

Original Article**Analysis of Prolonged Pediatric Intensive Care Stay in Children with Diabetic Ketoacidosis****Sandip Kumar Singh*, Shikha Rijal, Vijay kumar Sah, Babita Khanal and Arun Giri**

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Article Received: 26th April, 2020; Accepted: 20th June, 2020; Published: 30th June, 2020DOI: <http://dx.doi.org/10.3126/jonmc.v9i1.29530>**Abstract****Background**

Diabetic ketoacidosis is one of most serious complication of diabetes requiring intensive care management. We aim to analyze various factors responsible for prolonged duration of stay in pediatric intensive care unit in a child with diabetic ketoacidosis.

Materials and Methods

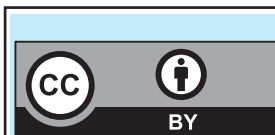
This was a hospital based prospective observational study conducted in Nobel Medical College Teaching Hospital among children with diabetic ketoacidosis over the period of one year. A total of 22 cases with diabetic ketoacidosis aged 1 month to 18 years were included and clinical profile, laboratory reports including blood gas analysis were documented.

Results

Among cases of diabetic ketoacidosis, 4 (18%) cases were of mild diabetic ketoacidosis, 4 cases (18%) were of moderate diabetic ketoacidosis and 14 cases (64%) were of severe diabetic ketoacidosis. Mean duration of Intensive care stay in new cases of diabetic ketoacidosis was 69.46 hours which was significantly higher compared to old cases (30.66 hours) suggested by p value < 0.0001. In 15 cases (68%), acidosis resolved in less than 48-55 hours, whereas 7 cases (32%) required more than 48-55 hours for resolution of acidosis, hence required longer Intensive care stay. Cases who required prolonged Pediatric Intensive care stay, sepsis was contributing factor in 3 cases (42.85%), one case (14.28%) has associated muscular dystrophy and 3 cases (42.85%) had hyperchloremia at the end of 48 hours.

Conclusion

Presence of sepsis and hyperchloremia are important reasons for prolonged stay in Intensive Care Unit in diabetic ketoacidosis patients. Other associated chronic illness can also prolong intensive care stay in diabetic ketoacidosis patients.

Keywords: *Diabetic ketoacidosis, Hyperglycemia, Sepsis*

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Introduction

Diabetic ketoacidosis (DKA) is serious complication of diabetes and common cause of Pediatric Intensive Care (PICU) admission in children. DKA comprises of hyperglycemia, ketonemia/ketonuria, and anion gap metabolic acidosis. Patients are discharged from PICU, once acidosis is resolved (glucose < 200 mg/dl, serum bicarbonate \geq 18 mEq/l, pH > 7.3 and AG \leq 12 mEq/l [1]. However, use of serum bicarbonate as marker of resolution of acidosis have limitations (due to dependence on pCO₂) [2].

Management of DKA requires fluid and electrolyte replacement depending on severity. There is total body potassium deficit, despite normal or elevated serum potassium level, requiring potassium supplementation. Bicarbonate administration is rarely indicated. Most serious complication associated with DKA is cerebral edema. Others are hypoglycemia, hypokalemia, hypophosphatemia, venous thrombosis, rhabdo-myolysis, and renal failure [3]. DKA resolves within 48-72 hours depending on the severity. Use of fluid with high chloride results in hyperchloremic acidosis due to preferential excretion of ketones over chloride by kidneys [4]. This can mask resolution of ketoacidosis when only base deficit is used to monitor biochemical improvement [5]. When hyperchloremia develops, low serum bicarbonate can be easily misinterpreted as ongoing ketosis and results in prolonged PICU stay [6].

In our study, we described demographic characteristics of children with DKA and analyzed different causes for prolonged PICU stay (> 48-55 hours) in children with DKA. We also intend to see whether sepsis and hyperchloremia (> 115 meq/l) results in prolonged stay in PICU.

Materials and Methods

The study is a prospective observational study conducted on children with Diabetic ketoacidosis admitted in Pediatric Intensive Care Unit of Nobel Medical College during 12 months period from December 2018 to November 2019. This study was started after acquiring approval from the Institutional Review Committee of Nobel Medical College (IRC). Written consent was acquired after the patient or patient party was explained about the study, its advantages, and disadvantages. All children (1month to 18 years of age) admitted to PICU with diagnosis of Diabetic ketoacidosis were included in this study. Neonates meeting criteria of Diabetic ketoacidosis were excluded from the study. Using $n = z^2 \times p(1-p) / e^2$ with 5% margin of error, and population proportion of 1%

[7], sample size was calculated to be 16. However we collected total 22 cases in duration of one year.

Nobel Medical College's PICU is a 10 bedded tertiary referral center in Biratnagar, Nepal. All children were diagnosed and managed by ISPAD 2018 (International Society for pediatric and adolescent diabetes) clinical practice consensus guidelines. Detail history and clinical examination was performed. Polyuria, polydipsia, polyphagia, vomiting, abdominal pain, acetone breath, dehydration, altered sensorium, vitals and systemic examination were noted. Laboratory parameters: Blood glucose, urinary ketones, electrolytes, urea and creatinine, arterial blood gas (ABG), electrocardiogram (ECG), hemogram, blood and urine culture and chest X-ray were performed at admission. Blood sugar level (BSL) was performed hourly until acidosis resolved. ABG and serum electrolytes were done 4 hourly until child was transferred out to the ward. Blood glucose was performed by glucometer and also in the laboratory. Urinary ketones were measured by Ketostix. Patients were transferred out to the ward after clinical stabilization, and resolution of acidosis (Ph > 7.3 and HCO₃ >15 meq/l). All data was tabulated and statistically analysed using SPSS 11. Descriptive analyses were expressed as percentages, mean \pm standard deviation (SD), median with minimum and maximum values. Chi square test were used for comparison of categorical variables. P-value < 0.05 was considered statistically significant with confidence interval (CI) of 95%.

Results

A total of 22 cases of DKA were analyzed during one year duration of study. Ten cases were male (45%) whereas 12 cases (55%) were female. The median age of presentation was 7.9 years (IQR 5.0-12.1) and duration of illness prior to admission was 4.8 days (IQR 3-15). The median weight was 23 kg (IQR 11.8-28.5) and median height was 116.8 cms (IQR 93.8-138). Four (18.2%) cases were of age less than 5 years, 7 cases (31.8%) were between 5-10 years of age, and 11 (51%) cases were more than 10 years of age. The most common presenting complaint was vomiting (72.7%), followed by polyuria (68.2%), pain abdomen (63.6%), polydipsia (27.7%) and polyphagia (16.8%). Among 22 cases 12 (55%) were new cases of diabetes whereas 10 (45%) were old cases of diabetes under regular insulin therapy.



Table 1: Demographic Features and Characteristics of DKA Cases on Admission

Characteristics	Results
Mean age at diagnosis (year)	7.9 (IQR 5.0-12.1)
Median duration of symptoms	4.8 days (3-15)
Gender, n (%)	Male 10 (45.5 %)
	Female 12 (54.5 %)
Age at diagnosis (year), n (%)	< 5 years 4 (18.2 %)
	5-10 years 7 (31.8 %)
	> 10 years 11 (50 %)
DKA	New Cases 12 (54.5 %)
	Established diabetes 10 (45.5 %)
	Vomiting 16 (72.7 %)
Symptoms at time of presentation	Polyuria 15 (68.2 %)
	Pain abdomen 14 (63.6 %)
	Polydipsia 6 (27.7 %)

Among cases of DKA, 4 (18%) cases were of mild DKA, 4 cases (18%) were of moderate DKA and 14 cases (64%) were of severe DKA. These children were managed in PICU until acidosis was resolved. In 15 cases (68%), acidosis resolved in less than 48-55 hours, whereas 7 cases (32%) required more than 48-55 hours for resolution of acidosis, hence required longer PICU stay.

Table 2. showing demographic characteristics of children based on DKA classification

Characteristics	Mild DKA	Moderate DKA	Severe DKA
Number of cases	4 (18%)	4(18%)	14(64 %)
New cases	2 (16.7%)	3 (25%)	7 (58.3%)
Mean duration of PICU stay	42.75 Hours	42.75 Hours	59.78 Hours
Prolonged PICU stay(> 48-55 hours)	None	1 (4.54%)	6 (27.3%)
Hyperchloremia at 48 Hours	None	1 (4.54%)	2 (9.1%)
High Anion gap metabolic acidosis at 48 Hours	None	None	3 (13.6%)

Mean duration of PICU stay was 58.13 hours. Children with mild to moderate DKA required shorter PICU stay (42.75 hours) compared to children with severe DKA (59.78 hours). Mean duration of PICU stay with children with DKA was different between new onset diabetes compared to old cases of Diabetes under insulin therapy. Mean duration of PICU stay in new cases was 69.46 hours which was significantly higher compared to old cases of Diabetes (30.66 hours) suggested by p value < 0.0001. In 15 cases (68%), acidosis resolved in less than 48-55 hours, whereas 7 cases (32%) required more than 48-55 hours for resolution of acidosis, hence required longer PICU stay. Among 7 cases that required PICU stay for > 48-55 hours (6 cases were of severe DKA and 1 cases of mild to moderate DKA). Cases who required prolonged PICU stay (>48-55 hours), sepsis was contributing factor in 3

cases (42.8%), one case (14.3%) has associated muscular dystrophy and 3 cases (42.8%) had hyperchloremia (serum chloride > 115 meq/l) at the end of 48 hours. Children with sepsis required PICU stay for mean duration of 70.38 hours compared to 46.12 hours in children without sepsis. This difference in PICU stay was statistically significantly with p value of < 0.001. Similarly, in children with hyperchloremia PICU stay was significantly increased as compared to children without hyperchloremia (66.16 hours and 53.32 hours respectively) with p value of 0.002.

Table 3. Showing Laboratory Profiles among the children with DKA

Laboratory Profile	Severity of DKA	Result
Admission pH	Mild DKA	7.23± 0.52
	Moderate DKA	7.12 ± 0.44
	Severe DKA	6.99 ± 0.68
Admission PaCO ₂ mean (SD) (mmHg)	Mild DKA	18 ± 0.8
	Moderate DKA	12 ± 0.92
	Severe DKA	7 ± 1.2
Admission HCO ₃ mean (SD) (meq/L)	Mild DKA	12.3 ± 1.2
	Moderate DKA	7.26 ± 0.88
	Severe DKA	3.11 ± 0.68
Number of Complications during PICU stay, n (%)	Hypokalemia	8 (36.4)
	Hyponatremia	6 (27.3)
	Hyperchloremia	7 (31.8%)

Among all cases of DKA, hyperchloremia was present in 7 cases (31.81%) at end of 48 hours of PICU stay, whereas 15 cases (68.18%) had normal chloride level at end of 48 hours of PICU stay. Among the 7 cases with hyperchloremia at end of 48 hours, 1 case (14.3%) had high anion gap metabolic acidosis and 6 cases (85.7%) had normal anion gap at 48 hours. High anion gap metabolic acidosis at end of 48 hours was seen in 3 cases (13.6%), whereas 19 cases (86.4%) had normal anion gap at end of 48 hours. Complications were seen like hypokalemia in 36.4 % of cases and hyponatremia in 27.3 % of cases. Out of 22 cases of DKA, all cases survived, 5 cases (22.72%) were directly discharged from PICU whereas 17 cases (77.27%) were shifted to ward and later discharged. None of the patients developed cerebral edema and the median number of days for the patient to be discharged was 13 (IQR 9.5-15). The median dose of insulin at discharge was 19.2 Unit (11.5-29).

Discussion

The outcome in management of DKA depends on early recognition of the condition, fluid and electrolyte replacement, insulin infusion, treatment of precipitating factors and early recognition of complications and its management. In this study, DKA was managed with ISPAD 2018



protocol. Females comprised more than half of total cases which is different compared to study done by Jayashree et al [8]. Female predominance can be attributed to hormonal influences leading to more brittle nature of disease and higher incidence of autoimmune conditions in females. The most common presenting complaint in our study were vomiting (72.7%), followed by polyuria (68.2%), pain abdomen (63.6%), polydipsia (27.7%) and polyphagia (16.8%). This finding is similar to study done by Jayashree et. al [8]. More than half of the cases (51%) presented during adolescent period (10-19 years). This finding can be explained by fact that peak incidence of diabetes is seen in children during early pubertal period (between 10-14 years of age). In our study 12 cases (54.5%) were new cases of T1DM presenting as DKA, this also explains majority of children presenting during adolescent period. Lone et al. [9] reported similar findings, in their study 55% of children with DKA were above 10 years of age. Similarly, study done by Naeem et al. [10] also reported highest number of DKA episodes in children, who aged 10 - 14 years.

As shown in our study, 55% of our patients were newly diagnosed diabetes, this is in contrast to western studies, western data showed it to be 25% [11]. This difference in incidence can be explained by late presentation to hospital in developing countries. Beside late presentation, delay in diagnosis and lack of awareness could also be attributing factors. Severe DKA was seen in 64% of cases in our study, similar to study by Guisado-Vasco et al' [12] which showed incidence of severe DKA in 49.4% cases. This can also be attributed to delay in diagnosis by primary care physician and lack of access to healthcare workers and healthcare centers. Beside common complications observed (i.e. hypokalemia, hypoglycemia, hyponatremia), we found higher incidence of hyperchloremia (31.81%) in our study and hyperchloremia result in delayed resolution of acidosis and delayed recovery from DKA [13]. Higher incidence of hyperchloremia can be explained by use of Normal saline (NS) as initial fluid of choice for expansion of intravascular volume in our study. Other complications observed in our study were hypokalemia (36.36%), hyponatremia (27.27%). All of these complications are higher than what are reported already by Jayashree et al [8]. In this study, all cases recovered without lethal complications and there were no mortality. Whereas, some studies showed that, among children with severe DKA 10% - 25% of survivors can have residual

morbidity. Incidences of significant residual morbidity are less described in recent studies, due to better awareness about diabetes in children and early recognition of condition and early intervention if associated with complications. Although till date, the recommended fluid therapy for DKA is isotonic fluids for initial management and this therapy can lead to hyperchloremia but newer studies are in favor of use of balanced solution or low chloride fluids like plasmalyte. Use of plasmalyte will decrease incidence of hyperchloremia and its adverse effects. In our study, DKA resolution was earlier in old cases compared to new cases, due to early diagnosis, better insulin sensitization. Similar finding were seen in a study done in 117 children admitted with DKA in a hospital in Pakistan, where longer continuous insulin infusion were needed in patients, who had no diagnosis of diabetes prior to admission [9]. Common causes of prolonged stay in PICU in child with DKA were sepsis, hyperchloremic acidosis and associated neuromuscular disorder in our study. Among all the causes of prolonged PICU stay in children with DKA, sepsis and hyperchloremia were strongly associated, as evidenced by p value of <0.001 and 0.002 respectively. This result is similar to study done by Varadarajan P in 2014 [14] which showed sepsis is strongly associated with prolonged acidosis and prolonged hospital stay.

Conclusion

Presence of sepsis is one of the important reasons for prolonged stay in PICU in DKA patients. Hyperchloremia is also seen as strong reason for prolonged PICU stay in DKA patients. Any patients, whose metabolic acidosis is persisting beyond 48 hours with normal anion gap, underlying hyperchloremia should be suspected and addressed by reduction of IV fluids or use of fluids containing low chloride level. However to generalize the statement, multicenter studies with larger study groups are required. This result would be of help to practicing pediatrician and pediatric intensivist for recognizing DKA patients requiring prolonged PICU stay.

Conflicts of interests: None

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