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Original Article

Role of Capillary Blood Ketone Assay in Management of Diabetic Ketoacidosis in Paediatric Intensive Care Unit

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ABSTRACT

Objective: To assess the role of capillary blood ketone assay in managing Diabetic Ketoacidosis in the Paediatric Intensive Care Unit.

Study Design: Prospective longitudinal study.

Place and Duration of Study: Paediatric Intensive Care Unit of Children's Hospital, University of Child Health Sciences, Lahore Pakistan, from Jul to Dec 2021.

Methodology: Patients with Diabetic ketoacidosis fulfilling the inclusion criteria and admitted during the study period were enrolled, and treatment was given according to standard protocol. On admission, capillary blood ketones were measured after 4-6 hours, and serial blood glucose, serum electrolytes, serum creatinine and venous blood gas were done.

Results: Out of 554 admissions, 55(9.9%) patients with diabetic ketoacidosis were enrolled. The mean age was 8.2±3.5 years, with 28(50.9%) females. Among 33(60%) newly diagnosed cases, 13(23.6%) were moderate and 41(74.5%) with severe diabetic ketoacidosis. 12(21.8%) cases developed AKI, 5(9.1%) required continuous renal replacement therapy, 10(18.2%) needed mechanical ventilation, and 2(3.6%) expired. A positive statistical correlation was observed between capillary blood ketones and standard acidosis markers on admission.

Conclusion: Capillary blood ketone assay has a significant role in managing Diabetic Ketoacidosis by prompt diagnosis, early initiation of treatment and early stoppage of insulin infusion at resolution of ketosis without waiting for blood gas parameters to normalise. Its use should be encouraged in PICUs, especially in low-resource settings, because of its cost-effectiveness.

Keywords: Capillary blood ketone, Diabetic ketoacidosis, Ketosis, Paediatric intensive care unit.

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INTRODUCTION

In children, Diabetic ketoacidosis (DKA) presents as an acute life-threatening emergency. At diagnosis, 30% of paediatric patients with Type-I diabetes present with diabetic ketoacidosis, while others may develop during their disease.[1] One local study mentioned DKA cases increasing in PICU from 1.8% in 2010 and 3.4% in 2015.[2] Over the last few years, the focus of DKA management has changed from being glucose-centred to ketone-centred.[3] "The criteria for the diagnosis of DKA include hyperglycemia (blood glucose >11 mmol /L [≈200mg/dL], metabolic acidosis (venous pH <7.[3] or serum bicarbonate <15 mmol/L, ketonemia (blood ß-hydroxybutyrate ≥3mmol/L) or moderate to large ketonuria.[4]

Advancing technology and frequent use of ketone meters have emphasised making treatment decisions based on their readings, as beta-hydroxybutyrate (BOHB) is the predominant ketone body in DKA, which is tested by these ketone meters.[5] The urine ketone measurement is a relatively cheap detection method. However, its limitations include delay in diagnosis due to decreased urine production and severe dehydration. Despite the correction of ketosis, insulin infusions are continued longer because of the continuous excretion of urinary ketones.[6] In low-resource settings, urinary ketones are still commonly used despite these limitations.[7,8]

Regarding the use of capillary blood ketones, the literature supports its role not only in the diagnosis of DKA but also in monitoring treatment response.[9,10] Data is lacking regarding its use in Diabetic Ketoacidosis management in paediatric intensive care units (PICU), so we have undertaken this study to look for the role of capillary blood ketones in management of Diabetic Ketoacidosis in PICU by assessing the statistical correlation between capillary blood ketones and standard acidosis markers like pH, HCO3, Anion Gap and Base Deficit.

METHODOLOGY

The prospective longitudinal study was conducted at the Paediatric Intensive Care Unit of Children's Hospital, University of Child Health Scien-

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ces, Lahore, from July to December 2021 after approval from the Institutional Review Board (2021-296-CHICH dated June 16, 2021). The sample size was calculated by Open Epi software version-3, using the 3.7% prevalence of DKA in type one diabetes mellitus in the paediatric population of Pakistan.[2]

Inclusion Criteria: Diabetic ketoacidosis patients of either gender, with aged from 1 month to 16 years, admitted to PICU, were included in the study.

Exclusion Criteria: Patients who left against medical advice during the data collection procedure were excluded from the study.

Diagnosis of Diabetic Ketoacidosis was made using ISPAD 2018 guidelines which included "venous BG >200 mg/dl, pH <7.30 and HCO3 <10 along with evidence of ketosis (blood or urine) and severity of DKA was categorised by the degree of acidosis: mild (pH 7.2-7.3), moderate (pH 7.1-7.2), or severe (pH <7.1 "4 Capillary blood ketone level ≥3mmol/L was labelled as ketoacidosis. Acute Kidney Injury was labelled based on serum creatinine values using KDIGO criteria.[10] serum chloride level >106mEq/L (laboratory reference value) was labelled as hyperchloremia. On Call GK Dual Blood Glucose and Ketone Meter (ACON laboratories, USA) was used, a handheld device that requires only a blood drop to measure both blood ketone (BOHB) and blood glucose and the results were seen within 30 seconds.

Figure: Dual Glucose and Ketone meter for measurement of both glucose and BOHB by a drop of blood.

All patients are given treatment according to standard DKA protocol, which comprises intravenous fluids, regular insulin infusion @ 0.1 Units/kg/h, and a serial clinical assessment of vitals and mental status. Bedside blood ketones were initially measured at admission, then 4-6 hourly till resolution of DKA (pH >7.3, HCO3 >15, and AG <12) using a ketone meter. Other tests included hourly bedside blood glucose, venous blood gas intermittently & serum electrolytes 4-6 hourly.

Statistical Package for Social Sciences (SPSS) version 25.0 was used for the data analysis. Quantitative variables were expressed as Mean±SD and qualitative variables were expressed as frequency and percentages. Independent sample t-test and Chi-square test were applied to explore the inferential statistics. Pearson's correlation coefficient was applied at two points: initially at diagnosis and then at resolution of DKA. The *p*-value of 0.05 or less was taken as significant.

RESULTS

Out of 554 admissions, 55(9.9%) patients with DKA were diagnosed. Mean age of 8.2±3.5 years was noted with 28(50.9%) females. 33(60%) patients were newly diagnosed cases. We had 13 patients (23.6%) with moderate DKA, while 41 patients (74.5%) presented with severe DKA. Detailed demographic and clinical characteristics are given in Table-I. On admission, the mean blood glucose was 416.5±123.4 mg/dL and the mean blood ketone 6.36±1.18 mmol/L, while in blood gas, we noted a mean pH of 7.03 ± 0.14, HCO3 4.49±2.40 mmol/L, Base deficit -26.25±5.31 mmol/L & Anion gap 29.98±8.42. A detailed comparison of metabolic characteristics is given in Table-II. Hyperchloremia was documented in 43.6% of cases. 12(21.8 %) patients developed AKI, and 5(9.1%) required continuous renal replacement therapy. Ten patients (18.2%) needed mechanical ventilation, and the mean stay in the hospital was 4.9±4.5 days. 2(3.6%) patients with severe DKA expired during our study period. Table-III compares capillary ketones with acidosis parameters on two occasions; on admission and at resolution. A significant positive correlation was observed between capillary blood ketones and acidosis markers (HCO3, BD) on admission; however, no statistical correlation was observed at the time of resolution of acidosis.

Table-I: Patients demographics and clinical characteristics (n=55)

Variables	Values
Age (years)	8.2±3.5(2-15)
Male	27(49.1%)
Female	28(50.9%)
Insulin Dependent Diabetes Mellitus	
New cases	33(60%)
Old cases	22(40%)
Severity	
Mild	1(1.8%)
Moderate	13(23.6%)
Severe	41(74.5%)

Table-II: Metabolic Characteristics at Admission and on Resolution (n=55)

Lab Parameters	On Admission	On Resolution
pH	7.03(6.80-7.32)	7.33(7.28-7.46)
HCO3	4.49(1.60-11.40)	14.09(8.90-20.90)
Anion Gap	29.98(10-45)	18.46(5.30-30.70)
Base Deficit	-26.25 (-14.80 to-37.80)	-8.89 (-3.80 to -13.90)
Capillary Blood Ketone	6.36(3.5-8.0)	1.41(0.60-2.80)
Blood Glucose	463.22(103- >600)	174.12(102-262)
Sodium	134.57(120-148)	139.76(130-155)
Potassium	4.26(2.50-6.10)	3.79(2.10-5.30)
Chloride	99.6(82-124)	107.5(97-128)
Creatinine	0.95(0.35-5.10)	0.74(0.30-2.02)

Table-III: Comparison of β-HOB with Standard Acidosis Markers on admission and at DKA resolution (n=55)

Variable	Pearson Correlation & *p*-value	On Admission	On Resolution
pH	Pearson Correlation	-0.332	-0.063
	p-value	0.013	0.650
HCO3	Pearson Correlation	-0.451	-0.251
	p-value	0.001	0.064
Base Deficit (BD)	Pearson Correlation	0.465	0.132
	p-value	<0.001	0.337
Anion Gap (AG)	Pearson Correlation	0.275	0.224
	p-value	0.042	0.100

DISCUSSION

Diabetic ketoacidosis is associated with significant morbidity and mortality, while delayed diagnosis and treatment can prove lethal to the patient. Capillary blood ketone testing can change the future of DKA management by making early diagnosis without exhausting our lab resources in low-resource settings. Secondly, early stoppage of continuous insulin infusion at a resolution of ketosis will shorten the length of stay in our PICUs, along with avoiding hyperchloremia due to prolonged chloride-rich fluid administration.

During the six-month duration, we received 9.9% cases of DKA, which is more than 1.5% and 2.5% from different PICUs of Karachi.[2,11] In our study, the mean age was 8.2±3.5 years, comparable to other studies.[2,11,12] Female predominance (50.9%) was seen in our study, similar to these local and international studies 2, 11, 13, while other studies reported male predominance.[12-15] 60% of cases in our study were newly diagnosed, similar to many other studies 2,12,14 but contrary to some international studies where reported figures are 25% and 35.8%, respectively.[1,15]

In our study, DKA severity was reported as 1.8% mild, 23.6% moderate and 74.5% severe. These figures of moderate and severe DKA are comparable with a study by Aslam *et al*.[12] Our reported figure of severe DKA is high, most probably due to delayed presentation and late referrals from the periphery, while we had 1.8% cases of mild DKA; this figure is small as mild cases are mostly being managed in the special care unit of our Paediatric Endocrinology unit.

In our study, two patients of DKA had urinary ketones <1, but capillary blood ketones were high along with hyperglycemia and clinical picture, so they were promptly diagnosed and managed. A study by Rashid *et al*. mentioned a 25-30% error in diagnosing DKA using urinary ketone measurements.[16] So capillary ketone testing should be encouraged in PICUs because it is easy to use, cost-effective and helps in rapid diagnosis and management of DKA. A similar role is seen in one study done in the Emergency Department.[17] Many studies have mentioned the role of capillary blood ketones in sick day management of people with diabetes during home monitoring, thus preventing DKA episodes & reducing hospitalisation.[18]

Hyperchloremia was documented in 43.6% of cases, which is less than the mentioned figures of 60% and 90% in other studies,[11,19] reasons being early switching to an insulin sliding scale once ketosis is resolved by ketone meter readings rather than relying on values of standard acidosis markers. Few published reports have mentioned discontinuation of continuous insulin infusion at a resolution of ketosis by readings of ketone meters.[20] AKI reported in 21.8% of our cases, with variable figures reported in literature ranging from 7% to 64.2%.[12]

In our study, the total length of stay was 4.89±4.47 days, more than the local study.[2] Reason for long hospital stays is attributed to delayed presentation with more complications, especially in new cases where parents had poor knowledge about the disease and its symptoms; secondly, late referral from peripheries and mismanaged cases.

CONCLUSION

Capillary blood ketone assay has a significant role in managing Diabetic Ketoacidosis by prompt diagnosis, early initiation of treatment, and early switching off the insulin infusion at a resolution of ketosis without waiting for blood gas parameters to normalise.Its use should be encouraged in Paediatric Intensive Care Units, especially in low-resource settings, because of its cost-effectiveness.

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Conflict of Interest: None

Author's Contribution:

Following authors have made substantial contributions to the manuscript as under:

FK & MS: Conception, study design, drafting the manuscript, approval of the final version to be published.

AA & AJ: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

NS & GS: Critical review, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Neu A, Willasch A, Ehehalt S, Hub R, Ranke MB. Ketoacidosis at onset of type 1 diabetes mellitus in children-frequency and clinical presentation. Pediatr Diabetes 2003; 4(2): 77–81. https://doi.org/10.1034/j.1399-5448.2003.00007 .x
2. Abbas Q, Arbab S, Haque A. Spectrum of comp-lications of severe DKA in children in pediatric Intensive Care Unit. Pak J Med Sci 2018; 34(1): 106-109. https://doi.org/10.12 669/pjms.341.875.
3. Dhatariya K. Blood Ketones: Measurement, interpretation, limitations, and utility in the management of diabetic ketoacidosis. Rev Diabet Stud 2016; 13 (4): 217-225.
4. Wolfsdorf JI, Glaser N, Agus M, Fritsch M. ISPAD clinical practice consensus guidelines 2018: Diabetic ketoacidosis and the hyperglycemic hyperosmolar state. Pediatr Diabetes 2018; 19 (Suppl 27): 155-77. https://doi.org/10.1111 /pedi.12701.
5. Pulungan AB, Juwita E, Pudjiadi AH, Rahmayanti S, Tsaniya I. diabetic ketoacidosis in adolescents and children: A prospective study of blood versusurine ketones in monitoring therapeutic response. Acta Med Indones 2018; 50(1):46-52.
6. Wallace TM, Matthews DR. Recent advances in the monitoring and management of diabetic ketoacidosis. Int J Med 2004; 97(12): 773–780. https://doi.org/10.1093/qjmed/hch132
7. Xu Y, Bai J. Clinical profile of diabetic ketoacidosis in tertiary hospitals in China: a multicentre, clinic-based study. Dia-betic Med 2016; 33 (2): 261–268. https://doi.org/10.1111/dme.1 2820
8. Bektas F, Eray O, Sari R, Akbas H. Point of care blood ketone testing of diabeticpatients in the Emergency Department. Endocr Res 2004; 30: 395-402. https://doi.org/10.1081/ec-200035231.
9. Brooke J, Stiell M, Ojo O. Evaluation of the accuracy of capillary hydroxybutyrate measurement compared with other measurements in the diagnosis of diabetic ketoacidosis: A systematic review. Int J Environ Res Public Health 2016; 13: 837. https://doi.org/: 10.3390/ijerph13090837.
10. Kellum JA, Lameire N, Aspelin P, Barsoum RS, Burdmann EA, GoldsteinSL, et al. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO clinical practice guideline for acute kidney injury. Kidney Int Suppl 2012; 2:1-138. https://doi.org/10.1038/kisup.2012.1
11. Shahzad M, Haque A, Mirza S, Jurair H, Ahmed AR, Khalid M, et al. Role of capillary blood ketone assay in diagnosis and management of diabetic ketoacidosis in pediatric intensive care unit. J Pediatr Crit Care 2020; 7: 316-320. https://doi.org/10.4103/JPCC.JPCC_105_20.
12. Aslam A, Sultana N, Sarwar M, Jamil A, Kausar F, Waqar U, et al. Spectrum of complications in children with moderate to severe dka admitted in pediatric intensive care unit of a tertiary care hospital. J Rawalpindi Med Coll 2022; 26(2). https://doi.org/10.37939/jrmc.v26i2.1835
13. 13) Safaei A, Maleknejad S, Ebrahimi Kelachaye M. Diabetic ketoacidosis and its complications among children. Acta Med Iran 2011; 49(2): 113-114.
14. Jayashree M, Singhi S. Diabetic ketoacidosis: predictors of outcome in a pediatric intensive care unit of a developing country. Pediatr Crit Care Med 2004; 5(5): 427- 433. https://doi.org/10.1097/01.PCC.0000137987.74235.5E
15. Atkilt HS, Turago MG, Tegegne BS. Clinical characteristics of diabetic ketoacidosis in children with newly diagnosed Type 1 diabetes in Addis Ababa, Ethiopia: a cross-sectional Study. PloS One 2017; 12(1): e0169666. https://doi.org/10.1371/journal.pon.0169666
16. Rashid MA, Chowdhury HS, Haque M, Faruque MO, Chowdhury MR, Ali L, et al. Role of measurement of blood ketone bodies in the management of diabetic ketoacidosis. Int J Nutr Pharmacol Neurol Dis 2013; 3: 335-340. https://doi.org/10.4103/2231-0738.119840
17. Klocker AA, Phelan H, Twigg SM, Craig ME. Blood β-hydroxybutyrate vs. urine acetoacetate testing for the prevention and management of ketoacidosis in Type 1 diabetes: a systematic review. Diabet Med 2013 ; 30(7): 818-824. https://doi.org/10.1111/dme.12136.
18. Laffel LM, Wentzell K, Loughlin C, Tovar A, Moltz K, Brink S,et al. Sick day management using blood 3-hydroxybutyrate (3-OHB) compared with urine ketone monitoringreduces hospital visits in young people with T1DM:A randomized clinical trial. Diabt Med 2006; 23: 278-284. https://doi.org/10.1111/j.14645491.2005.01771.x
19. Taylor D, Durward A, Tibby SM, Thorburn K, Holton F, Johnstone IC, et al. The influence of hyperchloremia on acid base interpretation in diabetic ketoacidosis.Intensive Care Med 2006; 32: 295-301. https://doi.org/10.1007/s00134-005-0009-1.
20. Prisco F, Picardi A, Iafusco D, Lorini R, Minicucci L, Martinucci ME, et al. Blood ketone bodies in patients with recent-onset type 1 diabetes (a multicente study). Pediatr Diabetes 2006; 7: 223-228. https://doi.org/10.1111/j.1399-5448.2006.00187.x