The Impact of the COVID-19 Pandemic on Diabetic Ketoacidosis Admissions to a COVID-19-Free Hospital

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Abstract

Background: COVID19 infection is associated with worse outcomes in patients admitted with diabetic ketoacidosis (DKA). The indirect impact of the pandemic on DKA admissions to COVID19 free hospitals has not been evaluated. In this study, we evaluate the characteristics and outcomes of DKA admissions before and during the pandemic. Materials and Methods: This retrospective study included 146 episodes of DKA for patients aged 16 years and above admitted to Tawam Hospital, A COVID-19-free hospital, between April and October from 2017 to 2020. Sociodemographic, clinical, and laboratory data were retrieved from the electronic records. Data from the (2017–2019) period were compared to those during the COVID19 pandemic in 2020. Results: We evaluated 79 pre-COVID19 and 67 during the COVID19 admissions. During the pandemic, patients were older (30 vs. 23 years, P 0.2) with higher proportions of male sex (66% vs. 25%) and non-Emirati nationals (Arabs 17.9% vs. 12.7% and South Asian 20.9% vs. 3.8%). In addition, only 64.2% of patients had medical coverage compared to 92.4% in pre-COVID19 time. More patients with newly diagnosed diabetes (25.4% vs. 7.6%) and type 2 diabetes mellitus (32.8% vs. 17.7%) were encountered during the pandemic. Overall, there was no significant difference in severity, time to resolution, and mortality. Length of stay was longer for DKA admissions during the pandemic (4 vs. 3 days). Conclusion: In our COVID-19-free hospital, the pandemic has led to an increased rate of DKA admissions and significant change in the sociodemographic characteristics of patients with DKA. Clinical care, patients’ management, and outcomes were not adversely affected. Assessing the indirect impact of the pandemic is essential for future service planning.

Keywords: COVID1-9, diabetes, ketoacidosis, pandemic

Introduction

The severe acute respiratory syndrome coronavirus-2 was described for the first time in December 2019 in Wuhan, China. The first case of COVID19 was confirmed in the United Arab Emirates (UAE) on January 29, 2020. Over 4.3 million deaths from coronavirus disease-2019 (COVID19) infection have been recorded globally by August 2021.[1] The indirect effect of the pandemic on non-COVID19 diseases has been recognized across different subspecialties, including a delay in diagnosis and treatment of cancer and a decreased rate of admissions for adults with cardiovascular diseases.[2,3] Concerning diabetes, initial data from the United States showed a 10% decrease in hyperglycemic crisis ER visits 10 weeks following the emergency declaration.[4] In addition, delay in presentation of children with Type 1 diabetes mellitus (T1DM) with increased frequency of severe diabetic ketoacidosis (DKA) at presentation has been reported.[5,6] In addition, more children with new-onset T2DM presented in DKA in 2020 compared to previous years.[7]

While DKA incidence increased in adult COVID19 patients,[8,9] studies showed no difference in severity or duration of DKA during the pandemic compared to the pre-COVID19 period. However, it highlighted an increased incidence of DKA in people with type 2 diabetes mellitus (T2DM) during the pandemic.[10-12] A recent population-based study showed a modest increase in DKA admissions during the COVID19 pandemic compared with three preceding years and that this trend was accounted by

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a significant rise in DKA admissions in people with preexisting T2DM and newly diagnosed diabetes despite a concurrent reduction in admissions in people with T1DM.\cite{13}

Like many healthcare facilities across the globe, the pandemic led to significant healthcare infrastructure changes in in-service distribution and allocation. Tawam and Al Ain are the two largest governmental hospitals in Al Ain City. They are both managed by Abu Dhabi Healthcare Company (SEHA), the largest and most comprehensive healthcare network in the UAE. Historically, UAE citizens, employees, and selected insurance coverage holders are followed in Tawam hospital, while non-Emirati nationals and other insurance coverage are followed in Al Ain Hospital. During the pandemic, SEHA has restructured its services in Al Ain City starting April 1, 2020. Accordingly, Al Ain hospital, with 300 beds, was classified as a COVID19 facility and, Tawam, the 500-bed hospital, is identified as the COVID19-free hospital. Consequently, many physicians and services were relocated and integrated into the appropriate facility.

This study aimed to assess the impact of the pandemic on DKA admission rates and outcomes at Tawam hospital, the COVID19 free hospital, in Al Ain City, UAE. We evaluated patients’ sociodemographic features, clinical and biochemical characteristics, precipitating factors during 6 months of the COVID19 pandemic in 2020 and compared that with a similar time frame in the three preceding years (2017–2019) in COVID19 negative patients.

**Materials and Methods**

The electronic medical records of patients admitted with DKA to Tawam Hospital aged 16 years and above were reviewed from April 1 to the end of October for 2017–2020. The pre-COVID19 years included 2017–2019, and 2020 represents the COVID19 year. The DKA episodes were identified using ICD 10 CM codes (E10.10, E10.11, E13.10, and E13.11). The DKA diagnosis and treatment is based on a modified hospital protocol derived from international guidelines.\cite{14,15} The following variables were collected: Age, sex, nationality, insurance coverage, type and duration of diabetes, medications use, prior history of DKA, precipitating factors, vital signs, body mass index, comorbidities, DKA complications, duration of hospital stay, time for DKA resolution and DKA relapse. Microvascular (diabetic nephropathy, foot ulcer, retinopathy, and peripheral neuropathy) and macrovascular (peripheral vascular disease, ischemic heart disease, and cerebrovascular disease) complications of diabetes were also recorded. The initial biochemical parameters: Venous blood gas result (\(\text{pH}, \text{HCO}_3^-, \text{glucose}\)) and blood investigation (sodium, potassium, chloride, urea, glucose) were collected. HbA1c value during admission or within the last 3 months period was retrieved. DKA severity was classified using American Diabetes Association criteria based on \(\text{pH}\) value; mild (\(\text{pH} 7.3–7.25\)), moderate (\(\text{pH} 7.24–7\)), and severe (\(\text{pH} < 7\)).\cite{14}

**Statistical analysis**

Statistical analysis was performed using statistical software (Stata 13, Stata Corp LP, Texas, USA). Proportional outcomes were presented as numbers and percentages. Continuous values were expressed as median with interquartile range (IQR). Chi-Square and Fisher’s exact tests were performed for categorical variables and Mann–Whitney U test for nonnormally distributed continuous variables. A two-tailed probability value of <5% was considered statistically significant.

**Results**

A total of 146 DKA episodes were included in the study; 79 during the pre-COVID19 years and 67 cases during the COVID19 year [Figure 1]. Table 1 shows the sociodemographic characteristic of all patients. The overall age (median and IQR) was 26 (19–39) years with numerically older patients during the pandemic compared to pre-COVID years (30 vs. 23 years, respectively, \(P = 0.2\)). During the pandemic, 66% of the patients were males compared to 25% in the pre-COVID19 years. Emiratis, Arabs, and South Asians constitute 56.7%, 17.9%, and 20.9% during the COVID19 year compared to 81%, 12.7%, and 3.8% in the pre-COVID years, respectively (\(P < 0.003\)). The proportion of patients with medical insurance dropped from 92.4% in the pre-COVID19 years to 64.2% in COVID19 (\(P < 0.0001\)). DKA episodes in T2DM increased from 17.7% prepandemic to 32.8% during the pandemic (\(P = 0.016\)). Similarly, DKA in patients newly diagnosed with diabetes was more encountered during the pandemic (25.4% vs. 7.6%, \(P = 0.005\)). A higher proportion of patients were on insulin at baseline in pre-COVID19 years compared to COVID19 years (86.1% vs. 65.7%, \(P = 0.006\)). History of previous DKA admission was reported in two-thirds of the patients (75.6%) in the pre-COVID years compared to COVID19 year [Figure 1]. Table 1 shows the sociodemographic characteristics, precipitating factors during 6 months of the COVID19 pandemic in 2020 and compared that with a similar time frame in the three preceding years (2017–2019) in COVID19 negative patients.

**Figure 1:** Number of diabetic ketoacidosis episodes per month between April and October during Pre-COVID19 years (2017–2019) and during COVID year (2020) at Tawam Hospital. Al-Ain. United Arab Emirates

Asians constitute 56.7%, 17.9%, and 20.9% during the pandemic, 66% of the patients were males compared to 25% in the pre-COVID19 years. Emiratis, Arabs, and South Asians constitute 56.7%, 17.9%, and 20.9% during the COVID19 year compared to 81%, 12.7%, and 3.8% in the pre-COVID years, respectively (\(P < 0.003\)). The proportion of patients with medical insurance dropped from 92.4% in the pre-COVID19 years to 64.2% in COVID19 (\(P < 0.0001\)). DKA episodes in T2DM increased from 17.7% prepandemic to 32.8% during the pandemic (\(P = 0.016\)). Similarly, DKA in patients newly diagnosed with diabetes was more encountered during the pandemic (25.4% vs. 7.6%, \(P = 0.005\)). A higher proportion of patients were on insulin at baseline in pre-COVID19 years compared to COVID19 years (86.1% vs. 65.7%, \(P = 0.006\)). History of previous DKA admission was reported in two-thirds of the patients (75.6%) in the pre-COVID19 years compared to 42.2% during the pandemic. There was no significant difference in comorbidities between the groups except for active cancer patients presenting with DKA during the pandemic, of whom two were related to steroid and another two to sodium-glucose cotransporter-2 inhibitor (SGLT2i) use.

The clinical and initial biochemical findings of the patients admitted with DKA are depicted in Table 2. Insulin omission/noncompliance (39.2%) followed by infection (24.1%) were the major DKA precipitating factors.
Almost half the patients (49%) had moderate DKA with no difference between the two groups. Outcomes and complications are shown in Table 3. Almost two-thirds of patients in both groups were admitted to the intensive care unit (ICU) or high dependency unit (HDU). Compared to prepandemic, the median time to DKA resolution was numerically longer (17 h vs. 13 h, \( P = 0.13 \)) during COVID19 year. The median length of hospital stay was longer during COVID19 years than pre-COVID19 years (4 vs. 3 days, \( P = 0.006 \)). The majority of patients had no complications with no difference between the two groups regarding in-hospital mortality and need for mechanical ventilation.

**Discussion**

To the best of our knowledge, this is the first regional study to evaluate the characteristics and treatment outcomes of DKA admissions in COVID-19.
DKA during the COVID19 pandemic in a COVID19-free hospital. While the rate of DKA admissions increased during the pandemic in our hospital, there were no significant differences in severity, duration, and complications. Our study reveals significant changes in patients’ sociodemographic characteristics. During the pandemic, higher proportions
We have observed that most in a mixed cohort of patients (COVID19 and non-COVID19 due to lack of medical coverage and perhaps limited resources. COVID 19 pandemic and noncompliance with medications from early presentation to the hospital in the setting of the South Asians with a higher risk of T2DM were admitted, fear to the change in patients' sociodemographic characteristics. Patients' fear of going to the hospital during the pandemic could also explain many differences. Moreover, noncompliance with medical treatment and regular follow-ups might have aggravated many patients' glycemic control, leading to worse hospital presentations.

In addition, our study showed more COVID19 free patients with T2DM presenting with DKA (32.8% compared to 17.7% prepandemic). This finding is consistent with previous studies, including both COVID19 positive and negative patients that showed over the presentation of T2DM associated DKA during the pandemic (33%–37% compared to 17%–21% pre-COVID19). These studies attributed this to the fact that patients with T2DM are likely to be older (age 53–60 years vs. 31–44 years pre-COVID19) and therefore at a greater risk of severe disease with COVID-19 infection. In our study, COVID19 negative patients presenting with DKA during the pandemic were older too (median 30 vs. 23 years pre-COVID19), nevertheless much younger than the age reported in cited studies. This observation could be attributed to several factors, including a shift in the patient population seen in our hospital during the pandemic as more South Asians with a higher risk of T2DM were admitted, fear from early presentation to the hospital in the setting of the COVID 19 pandemic and noncompliance with medications due to lack of medical coverage and perhaps limited resources.

The risk of euglycemic DKA in patients treated with SGLT2i is well recognized nowadays. We have observed that most of SGLT2i associated DKA admissions were seen during the pandemic (5 vs. 1). This observation may be attributed to the recent upsurge in the use of SGLT2 inhibitors and the improved recognition of SGLT2i-associated DKA among endocrinologists.

Of note, two out of five oncology patients admitted with DKA were on concomitant SGLT2i use. Cancer patients receiving chemotherapy are prone to dehydration, poor oral intake, and infection, all considered predisposing factors to SGLT2i-associated DKA. Many oncologists recognize the association of PD-1 or PD-L1 inhibitors with autoimmune endocrinopathies, including diabetes, as a rare side effect. While euglycemic DKA is an uncommon adverse event associated with SLGT2i, it is worth alerting oncologists about this relationship as more patients are using these drugs nowadays.

There was no difference regarding in-hospital mortality or need for mechanical ventilation between the two groups of patients. The cause of death was related to the underlying comorbidities in two T2DM patients and multiorgan failure in a young T1DM patient. Studies addressing DKA during the pandemic reported a higher mortality rate (10%–12% vs. 0%–2.3% pre-COVID19) in a mixed cohort of patients (COVID19 positive and negative patients) with significant comorbidities and multiorgan failure in those who died.

Our study observed DKA and vascular events like myocardial infarction and stroke only during the pandemic. This finding could be related to the change in the demographic of the patients seen during the pandemic, where patients from South Asia with a higher risk for cardiovascular disease were often seen.

### Table 3: Outcomes of diabetic ketoacidosis episodes between April and October 2020

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<tbody>
<tr>
<td>ICU/HDU admission</td>
<td>112 (76.7)</td>
<td>63 (79.8)</td>
<td>49 (73.1)</td>
<td>0.346</td>
</tr>
<tr>
<td>Time to DKA resolution (h)</td>
<td>16 (7.5-24)</td>
<td>13 (7-24)</td>
<td>17 (7.5-27)</td>
<td>0.130</td>
</tr>
<tr>
<td>Length of hospital stay (days)</td>
<td>3.61 (2-6.1)</td>
<td>3 (2-5)</td>
<td>4 (2.73-7.6)</td>
<td>0.006</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>3 (2.1)</td>
<td>1 (1.3)</td>
<td>2 (3)</td>
<td>0.594</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>7 (4.8)</td>
<td>2 (2.5)</td>
<td>5 (7.5)</td>
<td>0.248</td>
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<tr>
<td>Complications</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Nil</td>
<td>107 (73.3)</td>
<td>56 (70.9)</td>
<td>51 (76.1)</td>
<td>0.044</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>25 (17.1)</td>
<td>18 (22.8)</td>
<td>7 (10.5)</td>
<td></td>
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<tr>
<td>MI/stroke</td>
<td>4 (2.7)</td>
<td>0</td>
<td>4 (6)</td>
<td></td>
</tr>
<tr>
<td>Pulmonary edema</td>
<td>2 (1.4)</td>
<td>1 (1.3)</td>
<td>1 (1.5)</td>
<td></td>
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<tr>
<td>DKA relapse</td>
<td>2 (1.4)</td>
<td>0</td>
<td>2 (3)</td>
<td></td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>2 (1.4)</td>
<td>1 (1.3)</td>
<td>1 (1.5)</td>
<td></td>
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<tr>
<td>Venous thrombosis</td>
<td>1 (0.7)</td>
<td>1 (1.3)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>&gt;1 complication</td>
<td>3 (2.1)</td>
<td>2 (2.5)</td>
<td>1 (1.5)</td>
<td></td>
</tr>
</tbody>
</table>

*a*No reported complications of cerebral edema or rhabdomyolysis during the study period, *b*Pre-COVID; 1 Pulmonary edema + hypokalemia, 1 DKA relapse + hypokalemia/during COVID; 1 pulmonary edema + pancreatitis. ICU: Intensive care unit, HDU: High dependency unit, DKA: Diabetic ketoacidosis, IQR: Interquartile range
The drastic change in patients’ demographics dictated fundamental changes in our hospital practice and demanded many new protocols. Our hospital increased its capacity by opening new units and limiting elective admissions. Many new issues emerged, including introducing new medications to our pharmacy to accommodate patients’ economic means. In addition, the language barrier mandated the need for interpreters and frequent inpatient diabetic education sessions. Another challenge was to implement new policies to fund uninsured patients for a longer-term medication supply and a longer outpatient follow-up in our facility after discharge. The raised beds’ demand on the “only” public COVID19 free hospital in the city could have delayed shifting patients from ICU/HDU setting to the regular floor. These factors could clarify the marginally increased length of stay of DKA cases during the pandemic compared to prepandemic. Last and not least, the opening of our telemedicine service for postdischarge follow-up was essential to assure continuity of care.

This study highlights the importance of anticipating and coping with the indirect impact of natural and man-made disasters. Strategies to ensure patients’ access to outpatient and ambulatory health care facilities are of utmost importance. In addition, incorporating private health care in such responses may alleviate the burden of the public sector. The UAE is a country with a well-known high prevalence of diabetes in both native and expatriate populations.[24] The present study results complement the findings from the previously reported series from UAE during the COVID-19 pandemic[25] and outside of the COVID19 pandemic.[26-28]

Our study is an essential contribution in an area where there is a paucity of information. Using electronic medical records allowed extensive data extraction. Limitations of this study include the retrospective design and inconsistent collection of pertinent data like job status. It will also be ideal for comparing our data with DKA episodes admissions in Al Ain Hospital prepandemic, which was not feasible.

Nevertheless, the study underscores the adjustments of diabetes service in DKA admissions as an indirect effect of the COVID19 pandemic. In addition, our study highlights the success of the health authorities and leaders in the frontlines in ensuring adaptation to cope with the medical crisis due to the COVID 19 pandemic and to make sure that health delivery is granted to everyone as pledged by the leadership.

CONCLUSION

There is an increased rate of DKA admissions during the COVID-19 pandemic, even in hospitals designated as COVID-19-free institutions. This observation may reflect the significant shift in patients’ demographics and clinical profiles due to the reconfiguration of service provision mandated by the needed adaptations for the COVID19 pandemic. Nationwide pooling data from representative hospitals of different types and designations with a comprehensive assessment of classical and emerging risk factors should shed more light on the interplay between COVID19 and diabetes.

Authors’ contribution

All named authors have contributed substantially to the published work. They all confirm that they fulfill the ICMLE authorship criteria and have approved the final version of the article.

Compliance with ethical principles

The study was approved by Tawam Human Research Ethics Committee (MF2058–2020–755). Consent was waived due to the nature of the study being based on retrospective data collection with a lack of intervention.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES


