cohort 4 out of the 10 SGLT2i associated DKA in female patients were combined with UTI.

SGLT2i increase urinary glucose excretion and stimulate the release of glucagon from pancreatic alpha cells. Overall, this leads to decreased insulin requirements and shifting the insulin: glucagon ratio in favor of glucagon.[26] Therefore, exposure to precipitating factors (surgical stress, concurrent illness, reduced oral intake, alcohol use) that mandate increased insulin requirements may precipitate DKA in patients while using SGLT2i. To mitigate this risk, several prevention strategies have been suggested including proper patient selection for the use of SGLT2i excluding T1DM and avoidance of ketogenic diets.[27] Also, patients need continuous education about holding the SGLT2i during illnesses with decreased caloric intake or dehydration and need for early presentation to medical care. Additionally, healthcare providers should be educated about the necessity to suspend the drug during hospital admissions or preoperatively.[28]

Strengths and Limitations

Our study is the first study in the region to compare DKA in SGLT2i users versus non-users. It highlights the importance of addressing and recognizing this associated complication with SGLT2i which require healthcare provider awareness and patient education. However, it has its inherent limitations including the retrospective nature, small patient numbers, lack of data on the total number of patients using different SGLT2i during the study period and the incident rates per each agent and lack of information on the duration of SGLT2i use prior to DKA onset and total insulin doses used for DKA

management. It will be worth to expand this study to include other regional and national centers for a better insight into the prevalence and specifics of different SGLT2i and their associations with DKA.

Conclusions

In this single center study in the United Arab Emirates, SGLT2i related DKA was associated with lower blood glucose levels, lower SBP, worse hypovolemia, increased risk of AKI, and longer hospital stay when compared to non SGLT2i related episodes. Since the benefits of SGLT2i far outweigh potential risks, there is a need to raise healthcare professionals and patients' awareness about this potential association.

Declarations

Ethics approval and consent to participate

The Tawam Human Research Ethics Committee approved the study (MF2058-2022-826) and waived the requirement for consent due to the retrospective nature of the study, the anonymity of the data collection, and the lack of interventions.

Consent for publication

Not applicable.

Author contributions

Raya Almazrouei: Conceptualization; Data curation; Writing—original draft; Writing—review and editing. Bachar Afandi: Conceptualization; Data curation; Supervision; Writing—review and editing. Fatima AlKindi: Data curation; Investigation; Writing—review and editing. Romona Govender: Methodology; Writing—original draft; Writing—review and editing. Saif Al-Shamsi: Formal analysis; Methodology; Writing—original draft.

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Availability of data and materials

For confidentiality reasons, the original data cannot be shared. However, all results are presented in this manuscript.

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