Clinical, and Biochemical Profile of Pediatric Diabetic Ketoacidosis Patients in Al-zahraa Hospital Pediatric ICU

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ABSTRACT

Background: Diabetic ketoacidosis (DKA) is an acute and life-threatening situation that accounts for themajority of diabetes-related morbidity and mortality in children and adolescents who suffer from type 1 diabetes mellitus (T1DM).

Objective: To assess pediatric patients presented with DKA regarding aspects of presentation, findings, and management and probable risk factors associated with DKA.

Methods: a retrospective descriptive hospital-based study of 43 pediatric patients. Categorized into two groups, Group A: n=18, previously diagnosed T1DM children and Group B: n=25, newly diagnosed cases of T1DM admitted into Pediatric ICU at Alzahraa Hospital,during the period 2013 to 2017.The following data were analyzed: age, sex, weight loss, basic signs & symptoms, severity on admission, blood gas, blood glucose, glycated hemoglobin,risk factors, length of stay, and complications such as electrolyte disturbances were compared between the two groups.

Results: Newly diagnosed diabetics accounted for 25 (58.1%) of the patients. Patients in group B had longer hospital stay of 5.88±2.55 days.This study reported more nausea, vomiting, polydipsia, and polyuria, and showed more weight loss (p =.017)in group B. There was a significant relationship between hypokalemia and clinical severity (P = 0.012), and between lower bicarbonate,acidosis and severity of DKA (P <.001). No deaths occurred.

Conclusion: DKA was most prevalent in newly diagnosed T1DM cases. Significant differences in severity between groups were observed.Infections was the most common precipitating factors. No lethal complications were reported.

Keywords: Diabetes Mellitus Type 1, Diabetic ketoacidosis, children.

INTRODUCTION

Diabetic ketoacidosis (DKA) is a relatively common pediatric emergency. It's a major cause of morbidity and mortality in children with type I diabetes mellitus. DKA is commonly encountred clinicaly as the first presentation of newly diagnosed cases of typeI diabetes mellitus[(1)].

DKA at diagnosis of diabetes is common in children and adolescents. The worldwide incidence varies from approximately 13 to 80% [(2)].During the management of DKA, acid-base status, glycemia, and serum electrolytes are measured frequently to monitor the efficacy of treatment, detect complications of DKA and its treatment, and to determine resolution of DKA. Although there is some variation in the specific details of treatment protocols[(3)].

DKA is an acute life-threatening disease, which may be associated with acute and chronic complications. Acute complications can include hypokalaemia, deep vein thrombosis (DVT), cerebral oedema and death [(1)].Cerebraloedema is a rare complication, with an incidence of 0.5% to 0.9% [(4)].

It can result in medium- and long-term morbidity such as neurological dysfunction [(5)].In addition, the mortality rate of children in cerebral oedema with DKA is 40% [(6)]. The severity of diabetic ketoacidosis can be defined by blood gas results, as follows:

- Mild diabetic ketoacidosis - pH level of less than 7.3, bicarbonate level of less than 15 mmol/L
- Moderate diabetic ketoacidosis - pH level of less than 7.2, bicarbonate level of less than 10 mmol/L
- Severe diabetic ketoacidosis - pH level of less than 7.1, bicarbonate level of less than 5 mmol/L[(7)].

METHODOLOGY

This was a retrospective hospital-based study of 43 pediatric patients. Categorized into two groups, Group A: n=18, previously diagnosed T1DM children and Group B: n=25, newly diagnosed cases of T1DM admitted in Pediatric ICU at ALzahraa Hospital,during the periodfrom 2013 to 2017. All patients gave informed consent to take part in this research. Patients with inflammatory or infectious diseases, autoimmune and rheumatic diseases, cancer, haematological diseases, as well as those who were under treatment with anti-inflammatory drugs, were excluded.

Exclusion criteria included patients with incomplete documentation of DKA.Briefly, The data were collected by reviewing the medical records of the patients. We recorded the age, sex, presenting symptoms and signs at admission, precipitating factors like intercurrent illnesses, number of DKA admissions with reasons in children with established diabetes and investigations like complete blood

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counts, serum electrolytes, serum urea, serum creatinine, arterial blood gases, blood and urine culture and urinary ketone bodies.

Inclusion criteriaincluded patients admitted due to DKA. We verified that admission criteria were consistent with DKA definition by American Diabetes Association[8].

Statistical analysis

Data were coded and entered using the statistical package SPSS (Statistical Package for the Social Sciences) version 25.Data were summarized using mean, standard deviation, median,minimum and maximum in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. Comparisons between quantitative variables were done using the non-parametric Mann-Whitney test[9].For comparing categorical data, Chi square ($\chi 2$) test was performed. Exact test was used instead when the expected frequency is less than 5[10]. For all analysis, P-values less than 0.05 were considered as statistically significant. ROC curve was constructed with area under curve analysis performed to detect best cutoff value of significant parameters for detection of severe DKA.

RESULTS

The charts of 43 children fulfilled the criteria of DKA; 18 (41.9%) had established Type 1 diabetes and 25(58.1 %) children were newly diagnosed Type 1 diabetes. In group A, 55.6 % of subjects were female, while in group B 36% of subjects were female.

Table (1): Comparison between study groups as regards the baselinefeatures

Features	Group A,n=18 Previously diagnosed		Group B.n=25 Newly diagnosed		P value
	Mean	SD	Mean	SD	
Weight (kg)	41.22	16.63	25.42	11.39	.001
Age at presentation (years)	12.78	3.90	8.46	4.55	.002
Sex	Male 8	44.4%	16	64.0%	0.203
	Female 10	55.6%	9	36.0%	
Hospital stay(days)	4.17	2.09	5.88	2.55	.009

This table showed statistically significant difference between the two groups of patients as regard weight,age at presentation and hospital stay.

Table (2): Precipitating factors of study groups

Precipitating factors	Previously diagnosed Group A,n=18		Newly diagnosed Group B,n=25		P value
	Count	%	Count	%	
Unknown	2	11.1 %	10	40.0%	0.1
missed insulin dose	2	11.1%	0	0%	0.169
infection	14	77.7 %	15	60 %	0.220

The most common precipitating factor in the two groups was infection without significant difference.

Table (3): Clinical presentation of study groups

Symptoms	Previously diagnosed Group A,n=18		Newly diagnosed Group B,n=25		P value
	Count	%	Count	%	
Nausea & Vomiting	7	38.9%	18	72.0%	0.030
Abdominal pain	15	83.3%	16	64.0%	0.163
Polyuria&polydipsia	14	77.8%	24	96.0%	0.144
Weight loss	9	50.0%	21	84.0%	0.017
Fever	13	72.2%	16	64.0%	0.570

This table showed statistically significant difference between the two groups of patients as regard nausea and vomiting and weight loss.

Table (4): Grades of severity in study groups

Severity	Previously diagnosed Group A,n=18		Newly diagnosed Group B,n=25		P value
	Count	%	Count	%	
mild	5	27.8%	14	56.0%	0.012
moderate	11	61.1%	4	16.0%	
severe	2	11.1%	7	28.0%	

This table showed statistically significant difference between grades of severity in study groups. 61.1 % of subjects in group A had moderate grade of DKA followed by 27.8 % and 11.1 % had mild and severe status respectively.While in group B,the majority (56%) had mild DKA followed by severe grade 28% and mild grade 16 % with high significant statistical difference (p =.012).

Table (5):ROC- curve for detection of severe case

	Area Under the Curve	P value	95% Confidence Interval		Cut off	Sensitivity %	Specificity %
			Lower Bound	Upper Bound			
PH	0.956	<0.001	0.879	1.000	7.135	88.9	94.1
HCo3 (mmol/m)	0.920	< 0.001	0.770	1.000	5.95	88.9	100
K	0.776	0.012	0.620	0.932	4.65	100	50

By using ROC-Curve analysis, pH level at cutoff point7.135 detected severe cases of DKA with perfect accuracy, sensitivity=88.9% and specificity = 94.1% (p <0.001). HCO3 level at cutoff point 5.95 mmol/ml detected severe cases of DKA with perfect accuracy, sensitivity=88.9% and specificity =100% (p <0.001) and K level at cutoff point 4.65 mEq/Idetected severe cases of DKA with perfect accuracy sensitivity=100% and specificity =50% (p <0.012).

DISCUSSION

Diabetic ketoacidosis (DKA) is defined by the American Diabetes Association as hyperglycemia (plasma glucose > 200 mg/dL or approximately 11 mmol/L and venous pH < 7.3 and or bicarbonate (HCO3)< 15 mmol/L. DKA is the most common cause of death in children with T1DM.The most common rare and primary fatal complication of DKA is cerebral edema [(8)].

DKA is an acute complication of DM that was incurable before discovery of insulin and a leading cause for admission to the pediatric intensive care unit (PICU)[(11)].In addition, DKA is related to impaired cognitive functions, such as short-term memory and long-term intelligence [(12)].

In this study, our results were based on the data collection of 43 children with DKA admitted at Pediatric ICU in Alzahraa Hospital.We reported thatthe majority of patients (25 cases,58.1%) were newly diagnosed Type 1 diabetes mellitus and 18 cases (41.9 %) had established T1DM. In agreement with our study as regards those who found in their study that 50 (42.7%) cases had established T1DM and 67 (57.2 %) children were newly diagnosed T1DM[(13)], the explanation may be related to a lower awarness of symptoms of diabetes among parents. Or may be referred to a missed T1DM diagnosis at the first medical counseling visit for symptoms such as polyurea, polydipsia, weight loss. As mentioned earlier, some patients were misdiagnosed with gastroenteritis or respiratory infection and diagnosed with T1DM later, In disagreement with our work, thestudy that reported48.2% were newly diagnosed and 51.8% were previously diagnosed cases of diabetes[(14)].

In our work,the mean age at presentation was 12.7±3.9 years old in group A and 8.4 ±4.5years old in group B.There is a study that disagreed with our study, it revealed that the mean age of admission was 8.2±4.0 years old in previously diagnosed children and 9.5±4.3 years old in newly diagnosed children[(15)]. Regarding length of hospital stay, we found that newly diagnosed cases had longer mean hospital stay (5.88 days) as compared to previously diagnosed

(4.17 days).In agreement with our study,that of Kumar and Manjusha[16]whoreported that the duration of stay in PICU was longer in newly-diagnosed cases (4.5 days) compared to established cases (2.5 days)[16].

Our study found that the frequency of severe DKA was more found in newly diagnosed (28 %) than previously diagnosed (11.1%). Our finding was similar to that of Zubair et al.who reported that the frequency of severe DKA was 28.5% and 51% in previously diagnosed and newly diagnosed cases respectively [15].

Our result found that the major precipitating factor for DKA was infection (67.8%), most commonly pharyngitis,chest infection, tonsillitis, urinary tract infections, hepatitis A and gastroenteritis. This was in agreement with a study,which reported thatthe major precipitating factor for DKA was infection (most commonly viral fever, peritonitis, pneumonia and urinary tract infections)[17]. An earlier study from Pakistan was in disagreement with our study as their study showed that insulin omission precipitated DKA in upto 38% of pediatric patients with established diabetes[13].

In our study,the most common presenting symptoms were polyuria & polydipsia (88.4 %) followed by abdominal pain (72.1%),weight loss (69.8%),fever (67.4%) and Nausea & vomiting (58.1%). Syed et al.,[18]study agreed with our work.They observed the most commonly presenting symptoms were polyuria (86%), polydipsia (84.7%) followed by gastrointestinal symptoms, including nausea or vomiting(47.2%) and abdominal pain (43.1%).While a study in disagreement with our result,found that the commonest presenting complaints in both groups were respiratory distress(87.1%) and vomiting (77.7%)[13].

In regard toelectrolyte disturbance,there was no difference between newly and previously diagnosed in relation to hypokalemia and hyponatrmia as a complication of treatment in DKA.This finding was similar with that of Zubair et al. [15].

In current work, all cases recovered without lethal complications and no deaths occurred where95.3 % (41cases) of studied patients were recovered and 4.7 % (2cases) were referred to fever hospital. This might be attributedto the intensive, appropriate and careful treatment and physicians'experience in our pediatric critical care.

Our result found that hypokalemia, acidosis and decreased biacabonate were significantly associated with the degree of severity of DKA (p values of 0.012,< 0 .001 and < 0.001 respectively). The severity of DKA showed significant association with acidosis.This finding was similar to Syed et al. [18]and shabir et al. [19]who reported the severity of acidosis as a reflection of the severity of DKA.In addition, there was a significant relationship between hypokalemia and severity of DKA, which wasin agreement with another study reporeteda significant relationship between hypokalemia and clinical severity (P = 0.02) [20].

Our data indicated association between newly diagnosed diabetes and severity of DKA where 77.8% of newly diagnosed cases presented with severe grade of DKA. A study disagreed with our findings who indicated no association between newly diagnosed diabetes and severity of DKA[20].

In our work,we found no association between age and severity of DKA, which was in agreement with a study showed the same finding[20].Also Syed et al. [18]and shabir et al. [19]agreed with our study. There was a study that disagreed with our study, it reported that severe DKA was more frequent in the age group <5years old[21].

CONCLUSION

The majority of patients (25 cases,58.1%) were newly diagnosed Type 1 diabetes mellitus and 18 cases (41.9 %) cases had established T1DM.

Infection was the most common precipitating factor in previously and newly diagnosed T1DM.There was significant differences in clinical symptoms as nausea&vomiting and weight loss in previously and newly diagnosed T1DM. There was Significant differences in severity grades between previously and newly diagnosed T1DM.There was positive association between severity of DKA and low bicarbonate, hypokalemia and low PH.There was negative correlation between severity of DKA and age.Mild DKA was occuring more frequently than moderate and severe forms.All patients had good prognosis and no deaths were reported.

RECOMMENDATIONS

1- Public education about diabetes symptoms alone can reduce thefrequency of DKA through preventing a delayed diagnosis.

2-Regular follow up and early detection of infection in children of T1DM.

3-The vaccination status of the patient should be checked, and future vaccinations should be planned and added to diabetic children follow-up cards.

4- Further study to assess of the effect of puberty and sex hormones on glycemic control and development of DKA in adolescent.

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