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Seasonal Trends, Clinical Profiles, and Outcomes of Diabetic Ketoacidosis in Children and Adolescents with Type 1 Diabetes

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ABSTRACT

Type 1 diabetes mellitus (T1DM) is the most common endocrine disorder in children, and diabetic ketoacidosis (DKA) remains its most serious acute complication. While seasonal variation in DKA incidence has been reported globally, such data are lacking from Pakistan, where the pattern is unknown. **Objectives:** To describe the seasonal trends, clinical profiles, and outcomes of DKA in children and adolescents. **Methods:** This descriptive, cross-sectional, retrospective study was conducted at the Department of Pediatrics, The Aga Khan University Hospital, Karachi. Data were collected from 1st November 2024 to 1st April 2025. Medical records were reviewed retrospectively from January 2019 to December 2022. Children of both genders aged 1–18 years, diagnosed with DKA either as newly diagnosed or known cases of T1Dm, were included. Demographic data, season at the time of presentation, laboratory parameters, clinical course, outcomes, and complications were recorded. The data were analyzed using R software. **Results:** A total of 78 cases were included, with a mean age of 9.6 ± 4.8 years. The mean hospital stay was 3 days. Most patients presented with severe DKA (55.1%). The highest frequency of cases occurred in winter (38.5%), followed by spring (24.4%), summer (23.1%), and autumn (14.1%). Autumn had the highest proportion of severe DKA (82%). Hyponatremia was the most common laboratory abnormality (47.43%). **Conclusions:** Seasonal variation showed slightly higher occurrence of DKA in winter, with most newly diagnosed children presenting with severe DKA. The majority of children (96.2%) had recovered.

INTRODUCTION

The most common endocrine disease in children is T1DM. T1DM is diagnosed in 65000-78000 children each year on average, and close to 80% of them are initially presented with DKA [1, 2]. DKA is a severe acute complication of relative insulin deficiency and is marked by the typical triad of biochemical variables: hyperglycaemia, ketonaemia and/or ketonuria, and acidaemia. The clinical manifestations are dehydration, tachypnoea, gastrointestinal symptoms, and a low level of consciousness induced by a fluctuating duration of polyuria, polydipsia, and weight loss [3]. Close fluid resuscitation, insulin promptly, electrolyte imbalances restoration, and control of contributory factors are the primary DKA management methods. The causes of the electrolyte disturbances can be attributed to osmotic fluid shifts caused by hyperglycemia [4]. According to the International Diabetes Federation (2019), in Pakistan, the rate of IDDM is 0.5 cases per 100,000 children per year [5]. DKA is on an absolute rise as it has an increasing incidence of diabetes [6]. The change is more of an issue in developing nations, where death as a result of DKA is very high [7]. The frequency of DKA in newly diagnosed diabetes

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and known cases was reported in local studies done in Pakistan to be 6.7% and 2.2%, respectively. DKA is the most prevalent hyperglycaemic crisis in diabetic children aged below 10 years and a significant cause of death [8]. Risk factors associated with DKA are younger age, diagnostic errors, ethnic minority, low BMI, infection, and delayed treatment initiation. While higher parental education and first-degree relatives with diabetes are protective factors [9]. As per the World Bank Climate Change Knowledge Portal, Pakistan lies in a temperate zone, and four seasons are recognized here. 1. Winter from December to February. 2. Spring from March to May. 3. Summer, from June to September, and 4. the Autumn from October till November [10]. Seasonal variation is an environmental factor that can trigger the onset of type 1 diabetes and DKA in genetically predisposed individuals. The data about the seasonal variation of DKA varies across the globe. Literature showed no significant increase in DKA in winters [10] versus the seasonality being a major triggering factor in winter and/or spring [10, 11], summer [12-14], fall [15], fall and winter [16-18]. A single study reported from Pakistan has shown an increased incidence in winter [18].

Hence, we have very limited data regarding seasonal variation in DKAin children. This study will help in identifying regional seasonal variations of DKA in children. It will enable physicians to educate parents of children living with diabetes about the periods when their children are more susceptible. It will also enable us to identify the laboratory abnormalities frequently encountered in DKA and the overall outcomes. The results can be utilised to establish protocols for considering essential testing for DKA in emergency settings in resource-limited hospital settings. This study aimed to assess the seasonal trends, clinical profile, and outcomes of diabetic ketoacidosis in children and adolescents.

METHODS

This retrospective cross-sectional study was conducted at the Department of Paediatrics and Child Health, The Aga Khan University Hospital, Karachi, Pakistan. The study was conducted after ERC approval, from 1st November 2024 to 1st April 2025. A retrospective record review was done for all children and adolescents aged 1-18 who presented with DKA from January 2019 to December 2022. After fulfilling the criteria, 78 children were included in the study. The study was conducted in accordance with the Declaration of Helsinki and GCP principles, with an ERC Full Review exemption obtained from AKUH (Approval ID: 2024-10447-31663); all data were anonymized and securely managed to ensure confidentiality. Written informed consent was taken. Inclusion criteria were children of either gender diagnosed with T1DM (newly diagnosed as well as known cases) with an age group from 1 to 18 years, presenting with DKA, satisfying ISPAD 2024 criteria. Exclusion criteria included children less than 1 year of age, newly diagnosed T1DM without DKA, and children with diabetes other than T1DM. Exemption from the Institutional Ethical Research Committee was acquired as the study involved retrospective review of existing medical records and laboratory data without any direct participant contact or disclosure of identifiable information. Demographics of all children were noted. The data including age, gender, known diabetic/ newly diagnosed, residence, season at the time of diagnosis of DKA, length and type of symptoms before presentation, capillary and serum blood glucose on arrival, venous pH, electrolytes, urine ketones, Bun, creatinine levels, SGPT, PT, INR, GAD-65 antibodies, GCS on arrival, admission disposition, length of stay, complications, indication of bicarbonate administration and outcome were recorded. DKA was defined according to ISPAD 2024 as hyperglycemia (blood glucose >200 mg/dl) with venous pH <7.3 or serum bicarbonate <18 mmol/L and ketonemia (blood ß-hydroxybutyrate≥3 mmol/L) or moderate to large ketonuria (≥2+). Mild DKA was labelled as venous pH <7.3 or serum bicarbonate <18 mmol/L, moderate DKA as venous pH <7.2 or serum bicarbonate <10 mmol/L, and severe DKA as venous pH <7.1 or serum bicarbonate <5 mmol/L. A structured proforma designed after a thorough literature review was filled out from reviewing labs and confidential files, and data was recorded on Google Forms. The statistical analysis was conducted using R Studio (version 4.4.3, R Core Team, 2025). Initially, quantitative variables were summarized using the mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. The normality of the distribution of quantitative variables was assessed using the Shapiro-Wilk test. Associations between categorical variables were determined using the Chi-square (χ^2) test or Fisher's exact test. A p-value of ≤ 0.05 was considered statistically significant. The computational workflow relied on specialized R packages, including tidyverse (encompassing dplyr for manipulation and ggplot2 for visualization), lubridate (for efficient handling of date-time objects), summarytools (for descriptive statistics), and gtsummary and gt (for generating high-quality, publication-ready tables). Multivariate logistic regression was applied afterwards.

RESULTS

The mean age was 9.6 ± 4.8 years, with 55.7% female and 43.6% male. The majority of patients (92.3%) belonged to urban areas. In our cohort, 62.8% patients were newly diagnosed (n=49). Among known diabetic patients (n=29), a previous history of DKA was positive in 15 patients, out of which 2 children had a history of DKA twice, one child had DKA 5 times, while 12 children had DKA once before. The

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mean duration of symptoms was 3.5 days. 13 patients presented with one symptom only, while the majority of children (60.2%) presented with classic symptoms of DKA. 11 parents reported weight loss along with these symptoms (14.1%). Preceding symptoms of viral infection, such as fever, cough, and flu, were positive in 33.3% (Table 1).

Table 1: Baseline Characteristics of Our Study Population

Variables	Mean ± SD (95% CI) or n (%)	Missings (n)
Age		
Years	9.59 ± 4.81 (8.51, 10.68)	–
Age Categories		
Child	33 (42.31%)	–
Adolescent	45 (57.69%)	–
Gender		
Male	34 (43.59%)	–
Female	44 (56.41%)	–
Residence		
Rural	6 (7.69%)	–
Urban	72 (92.31%)	–
Type I Diabetes		
Known Case	29 (37.18%)	–
Newly Diagnosed	49 (62.82%)	–
Diagnosis (years) (for Known Cases Only)	4.13 ± 2.94 (3.01, 5.25)	–
Symptom Duration		
Days	7.21 ± 9.76 (5.01, 9.41)	–
Recent Viral Infection		
Yes	26 (33.33%)	–
No	52 (66.67%)	–
Length of Stay		
Days	2.92 ± 1.63 (2.56, 3.29)	–
DKA Severity		
Mild DKA	9 (11.54%)	–
Moderate DKA	26 (33.33%)	–
Severe DKA	43 (55.13%)	–
DKA Resolution Time		
Hours	22.58 ± 15.38 (19.09, 26.08)	1
Admission Disposition		
PICU	32 (41.03%)	–
SCU	34 (43.59%)	–
Ward Bed	12 (15.38%)	–
Outcome		
Left Against Medical Advice	3 (3.85%)	–
Recovered and Discharged	75 (96.15%)	–

During the hospital course, the mean length of stay was 3 days, while the time taken for the resolution of DKA was 22.6 ± 15.4 hours. Most of the patients presented with severe DKA (55.1%), followed by moderate (33.3%) and mild DKA (11.5%), respectively. Findings show moderate and severe DKA were more common among female than male, with no statistical significance. Newly diagnosed cases presented with severe DKA compared to known cases of T1DM. The observed association was found to be statistically significant (Table 2).

Table 2: Severity of Diabetic Ketoacidosis (DKA) Stratified by Gender and Diabetes Type

Variables	Mild DKA	Moderate DKA	Severe DKA	Total
Female	2 (4.5%)	17 (39%)	25 (57%)	44 (56%)
Male	7 (21%)	9 (26%)	18 (53%)	34 (44%)
Total	9 (12%)	26 (33%)	43 (55%)	78 (100%)
Known Case	7 (24%)	13 (45%)	9 (31%)	29 (37%)
Newly Diagnosed	2 (4.1%)	13 (27%)	34 (69%)	49 (63%)
Total	9 (12%)	26 (33%)	43 (55%)	78 (100%)

Fisher's exact test = 3.73, p=0.081. Fisher's exact test = 14.92, p=0.001.

The overall number of cases increased over the years from 2019 to 2022. Cases were reported more in winter (38.5%), followed by nearly equal occurrence in spring and summer (24.4% and 23.1% respectively), and followed by the least in autumn (14.1%) (Figure 1).

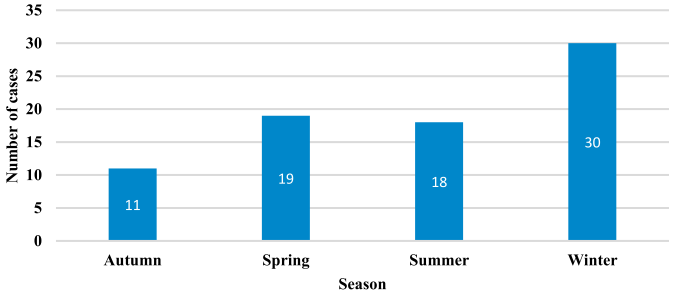

Figure 1: Distribution of DKA Across Seasons

Autumn had the highest proportion of severe DKA (82%), while winter had the highest proportion of mild/moderate cases (57%). Despite these variations, the p-value is 0.2, indicating no statistically significant association between the season and DKA severity (Table 3).

Table 3: Severity of Diabetic Ketoacidosis (DKA) Stratified by Season

Season	Mild/Moderate DKA	Severe DKA	Total
Autumn	2 (18%)	9 (82%)	11 (14%)
Spring	9 (47%)	10 (53%)	19 (24%)
Summer	7 (39%)	11 (61%)	18 (23%)
Winter	17 (57%)	13 (43%)	30 (39%)
Total	35 (45%)	43 (55%)	78 (100%)

Fisher's exact test = 6.44, p=0.20.

Urinary ketone results, as serum ketone testing is not available in our hospital (Table 4).

Table 4: Laboratory Parameters on Arrival of the Study Population

Variables	Mean ± SD (95% CI) or n (%)	Missings (n)
Previous HbA1c (%)	11.46 ± 2.56 (10.42–12.49)	03
Current HbA1c (%)	12.14 ± 2.63 (11.55–12.73)	–

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Capillary Blood Glucose	431.47 ± 103.39 (408.16–454.79)	–
Serum RBS (mg/dl)	480.80 ± 157.09 (438.33–523.27)	23
Venous pH	7.10 ± 0.14 (7.07–7.14)	–
Urinary Ketones 2+	13 (16.67%)	–
Urinary Ketones 3+	14 (17.95%)	–
Urinary Ketones 4+	51 (65.38%)	–
Serum Sodium (mEq/L)	135.29 ± 6.39 (133.85–136.74)	–
Serum Potassium (mEq/L)	4.22 ± 0.85 (4.02–4.41)	–
Serum Bicarbonate (mEq/L)	6.62 ± 3.63 (5.81–7.44)	–
Serum BUN (mg/dl)	13.01 ± 7.49 (11.22–14.81)	9
Serum Creatinine (mg/dl)	0.88 ± 0.44 (0.77–0.98)	9
SGPT (U/L)	20.15 ± 5.98 (18.06–22.23)	44
Prothrombin Time (seconds)	13.93 ± 2.99 (10.79–17.07)	72
CRP (mg/L)	22.62 ± 53.58 (–4.03–49.26)	–
Procalcitonin (ng/ml)	4.63 ± 10.35 (0.04–9.22)	56
Positive Cultures		
Blood CS	4 (5.13%)	–
None	71 (91.03%)	–
Urine CS	3 (3.85%)	–
Organisms in Positive Cultures		
Acinetobacter and Streptococcus Species	1 (1.28%)	–
Bacillus Species	1 (1.28%)	–
Candida Albicans	2 (2.56%)	–
Staph (Not Aureus)	2 (2.56%)	–
GAD-65 Antibodies		
Negative	9 (11.54%)	–
Positive	10 (12.82%)	–
Not checked	59 (75.64%)	–

Values are presented as Mean ± SD (95% Confidence Interval) unless otherwise stated.

In our study, the sodium level on arrival was reported with a mean and S.D. of 135.3 ± 6.4 mEq/L; the commonest electrolyte imbalance was hyponatremia (47.4%), which was severe in 2 children, moderate in 12 children, and mild in 23 children. Potassium level on arrival was 4.2 ± 0.9 mEq/L. Hypokalemia was observed in 14 patients (17.94%), out of which none of the patients had a potassium level <2.5mEq/L. Serum bicarbonate level on arrival was reported low in all patients, consistent with DKA, with a mean and S.D of 6.6 ± 3.6. In the extended clinical profile, SGPT was deranged in one child, who was diagnosed with Acute Viral Hepatitis A. Among septic markers, CRP was done in 18 patients with a mean and S.D of 22.6 ± 53.6, and procalcitonin was sent in 22 patients, with a mean and S.D of 4.6 ± 10.4. Regarding cultures, blood cultures were positive in 4 children (5.1%), urine CS was positive in 3 children (3.8%), while cultures were negative in the majority (91%). Among the positive blood cultures, Bacillus and Staphylococcus, not Aureus, were likely contaminants; all three cultures of urine reported Candida albicans. Serum GAD-65 antibodies were not sent in the majority (75.6%), because this test was introduced late in our centre. This is the single antibody being tested at our centre. After applying logistic regression, the two key factors retained in the Final Multivariable Model were present. Type I Diabetes-Newly Diagnosed (OR=3.14; p=0.041): This is a significant predictor. Being newly diagnosed is associated with 3.14 times the odds of the outcome compared to being a known case. Length of Stay (days) (OR=1.95; p=0.012): This is also a significant predictor. Every one-day increase in the length of stay increases the odds of the outcome by a factor of 1.95 (Table 5).

Table 5: Univariate Logistic Regression and Final Multivariable Model (Backward Elimination)

Predictor	Reference Category	Univariate OR (95% CI)	p-value	Final Model OR (95% CI)
Age	–	0.97 (0.88–1.07)	0.519	–
Age Category: Adolescent	Child	1.04 (0.42–2.58)	0.929	–
Season: Autumn	Summer	2.86 (0.53–22.57)	0.252	–
Season: Spring	Summer	0.71 (0.19–2.61)	0.603	–
Season: Winter	Summer	0.49 (0.14–1.58)	0.236	–
Gender: Female	Male	1.17 (0.47–2.89)	0.733	–
Residence: Urban	Rural	0.22 (0.01–1.48)	0.181	–
Type I Diabetes: Newly Diagnosed	Known Case	5.04 (1.92–14.17)	0.001	3.14 (1.05–9.64)
Diagnosis Years	–	0.83 (0.55–1.12)	0.282	–
Length of Stay (Days)	–	2.38 (1.47–4.28)	0.001	1.95 (1.22–3.50)
Outcome: Recovered and Discharged	Left Against Medical Advice	0.60 (0.03–6.56)	0.685	–
Season: Spring	Summer	0.71 (0.19–2.61)	0.603	–

DISCUSSION

This study presents a detailed overview of the clinical features and biochemical profile of patients with DKA, highlighting the association between seasonal variations and DKA presentation, along with a comprehensive description of laboratory characteristics in the paediatric population. In our study, the mean age of presentation was 9.6 years, with a slightly higher female predominance, aligning with previously published literature [19]. A high proportion of children with DKA had it as their initial presentation (62.8%), with a mean symptom duration of 3.5 days before presentation. This trend, reported globally [20, 21], highlights the challenge of delayed diagnosis, with most seeking care only after significant metabolic decompensation. Most patients were from urban areas (92.3%), reflecting disparities in access to quality healthcare. The highest number of DKA cases occurred in winter (38.5%), consistent with findings from Peshawar, Pakistan [8]. This may relate to the increased incidence of viral infections in colder months that unmask diabetes by contributing to islet autoimmunity and beta-cell destruction [22]. Seasonal variations also influence

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glycemic control, as reported in a Chinese adult study [23], though paediatric data remain limited. In our study, a slightly higher number of DKA cases were observed during the winter season; however, this variation was not found to be statistically significant. Therefore, our findings do not indicate a statistically significant association between seasonality and DKA occurrence. Overall, 60.2% presented with classic symptoms of polyuria, polydipsia, and polyphagia, while a few had only one symptom, highlighting the need for high clinical suspicion. Many had neuroglycopenic symptoms such as altered sensorium, emphasizing timely diagnosis to prevent cerebral edema. About 33.3% had preceding viral symptoms, suggesting mild viral illnesses as common DKA triggers, especially in winter. Although CRP and procalcitonin were elevated in some patients, no growth was reported in 91% of cultures, suggesting systemic inflammation rather than true sepsis. Literature supports that combining procalcitonin and fever can help identify bacterial infection and guide antibiotic use [24]. Biochemical findings matched diagnostic criteria for DKA. Consistent with delayed presentation, severe DKA was most common (55.1%), differing from findings in Peshawar [8]. Electrolyte disturbances were frequent, with hyponatremia in 47.4% and hypokalemia in 17.9%, both linked to osmotic diuresis and insulin therapy. Hypernatremia, though less common (7.7%), was noted and should be considered during fluid replacement to avoid complications. The average hospital stay was 3 days, similar to studies in the US and UK [25, 26], reflecting effective use of standardized ISPAD protocols. Despite being a lower-middle-income country, our outcomes align with those from developed nations, highlighting the success of these management strategies. An upward trend in DKA cases from 2019 to 2022 was observed, possibly reflecting a true rise, better diagnostics, or increased awareness. However, it also raises public health concerns and calls for an investigation into environmental, socioeconomic, and systemic contributors. Potential confounders such as socioeconomic status, comorbidities, and healthcare access were not fully accounted for and may have influenced the observed associations. Larger multicentre studies are needed to confirm our observations and delineate population-specific patterns of seasonal variation and outcomes.

Study limitations include its single-centre design and small data size, restricting its generalizability. The true correlation of seasonal trigger of DKA cannot be accurately determined without larger cohorts. As the study was conducted in a tertiary care hospital, outcomes may differ across other secondary care facilities in Pakistan. Another limitation of our study is missing laboratory data for several variables. Tests like GAD-65 antibodies were not done in 75.6% of patients, while CRP and procalcitonin were available for few, hence, limiting full assessment of laboratory profiles. Larger multicentre studies are needed to confirm our observations and delineate population-specific patterns of seasonal variation and outcomes.

CONCLUSIONS

This study delineates the clinical spectrum and biochemical characteristics of paediatric DKA, showing the predominance of severe presentations and a high proportion of new-onset diabetes at diagnosis. The findings underscore persistent diagnostic delays, reaffirming the need for earlier recognition. Although a seasonal peak in winter was observed, consistent with regional and global trends, it did not reach statistical significance, suggesting multifactorial influences beyond climatic factors. Outcomes achieved through standardized ISPAD-based management highlight the potential for high-quality care even within resource-constrained settings.

Authors' Contribution

Conceptualization: BR
Methodology: BR, BS, HHZ, MA, FM, KNH
Formal analysis: HHZ, SH, MA, FM
Writing and Drafting: BR, KNH
Review and Editing: BR, BS, HHZ, MA, FM, KNH, SH

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

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