ARTICLE

Impact of the COVID-19 Pandemic on children diagnosed with diabetic ketoacidosis admitted in a tertiary pediatric hospital

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OBJECTIVES: This study aims to determine the effect of the COVID-19 pandemic on the incidence, severity, and outcome of children diagnosed with diabetic ketoacidosis admitted in a tertiary pediatric hospital.

MATERIALS AND METHODS: Two groups were identified as the basis for classification: pre-pandemic (2017 to 2019) and COVID-19 pandemic (2020 to 2022). The Mann-Whitney U test was utilized to test for the differences in continuous variables, while Pearson's chi-squared test was used to test for differences in categorical variables.

RESULTS: The study involved 136 participants, 63 of whom were recorded in the pre-pandemic period and 73 during the COVID-19 pandemic period. Data revealed no conclusive relationship between sex (p=0.578), age (p=0.225), or height (p=0.876) across the two time frames. However, data showed significant difference between the weight (p=0.007) and BMI (p=0.003) of children with DKA pre-pandemic and during pandemic. This implies that marked changes in weight and BMI reflect possible changes in health behaviors, healthcare access, or other variables that may have altered during the COVID-19 pandemic. Furthermore, there was no discernible difference between pre-pandemic and COVID-19 in terms of severity, incidence, or the amount of time between the onset of symptoms and consultation.

CONCLUSION: The demographic and clinical characteristics of patients with DKA across the two study periods indicate a degree of stability in patient profiles. Despite the unique circumstances of the pandemic, patient outcomes in terms of glycemic control and mortality were like those observed pre-pandemic. The significant difference in weight and BMI emphasizes how crucial it is to monitor and respond to modifications in the nutritional status and metabolic health of DKA patients during times of crisis, like the COVID-19 pandemic. Comprehending these changes can provide focused treatments aimed at promoting the best possible health outcomes for susceptible patient groups.

KEYWORDS: *Diabetic Ketoacidosis, Diabetes mellitus, Covid-19 pandemic*

INTRODUCTION

Diabetes Mellitus (DM) is a metabolic disorder caused by an absolute or relative insulin shortage and an excess of counter-regulatory hormones. Diabetic ketoacidosis (DKA) is a catastrophic condition seen in patients with Diabetes Mellitus, which could be the presenting manifestation of diabetic patients with both Type 1 and Type 2 DM. DKA in patients with confirmed DM may be triggered by inadequate glycemic management, omission of insulin, infection, or emotional stress. The prevalence of DKA rose in children and teenagers with type 1 diabetes mellitus (T1DM) throughout the COVID-19 pandemic.[9] Studies on its demographic profile, such as age, gender, family history of diabetes, BMI z-scores, and laboratory tests have been established. However, reports on incidence and prevalence are somewhat underrepresented in the Philippines during the COVID-19 pandemic.[1] We investigated how this pandemic affected the lives of children diagnosed with DKA. Symptoms such as weight loss, fatigue, polyuria, nocturia, vomiting, and other typical signs of diabetes may be mistaken for pharyngitis, the flu or another common virus, pneumonia, eating disorders, food poisoning, or urinary tract infections. These might lead to a delayed diagnosis of T1DM, which would then cause diabetic ketoacidosis to advance quickly and raise the risk of complications and mortality.[1,6]

Although the impact of COVID-19 varies by nation, societies are making an effort to cut down on the use of healthcare facilities by preventing virus transmission and reducing rates of illness and death. Children experience less mortality, problems, and frequency as compared to adult age groups.[3] Children who had COVID-19-unrelated diseases during the pandemic, such as diabetes mellitus (DM), were more likely to experience negative outcomes.[9] Several studies showed a notable rise during the COVID-19 pandemic of diabetic ketoacidosis. This may make it more difficult to diagnose T1DM in children, further delaying the initiation of insulin therapy.[6] These findings show the critical need for better prevention methods for DKA in T1DM patients, not just in pandemic situations but in all situations, especially in groups most impacted by health disparities.[2,4,7,11] However, there are limited data about the impact of the pandemic on T1DM in the Philippines.

This study aims to determine the effect of the Covid-19 pandemic on the incidence, severity, and outcome of children diagnosed with diabetic ketoacidosis admitted in a tertiary pediatric hospital. This study aims to: 1) compare the demographic data of children with diabetic ketoacidosis hospitalized in a tertiary pediatric hospital during pre-pandemic (2017-2019) and COVID-19 pandemic (2020-2022) period; 2) compare the incidence of DKA in children during pre-pandemic and pandemic between known and newly diagnosed T1DM children; 3) compare DKA

characteristics in children hospitalized in a tertiary pediatric hospital during pre-pandemic and pandemic in terms of: time interval between onset of symptoms and consultation, severity, length of hospitalization, survival/ mortality; and 4) compare glycemic control based on HbA1c between T1DM children diagnosed with DKA admitted in a tertiary hospital during pre-pandemic and pandemic.

Materials and Methods

This is a retrospective study design. Purposive sampling of children 6 months to 18 years old admitted at the Philippine Children's Medical Center (PCMC) who were diagnosed with diabetic ketoacidosis between 2017 to 2022 were included. Two groups were identified using the period of admission as the basis for classification pre-pandemic (2017 to 2019) and COVID-19 pandemic (2020 to 2022). Children aged less than 6 months were excluded due to the diagnosis of neonatal diabetes. Other types of diabetes mellitus such as Type 2 DM were also excluded.

Case records of children diagnosed with DKA was obtained from the Medical Records Section of PCMC. Data collected include demographic data (age, gender, family history, BMI), clinical symptoms, onset of symptoms, time interval between symptoms and consultation, laboratory tests used such as HbA1c, serum bicarbonate, and venous blood gas. Since the study is a descriptive, no intervention was involved.

Identifying outcomes were patterned from the studies of Al-Alburazzaq *et al.* and Dyzgalo, *et al*., wherein demographic information for each patient, laboratory findings, and clinical outcomes such as timely diagnosis and treatment, regimen, and length of hospital stay was gathered. Severity of DKA was based on the standard definition from the 2022 ISPAD Guidelines of Diabetic Ketoacidosis.

The standard deviation for continuous variables, frequencies (%) and numbers (n) for categorical variables was used. Comparison of the incidence is based on the rate of the DKA/ Total DM for the pre-pandemic and during pandemic period.

The Mann-Whitney U test was utilized to test for the differences in continuous variables, while Pearson's chi-squared test was used to test for differences in categorical variables.[1,6]

Only the information needed for the research was utilized after the study. The participants' identities were likewise treated with confidentiality. The study's data was anonymized, with no way for participants to be re-identified. A waiver consent was obtained from IR-EC and non-disclosure confidentiality agreement was signed.

Results

The study included 136 participants, 63 of whom were recorded in the pre-pandemic period and 73 during the COVID-19 pandemic period.

A Mann-Whitney test showed that there is no significant difference between the age, sex, and height of children with diabetic ketoacidosis hospitalized in a tertiary pediatric hospital during pre-pandemic and COVID-19 pandemic period (Table 1). The weight, and BMI however, showed a significant difference between the two groups with p values of 0.007 and 0.003, respectively. This implies that while age, sex and height remain largely similar across two time periods, there are marked changes in weight and BMI. This reflects possible changes in health behaviors, healthcare access, or other variables that may have altered weight and BMI outcomes during the COVID-19 pandemic compared to the pre-pandemic period. Further studies may be needed to understand the underlying reasons for these changes.

Table 1. Summary of Demographic Characteristics of T1DM Patients

Parameter	Pre- pandemic (N=63) (2017-2019)	COVID-19 Pandemic (N=73) (2020-2022)	p-value
Age (Median)	12	12	0.225
Sex (Male)	35	44	0.578
(Female)	28	29	0.578
Weight (kilograms)	30	40.9	0.007
Height (centimeters)	138	141	0.876
BMI (kg/m^2)	15.8	18.4	0.003

The overall incidence of DKA among old patients was 74%, with 61% occurring pre-pandemic and 47% during pandemic. Similarly, among newly diagnosed patients, the overall incidence was 62%, with 38% occurring pre-pandemic and 52% during pandemic. The chi-square test of independence indicated that there was no statistically significant difference between the incidence of DKA and the period of observation (Table 2).

Table 2. Incidence Rate Of DKA In Children During Pre-Pandemic And Covid-19 Pandemic Between Known And Newly Diagnosed T1dm Children

	Pre-Pandemic (2017-2019)	COVID-19 Pandemic (2020-2022)	Total
Old	61%	47%	74%
New	38%	52%	62%

A Mann-Whitney test showed that there is no significant difference between the time interval, severity, and length of hospitalization. While there was no statistically significant difference in the glycemic control between patients in the study period, one point difference translates to a significant clinical implication (Table 3).

Table 3. Clinical Characteristics Of Patients With DKA

Parameter	Pre-pandemic (N=63) (2017-2019)	During Pandemic (N=73) (2020-2022)	p-value
Time interval between onset of symptoms and consult (Hours)	72	96	0.619
Severity of acidosis			
Mild	10	12	22
Moderate	9	12	21
Severe	44	49	93
Length of Hospital stay	6.0	7.0	0.366
Outcome			
Discharged	60	70	130
Mortality	3 (4.8%)	3 (4.1%)	6
Glycemic Control Based on HbA1c	12.7	13.2	0.075

Discussion

The absence of a significant difference between the age of children with diabetic ketoacidosis hospitalized in a tertiary pediatric hospital during the pre-pandemic and during the COVID-19 Pandemic is different from the findings of Vorgučin *et al.* (2022), where children aged 10 -14 years reflect the highest frequency rate of diabetic ketoacidosis observed during the pandemic.[17] This could be related to a difference in the health care system between countries and health-seeking behavior among parents.

Furthermore, pre-pandemic and during COVID-19 pandemic data show that there was also no significant association between sex and year of children with diabetic ketoacidosis hospitalized in a tertiary pediatric hospital. Similarly, the height of children with DKA reflects no statistically significant difference. These findings are in consonance with the findings of Mastromauro *et al.*, that while there is a remarkable increase in the prevalence of DKA among children during the pandemic, there is no consequential differences in terms of the sex, and height of children with diabetic ketoacidosis pre-pandemic and during the COVID-19 pandemic.

Meanwhile, as to the weight and the body mass index (BMI), the findings reflect a significant difference between the children with diabetic ketoacidosis hospitalized during the pre-pandemic period and during the COVID-19 pandemic Period. This is in consonance with the findings of Lange *et al.* which reported that the rate of weight and BMI increased among the pediatric population during the COVID-19 pandemic due to a more sedentary lifestyle, increased calorie intake, reduced access to physical activities, and increased social isolation as compared to the pre-pandemic period.

As to the incidence of DKA in children during pre-pandemic and pandemic between known and newly diagnosed T1DM children, results showed no statistically significant difference between the incidence of DKA and year of observation. This supports the findings of Rabbone *et al.* which shows that there were no differences in the incidence of DKA before and during the COVID-19 Pandemic.

This research also compared the characteristics of DKA in children hospitalized in a tertiary pediatric hospital during pre-pandemic and pandemic. In terms of the time interval between the onset of symptoms and consultation of children with DKA, the findings showed no statistically significant difference between the time interval during the pre-pandemic period and the COVID-19 pandemic period. However, the 24-day difference has significant clinical implications. Patients during pandemic could have been at greater risk for complications due to the delay in diagnosis The findings of Duncanson, *et al.* showed that the fear of COVID-19 transmission in hospitals resulted in a more delayed diagnosis and higher complication rates.

Data also revealed that there was no significant association between the severity of DKA during the pre-pandemic and during the COVID-19 pandemic period. This is consistent with the findings of Ordooei, *et al.* where the frequency of mild and moderate DKA cases was not significantly different between the pre -pandemic and during the COVID-19 Pandemic. However, their findings reflect that there are significantly more severe DKA cases found during the pandemic than the pre-pandemic period.

In terms of the length of hospitalization of children with DKA during the pre-pandemic and COVID-19 Pandemic, the absence of significant difference reflects a more aggressive and focused management during the COVID-19 as there were less consultations. This is in contrast to the study of Chambers, *et al.* (2022) where children in a tertiary care children's hospital with DKA after the pandemic onset had higher lengths of hospitalization.

In terms of the association between the outcome of Children with DKA during the pre-pandemic and the COVID-19 Pandemic period, analysis did not indicate a statistically

significant association between the two variables. This could be attributed to the standardized care that has been in place in the management of DKA patients in our institution. The findings provide a different view from the study of Kiral *et al.* and Chambers *et al.* which postulate that children who had COVID-19-unrelated diseases during the pandemic were more likely to experience negative outcomes.

In terms of glycemic control based on glycosylated HbA1c, the study revealed no significant difference but the slightly higher HbA1c among children during the pandemic period could be related to higher glucose levels with sedentary lifestyle as a contributory factor. While studies reflect that the global quarantine and health protocols brought by the COVID-19 Pandemic negatively affect the access to quality of care for children with T1DM diagnosed with diabetic ketoacidosis, the findings reflect that there was no significant difference between the established quality of care during the pre-pandemic for T1DM children diagnosed with diabetic ketoacidosis and during the COVID-19 pandemic. The sustained quality of care could be attributed to the established health intervention protocols amid the COVID-19 pandemic.

The implications of this study are multifaceted. The allocation of healthcare resources for DKA patients remained unchanged throughout the course of the two periods. Potential changes in health behaviors or access to healthcare services during the pandemic emphasizes the need for interventions to address weight management and overall health during crisis situations like the Covid-19 pandemic. The importance of continued monitoring and adaptation of healthcare practices could provide valuable insights to address emerging trends in diabetic ketoacidosis. These findings could provide clinical management strategies and patient education programs designed to target potential risk factors discovered during the pandemic period.

Conclusions and Recommendations

The incidence of DKA during the study periods offer important information despite not achieving statistical significance. The demographic and clinical characteristics of patients with DKA across two study periods indicate a degree of stability in patient profiles. Despite the unique circumstances of the pandemic, patient outcomes in terms of glycemic control and mortality were similar to those observed pre-pandemic. Meanwhile, the significant difference in weight and BMI emphasize how crucial it is to monitor and respond to modifications in the nutritional status and metabolic health of DKA patients during times of crisis, like the COVID-19 pandemic. Comprehending these changes can provide focused treatments aimed at promoting the best possible health outcomes for susceptible patient groups.

This pioneering study also has limitations due to the limited international and local literature on the impact of COVID-19 on children with DKA. The lack of existing data and registry also emphasizes the need to enhance measures and programs for an integrated, comprehensive, and optimal treatment for pediatric patients with diabetic ketoacidosis, this includes the establishment of a nationwide registry of pediatric patients with diabetic ketoacidosis to better assess the impact of the COVID-19 pandemic and its implications to the post-pandemic phase on the continuum of care for T1DM and its outcomes.

Given that the COVID-19 pandemic has also seen the potential of telemedicine and the relevance of the field of telehealth, there is also a need to recommend mechanisms that would enhance the scope of services and accessibility of telemedicine for pediatric patients with diabetic ketoacidosis and platforms for allied specialists to provide inputs on the continuum of care, especially in the underserved and geographically isolated and disadvantaged areas. Hand in hand with the need to sustain the efforts for the health sector to encourage screening for symptoms of DKA and T1DM among children and increase health campaigns on the awareness to the issue of delayed presentation and early intervention.

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