# **ORIGINAL ARTICLE**

# Prerequisite of Insulin and Intravenous Fluid in the Treatment of Diabetic Ketoacidosis to Overwhelmed the Catastrophe

TARIQ TAHIR BUTT<sup>1</sup>, SOBIA MUHAMMAD ILYAS<sup>2</sup>, SYED MIR USMAN SHAH<sup>3</sup>, MUHAMMAD AZAM<sup>4</sup>, AMANULLAH KHOKHAR<sup>5</sup>, AYESHA SHAFIQUE<sup>6</sup>

<sup>1</sup>Associate Professor of Biochemistry, Sialkot Medical College, Sialkot

<sup>3</sup>Assistant Professor of Medicine, Postgraduate Medical Institute, Quetta

<sup>4</sup>Assistant Professor of Medicine, M. Islam Medical and Dental College Gujranwala

<sup>5</sup>Assistant Professor of Medicine, AI Tibri Medical College and Hospital, Malir Karachi/ Isra University Campus Hyderabad

<sup>6</sup>MS Biochemistry, University of the Punjab, Lahore

Corresponding author: Syed Mir Usman Shah, Email: mirusman573@hot.com, Cell: + 92 321 8002738

# ABSTRACT

**Introduction:** Ketoacidosis (DKA) is relatively common among the states of acute metabolic decompensation of diabetes. It usually transpires in patients with diabetes mellitus who have some type of infection and have poor compliance of insulin. Treatment entailed of correcting hyperglycaemia, dehydration, acidosis, electrolyte imbalance and antibiotic therapy in patients with any type of infection or treating another reason, if any. The aim of this study is to determine the requirement of insulin and intravenous fluid for the treatment of diabetic ketoacidosis to overcome the catastrophe

**Study Design:** It was a cross-sectional study, held in the Medicine of Sialkot Medical College, Sialkot for six-months duration from July 2021 to December 2021.

**Methods:** Sixty adult patients with DKA who met the exclusion and inclusion criteria who need the total volume of intravenous fluid (saline) required to manage diabetic ketoacidosis.

**Results:** The total numbers of selected patients were 60. Diabetic ketoacidosis was communal in patients with formerly detected diabetes (71.4%), and its frequency was higher in the poor and the rural population, no significant gender differences were found. Vomiting (53.3%), Nausea (36.7%), infection (38.3%) and abdominal pain (30%) were common, with polyuria (25%) and polydipsia (18.3%). The main causes were infection (38.3%) and failure to administer insulin (51.7%). In most cases, status of glycaemia was poor. Many of the cases had mild (43.3%) to moderate (56.7%) acidosis, and electrolyte disturbances were less frequent. Leucocytosis (90%) was consistently present even in the absence of any infection. The result (91.7% survival) is comparable to that of developing countries. For the treatment of CKD, 35% of patients with increased diuresis required 11 liters of fluid. 23.3% of patients required 91-100 insulin units, and maximum patients (31.7%) needed forty-eight hours to correct their acidosis.

**Conclusion:** Diagnosing diabetic ketoacidosis is not tough if noticed in time and can be treated successfully. In order to prevent mortality; adequate fluid replacement is mandatory.

Keywords: Diabetic ketoacidosis, diabetes, intravenous fluids and insulin.

# INTRODUCTION

In 2009, there were 140,000 hospitalizations for diabetic ketoacidosis (DKA), with an average stay of 3.5 days<sup>1</sup>. The annual indirect and direct hospitalization costs for DKA are \$ 2.4 billion. The most common factor causing DKA is skipping insulin<sup>2-3</sup>. Infectious stress, acute cardiovascular (myocardial infarction, stroke) and gastrointestinal diseases (pancreatitis, bleeding), endocrine disease (Cushing's syndrome, acromegaly), and recent surgery may result in the DKA development by causing increased levels of insulin counterregulatory hormones, dehydration and deteriorating of peripheral insulin resistance<sup>4</sup>. Medications, such as beta blockers, diuretics, antipsychotics, anticonvulsants and corticosteroids may influence volume status and carbohydrate metabolism and thus accelerate CKD5. Extra aspects that may result in CKD comprise eating disorders, psychological problems, the use of illegal substances and insulin pump malfunction. It is now accepted that new-onset type 2 diabetes may occur in DKA6. These patients are mostly African American or Asian, obese and have extremely level of resistant to insulin during presentation.

Amongst the decompensated and acute metabolic conditions of diabetes, diabetic ketoacidosis is comparatively communal<sup>7</sup>. It usually transpires in patients with diabetes mellitus who have some type of infection and have poor compliance of insulin<sup>8</sup>. Formerly undiagnosed people with DM may also presented with symptoms of DKA<sup>9</sup>. Accordingly, we assessed sixty patients with DKA for insulin and IV fluid requirements for treatment and outcomes<sup>10</sup>.Treatment comprised of correcting acidosis, electrolyte imbalance and dehydration as well as precipitating factor like antibiotics for infections.

### METHODS

This Cross-sectional study was held in the Medicine of Sialkot Medical College, Sialkot for six-months duration from July 2021 to

December 2021. for six-months duration from July 2021 to December 2021. The DKA management was carried out conferring to the Portland Protocol. Blood glucose was hourly measured and the insulin rate was regulated on a syringe pump conferring to the protocol of Portland. The chart of Intake and output is retained to verify that fifty percent of the fluid has been directed in order to avoid fluid overload and bicarbonate was not directed. DKA was taken as resolute when there is >18 meq / L of bicarbonate level with pH> 7.3. Subsequently, a subcutaneous split-mix insulin regime was initiated when the volunteers were able to ingest food ( $1/3^{rd}$  of regular insulin and  $2/3^{rd}$  intermediate-acting NPH insulin).  $2/3^{rd}$  of the over-all daily dosage was administered in the morning time and  $1/3^{rd}$  in the evening time.

# RESULTS

The total number of selected patients were 60. Thirty-five of the cases were men and twenty-five were women. (M: F = 1.8:1). The recently identified cases of diabetes mellitus were 35(58.3%) and known diabetic patients were 25(41.7%) of selectees. More specifically, at most 23.3% of the patients were 21-25 years of age. Table 1 labels the patient's distribution in the various age groups.

Table-1: shows the patients distributio	n conferring to age
---	---------------------

Age (years)	Number of patients (%)
≤ 20	10 (16.7)
21-25	14 (23.3)
26-30	8 (13.3)
31-35	5 (8.3)
36-40	6 (10)
41-45	10 (16.7)
46-50	3 (5)
51-55	2 (3.3)
56-60	2 (3.3)
≥ 61	0 (0)

<sup>&</sup>lt;sup>2</sup>Jinnah Postgraduate Medical Center, Karachi

Amongst the known diabetic patients, 50% received insulin, 25% received oral hypoglycemic drugs followed by insulin, and 25% received only oral hypoglycemic drugs.

Table-2: shows the patients distribution conferring to the precipitating  $\underset{\mbox{causes}}{\mbox{causes}}$ 

Cause	No of old cases	No of new cases
Infection (38.3%)	12	11
Omission of drugs/ insulin (51.7%)	19	12
New case (5%)	2	1
Surgery (5%)	2	1
Pancreatitis (6%)		

Omission of insulin and infection were the foremost reasons of the progression of CKD. In most cases, glycemic status was poor. Most of the patients had mild to moderate acidosis. In most cases, status of glycaemia was poor.

Table-3: shows the levels of RBS at admission

RBS mmol/l	No of subjects	%age
≤10	0	0
10-15	12	20
16-20	9	15
21-25	22	36.7
26-30	8	13.3
31-35	5	8.3
>35	4	6.7

Table-4: shows level of acidosis		
рН	Number of patients	Percentage
<7	6	10
7-7.24	32	53.3
7.25-7.30	22	36.7

For the treatment of CKD, 35% of patients with increased diuresis required 11 liters of fluid. 23.3% of patients required 91-100 insulin units, and maximum patients (31.7%) needed forty-eight hours to correct their acidosis.

Table-5: shows the Pre	requisite of fluid for	improvement of acidosis

Amount of (NS) fluid (L)	Number of patients
5	10
6	5
7	2
8	5
9	3
10	6
11	21
12	3
13	3
14	1
16	1

Table-6: shows the Insulin required for improvement in acidosis

Amount (unit )	Number of patients
< 80	12
81-90	10
91-100	14 (23.3%)
101-110	5
111-120	3
121-130	5
131-140	8
141-150	2
151-160	3

Table-7: shows the time required for improvement in acidosis

Time	Number of patients
24 hrs	13
48 hrs	19 (31.7%)
72 hrs	10
4days	4
5 days	4
6 days	5
7 days	5

### DISCUSSION

This research was conducted to test the intravenous insulin and fluid requirements in the treatment of diabetic ketoacidosis in order to overwhelmed the emergency experienced at the tertiary care Hospital. In Denmark, the ratio of women to men was 7.1: 6.1. A Taipei recent study institute that 68% of patients with DKA are women<sup>10-11</sup>. In India case series, the M: F proportion was 3:1.2. The cases of acidosis with mild to moderate level were managed in a general ward, as suggested in analysis held at the Atlanta in Emory University School of Medicine<sup>12-13</sup>. In this study, infection was the most common causing cause (36%). Infection was documented in 38.3% of cases. They probably had formerly undetected hyperglycaemia and the DKA was caused by the infection. The residual ten patients had a comparatively brief history of polyuria, polydipsia, rapid breathing and weight loss; acute pancreatitis was seen in one case only. Of the 35 known diabetic cases, 20 (57.1%) had insulin deficiency and DKA was developed within 1-19 days<sup>14-15</sup>. Infection was noticed in ten cases; acute pancreatitis was seen in two cases. In one patient, omitting insulin after gynaecological surgery aggravate DKA. Most of the patients had slightly low or normal levels of sodium and normal or slightly elevated levels of potassium. Comparable outcomes were obtained in studies in Pakistan and Atlanta<sup>16</sup>. Severe hypokalaemia, severe acidosis and hyponatraemia was seen in 4 patients. Afterwards initiating insulin and fluid therapy, nearly all subjects established hypokalaemia necessitating correction by intravenous potassium. A similar observation appeared in a national survey in Denmark. Most of the patients had very high blood sugar and ketonuria on urine ketos-tix test<sup>17-18</sup>. Patients were found to have a longer duration of ketonuria compared to biochemical and clinical enhancement as demonstrated by HCO3 and pH levels. A comparable opinion was conveyed very recently in one Indian study<sup>19-20</sup>. Correction of acidosis in the majority of patients (24%) took 48 hours, up to a maximum of 1-week. In the Emroy Medicine University study, the time required was between 11 and 15 hours. The results were quite comparable and satisfactory in established states. 5 (8.3%) cases who developed severe acidosis died. Mortality in developing countries ranged from 6 to 24%<sup>21-22</sup>. In our study, most patients required 91 to 100 units of insulin and 82 to 110 units of insulin, similar to the study at Emroy Medicine University. In the 1st 24 hours of inpatient treatment, every subject needed 4.12 litters of IV fluid approximately, 72 units of insulin and 60 mmol of potassium<sup>23-24</sup>.

#### CONCLUSION

DKA most often arisen in patients diagnosed with diabetes who had an infection and missed an insulin dose. New cases are common. Common features are polydipsia, polyuria, abdominal pain, vomiting and infection. These patients have poor glycaemic control. Severe acidosis is less common. Severe electrolyte disturbances are rare in mild to moderate acidosis, but after start of therapy; hypokalaemia develops. Leucocytosis is communal even in the absenteeism of infection, and ketonuria may continue or worsen with treatment despite biochemical and clinical enhancement. The general outcome is better with 10% death ratio.

#### REFERENCES

- Tran TT, Pease A, Wood AJ, Zajac JD, Mårtensson J, Bellomo R, Ekinci El. Review of evidence for adult diabetic ketoacidosis management protocols. Frontiers in endocrinology. 2017 Jun 13;8:106.
- Evans K. Diabetic ketoacidosis: update on management. Clinical Medicine. 2019 Sep;19(5):396.
- Razavi Z, Maher S, Fredmal J. Comparison of subcutaneous insulin aspart and intravenous regular insulin for the treatment of mild and moderate diabetic ketoacidosis in pediatric patients. Endocrine. 2018 Aug;61(2):267-74.
- Donihi A, Karajgikar ND, Manroa P, Acharya R, Codario RA, Reider JA, Salata RA, Korytkowski MT. Addressing pitfalls in management of diabetic ketoacidosis with a standardized protocol. Endocrine Practice. 2019 May 1;25(5):407-12.

- Islam T, Sherani K, Surani S, Vakil A. Guidelines and controversies in the management of diabetic ketoacidosis–A mini-review. World Journal of Diabetes. 2018 Dec 12;9(12):226.
- Rayman GE, Lumb A, Kennon B, Cottrell C, Nagi D, Page E, Voigt D, Courtney H, Atkins H, Platts J, Higgins K. Guidance on the management of Diabetic Ketoacidosis in the exceptional circumstances of the COVID-19 pandemic. Diabetic Medicine. 2020 Jun 18;37(7):1214-6.
- Haas NL, Gianchandani RY, Gunnerson KJ, Bassin BS, Ganti A, Hapner C, Boyd C, Cranford JA, Whitmore SP. The two-bag method for treatment of diabetic ketoacidosis in adults. The Journal of emergency medicine. 2018 May 1;54(5):593-9.
- Dizon S, Keely EJ, Malcolm J, Arnaout A. Insights into the recognition and management of SGLT2-inhibitor-associated ketoacidosis: it's not just euglycemic diabetic ketoacidosis. Canadian journal of diabetes. 2017 Oct 1;41(5):499-503.
- Cohen M, Leibovitz N, Shilo S, Zuckerman-Levin N, Shavit I, Shehadeh N. Subcutaneous regular insulin for the treatment of diabetic ketoacidosis in children. Pediatric diabetes. 2017 Jun;18(4):290-6.
- Rawla P, Vellipuram AR, Bandaru SS, Raj JP. Euglycemic diabetic ketoacidosis: a diagnostic and therapeutic dilemma. Endocrinology, diabetes & metabolism case reports. 2017 Sep 4;2017(1).
- Harrison VS, Rustico S, Palladino AA, Ferrara C, Hawkes CP. Glargine co-administration with intravenous insulin in pediatric diabetic ketoacidosis is safe and facilitates transition to a subcutaneous regimen. Pediatric diabetes. 2017 Dec;18(8):742-8.
- Rouf R, Rahim M, Latif ZA. Requirement of intravenous fluid and insulin in the management of diabetic ketoacidosis to overcome the crisis: experience in a specialized hospital. Journal of Medicine. 2018;19(1):18-21.
- Mohan M, Baagar KA, Lindow S. Management of diabetic ketoacidosis in pregnancy. The Obstetrician & Gynaecologist. 2017 Jan;19(1):55-62.
- Yung M, Letton G, Keeley S. Controlled trial of Hartmann's solution versus 0.9% saline for diabetic ketoacidosis. Journal of Paediatrics and Child Health. 2017 Jan;53(1):12-7.

- Basetty S, Kumar GY, Shalini M, Angeline RP, David KV, Abraham S. Management of diabetic ketosis and ketoacidosis with intramuscular regular insulin in a low-resource family medicine setting. Journal of Family Medicine and Primary Care. 2017 Jan;6(1):25.
- 16. Kreider KE. Updates in the management of diabetic ketoacidosis. The Journal for Nurse Practitioners. 2018 Sep 1;14(8):591-7.
- Nguyen AD, Luong CQ, Chu HC, Nguyen VK, Nguyen CV, Nguyen TA, Nguyen QH, Mai TD, Nguyen DV, Nguyen BQ, Tran TH. Successful management of severe diabetic ketoacidosis in a patient with type 2 diabetes with insulin allergy: a case report. BMC endocrine disorders. 2019 Dec;19(1):1-6.
- Laliberte B, Yeung SY, Gonzales JP. Impact of diabetic ketoacidosis management in the medical intensive care unit after order set implementation. International Journal of Pharmacy Practice. 2017 Jun;25(3):238-43.
- Shuster S, Borici-Mazi R, Awad S, Houlden RL. Rapid desensitization with intravenous insulin in a patient with diabetic ketoacidosis and insulin allergy. AACE Clinical Case Reports. 2020 Jul 1;6(4):e147-50.
- Long B, Willis GC, Lentz S, Koyfman A, Gottlieb M. Evaluation and management of the critically ill adult with diabetic ketoacidosis. The Journal of Emergency Medicine. 2020 Sep 1;59(3):371-83.
- Lee MH, Calder GL, Santamaria JD, MacIsaac RJ. Diabetic ketoacidosis in adult patients: an audit of factors influencing time to normalisation of metabolic parameters. Internal medicine journal. 2018 May;48(5):529-34.
- Kumar P, Sakwariya A, Sultania AR, Dabas R. Hypertriglyceridemiainduced acute pancreatitis with diabetic ketoacidosis: a rare presentation of type 1 diabetes mellitus. Journal of laboratory physicians. 2017 Oct;9(04):329-31.
- Alberti KG. History of the Treatment of Diabetic Ketoacidosis. InUnveiling Diabetes-Historical Milestones in Diabetology 2020 (Vol. 29, pp. 202-206). Karger Publishers.
- Castellanos L, Tuffaha M, Koren D, Levitsky LL. Management of diabetic ketoacidosis in children and adolescents with type 1 diabetes mellitus. Pediatric Drugs. 2020 Aug;22(4):357-67.