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DIABETIC KETOACIDOSIS CHARACTERISTICS AND DIFFERENCES IN TYPE 1 VERSUS TYPE 2 DIABETES PATIENTS

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ORIGINAL ARTICLE

DIABETIC KETOACIDOSIS CHARACTERISTICS AND DIFFERENCES IN TYPE 1 VERSUS TYPE 2 DIABETES PATIENTS

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Background: Diabetes is undoubtedly one of the most challenging health problems of the 21st century. It is well known that diabetes once develop can lead to several complications. Diabetic ketoacidosis (DKA) is one of the life-threatening complications of diabetes. This study was designed to determine the frequency of DKA in diabetes patients and find out the clinical and biochemical determinants of DKA. **Methods:** This descriptive study was conducted at Aga Khan University Hospital (AKUH) Karachi, Pakistan from January 2010 to February 2016. All known or newly diagnosed diabetic patients of >16 years of age irrespective of gender and type of diabetes were included. Information regarding patient's demographics, presenting symptoms, precipitating causes of DKA, biochemical profiles and outcome at the time of discharge was collected. **Results:** Majority (54.7%) had moderate and 12.4% had severe DKA at presentation. Previous history of DKA was found higher in type 1 diabetes patients (T1DM) (14%) as compare to (4%) type 2 diabetes patients (T2DM) (p<0.05). DKA severity was observed more (12%) in newly diagnosed (T1DM) (p<0.05). Comorbidities were found more (81%) in (T2DM) (p<0.05) Mortality was also observed higher in Type 2 diabetes patients (p<0.05). **Conclusion:** Majority of the diabetics had moderate to severe DKA at presentation. Mortality and morbidity related with DKA was found considerably higher among patients with T2DM while infection, myocardial infarction and stroke found as triggering factors in these patients.

Keywords: Diabetic ketoacidosis (DKA); T1DM; T2DM

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INTRODUCTION

Diabetic ketoacidosis (DKA) is a medical emergency which was once thought to occur in only type 1 diabetes patient but has now been proven to occur in type 2 diabetes as well. It occurs due to relative or complete lack of insulin in the body.[1–3]

Its prevalence is higher among type 2 diabetes mellitus (T2DM) patients as compared to type 1 diabetes mellitus (T1DM), and the proportion is expected to increase over the next 20 years; therefore, the presentation of DKA is likely to be higher in people with T2DM.[4] The overall prevalence of ketosis-prone T2DM is comparatively lower in Asian and white people and may represent fewer than 10% of cases of DKA.[5,6]

There are various parameters that need to be ascertained in both type 1 and type 2 diabetes patients who present with DKA, like age of presentation, presenting clinical features, precipitating cause and biochemical characteristics. Many studies have been conducted to observe the characteristics of DKA in both type 1 and type 2 diabetes mellitus[2,5,7] and various comparisons have been made worldwide but the local data of Pakistan is still scarce. The need for more studies is needed and justified in order to know valuable information about ketoacidosis in Pakistani diabetes patients. This information will help in increasing our knowledge and understanding of various factors related to DKA and help in differentiating the various characteristics of both type 1 and type 2 diabetes patients. In the present study, we aimed to determine the frequency of DKA in Pakistani diabetes population and comparison of clinical and biochemical characteristics of DKA in type 1 and type 2 diabetes.

MATERIAL AND METHODS

This retrospective study was conducted among 234 patients aged 16 years and above of either gender admitted with diagnosis of DKA to Aga Khan University Hospital (AKUH) Karachi, Pakistan during the period from January 2010 to February 2016. Patients aged below 16 years and non-diabetics presenting with ketoacidosis were excluded from the study. Informed written consent was obtained from hospital authorities to use the data of patients. No personal detail by any means related to any patient was revealed in regard of ethical considerations.

Computer coding was used to identify admissions with an ICD code for DM and DKA during the period of study. Diagnosis of DKA was made by the presence of an arterial pH lower than 7.30, an anion gap of less than 15 mmol/L, presence of hyperglycemia, i.e., blood glucose >250mg/dL, urine ketone levels of 'moderate'or 'large' i.e., equal to or more than 2+. DKA was

classified as mild, moderate or severe according to ADA criteria1 (see annexure). Serum osmolality was being calculated using the formula 2[measured Na (mEq/l)] + glucose (mg/dl)/18 and was measured in mosm/kg. Anion gap was calculated using the formula (Na+) − (Cl− + HCO3−) (mEq/L).

All patients presenting with DKA were admitted under medicine service and were managed by team of internist, medicine residents and interns while in emergency department and ward. Endocrinology team including an endocrinologist, fellow endocrinology and diabetes nurse were later involved as specialist team. All patients were managed as per the hospital's local management protocol of DKA.

Patients data was reviewed retrospectively regarding patient's demographics, presenting symptoms, precipitating causes of DKA, vital signs, biochemical profiles at presentation to the emergency department, amount of intravenous fluid administered, amount of insulin administered, duration of insulin infusion, time from presentation to resolution of urine ketones, insulin dose at discharge, and length of hospitalization and outcome at the time of discharge was collected. Precipitating factors of DKA were defined as conditions leading to the development of DKA, such as inadequate insulin dose or missed insulin doses, sepsis, infection, surgical stress etc. For patient presenting with more than one factor, the main cause was noted. Observation bias was controlled by reconfirmation of collected information from hospital's records by a second verifier. Confounding factors were rectified through restriction.

Subjects were classified as Type 2 DM if they had prior history of treatment (>1 years) with diet alone or oral hypoglycaemic agents (OHA), or as 'new onset' if the episode of DKA was the first manifestation of diabetes. Patients with new-onset DM were further classified as type 1 or type 2 if they discontinued insulin use without recurrence of DKA for at least 1 year respectively. Patients follow-up data was obtained by chart review or telephone contact when necessary.

Data was analysed by using SPSS version 19.0. Frequency and percentages were computed for categorical variables, i.e.; gender, type and duration of DM, previous episode of DKA, presenting symptoms and severity of DKA. Chi square test was used to compare the categorical variables between T1DM versus T2DM patients. Mean and Standard Deviation was computed for continuous variables, i.e.; age, BMI, duration of DM and biochemical parameters. T-test and ANOVA were used to compare Mean±Standard Deviation. P value less than 0.05 was considered as significant.

RESULTS

Data of 234 patients with diabetes was used in this study. Patients were divided into four groups, newly diagnosed type I (n=47), known type I (n=59), newly diagnosed type II (n=10) and known type II (n=118). Out of total 234 patients, 120 (51.3%) were males and 114 (48.7%) were females. Body mass index (BMI) was found significantly more in type 2 diabetes (p<0.05). Previous history of DKA was found more in known type I diabetes patients (14%) as compare to (4%) known type II diabetes patients (p<0.05). More than half (54.7%) of the subjects had moderate DKA and 12.4% of them had severe DKA at presentation. DKA severity was observed more (12%) in newly diagnosed type 1 diabetes patients (p<0.05). Comorbidities were found more (81%) in known type 2 diabetes patients (p<0.05) (Table-1).

Table-2 shows the presentation of biochemical parameters of the study participants. Haemoglobin levels were higher in newly diagnosed type 1 diabetes patients (p<0.001). WBC and platelet counts were high in known type 1 diabetes patients (p<0.05).No significant differences were found in other biochemical parameters. (Table-2)

Figure-1 shows the presenting symptoms of patients of type I and II diabetes. Polyphagia, polydipsia, polyuria, weight loss and abdominal pain was significantly higher in type 1 diabetes patients.

The comparison of DKA treatment of type I and type II patients are presented in Table-3. The amount of insulin given to the type 1 and 2 patients were same (p>0.05). Length of stay in hospital, ICU admission and ventilator support were also not different significantly in both groups (p>0.05). Precipitating factors like infection, myocardial infarction and stroke were found more in type 2 patients, while more type 1 patients were found non-compliant (p<0.05). Overall mortality due to DKA was 9.4% (22 out of 234 patients) and was higher in type 2 patients (p<0.05). Six out of 47 (12.8%) newly diagnosed type 1 patients and 16 out of 118 (13.6%) known type 2 diabetic patients had mortality due to DKA (p<0.05).

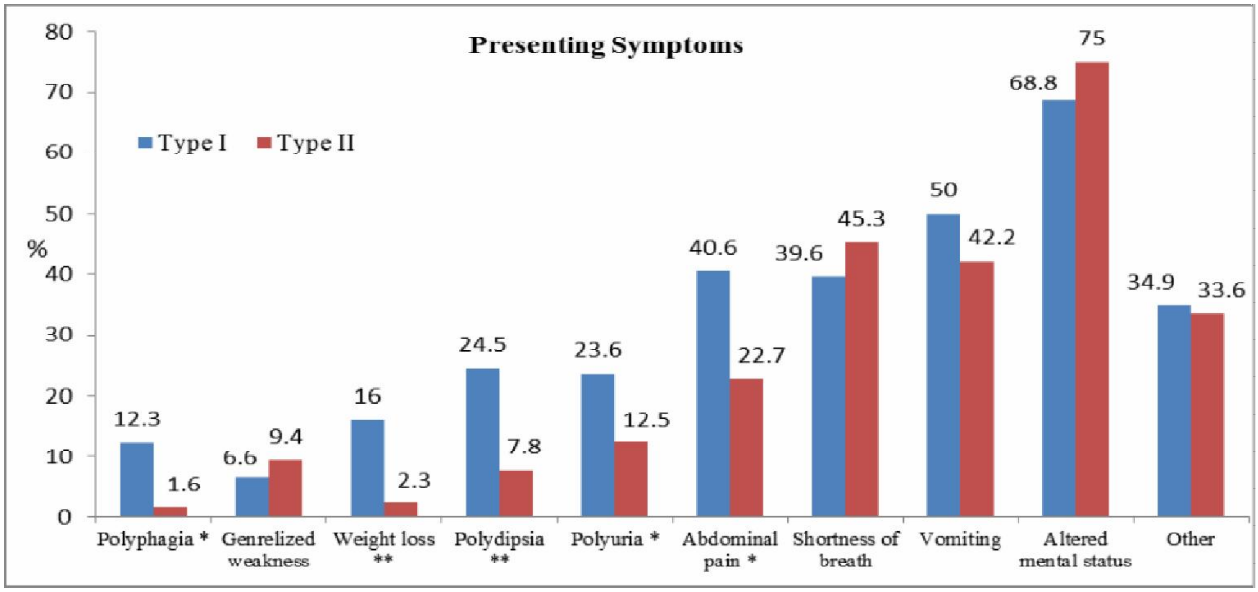

Figure-1: Presenting symptoms of type 1 and type 2 patients.

Other included Fits, cough, diarrhoea and nausea. Only moderate and severe altered mental status is presented.
*p<0.05, **p<0.0001

Table-1: Baseline characteristics of the study groups

	Newly diagnosed Type 1	Known type 1	Newly diagnosed Type 2	Known type 2
Number of patients	47	59	10	118
Age (years)	31.7±13.2	31.6±12.6	55.6±14.1	57.0±12.3
Sex				
Male	61.7 (29)	39 (23)	70 (7)	51.7(61)
Female	38.3(18)	61 (36)	30 (3)	48.3(57)
Duration of diabetes (years)	0.06±0.44	8.3±7.9	---	9.9±8.4
Less than a year	97.9 (46)	3.4 (2)	100 (10)	21.2 (25)
1-5 years	2.1 (1)	47.5 (28)	---	14.4 (17)
6-10 years	---	18.6 (11)	---	22 (26)
>10 years	---	30.5 (18)	---	42.4 (50)
BMI (kg/m²)	21.3±5.5	22.0±4.3	22.1±1.49	26.7±7.6
Previous episodes of DKA	0 (0)	23.7 (14)	0 (0)	3.4 (4)
Severity of DKA				
Mild	21.3 (10)	28.8 (17)	30 (3)	39.8 (47)
Moderate	53.2 (25)	59.3 (35)	60 (6)	52.5 (62)
Severe	25.5 (12)	11.9 (7)	10 (1)	7.6 (9)
Comorbidities	18.8 (9)	28.8(17)	50 (5)	68.6 (81)
Data presented as Mean±Sd and %(n)				

Table-2: Biochemical characteristics of subgroups of patients with DKA

	Newly diagnosed Type 1	Known type 1 diabetes	Newly diagnosed type 2	Known type 2 diabetes
Haemoglobin (gm/dl)	13.8±2.5	13.1±1.9	13.5±2.5	11.9±2.5
WBC Count (x10E9/L)	13.7±7.1	18±8.8	12.7±4.9	16.3±6.7
Platelet Count (x10E9/L)	256.3±121.9	339.6±143.8	231.6±104	306.8±145.3
BUN (mg/dl)	23.2±23.6	23.2±17.1	20.8±12.1	40.4±28.2
Creatinine (mg/dl)	1.7±2.2	1.6±1.4	1.6±0.5	2.3±1.9
Sodium (mmol/L)	133.4±9	132±7.8	134.2±6.7	130.9±8.8
Potassium (mmol/L)	4.1±1	4.8±1.2	4.5±0.8	4.9±1.1
Chloride (mmol/L)	99.3±10.8	97.4±10.4	98.9±6	96.5±9.5
Bicarbonate (mmol/L)	8.7±4.6	9.8±5.4	10.4±3.5	11.6±4.7
Arterial pH	7.2±0.2	7.2±0.1	7.2±0.1	7.2±0.1
PCO2 (mmHg)	22.6±9.4	20.6±7.3	28.6±12.3	25.3±9.3
PO2 (mmHg)	130.4±81.8	124.3±83	79.1±44.7	120.1±73.7
O2 Saturation (%)	92.6±12.6	92.2±15.5	80.3±27.1	92.4±11.7
Amylase	120.5±109.7	291.7±488.8	147.5±38.9	215.1±290.6
Lipase	155.6±175.2	155.4±282.5	84±22.6	208.2±502.3
Urinary Ketones	2.7±0.4	2.7±0.5	2.5±0.5	2.4±0.7
Random Blood Sugar	513.9±210.3	490.6±203.3	517.5±156.8	485.6±176.7
Serum osmolality (mosm/Kg)	304.4±31.6	303.6±24.5	310.7±29.5	303.5±28.4
Anion Gap	25.3±6.4	25.5±7.4	24.9±7.1	23.1±7.2
HBA1C %	12.3±3	11.9±2.8	12.8±2.3	10.7±2.7
Data presented as Mean±SD				

Table3: Mode of severity and outcome of DKA in type 1 and type 2 diabetes

Characteristic	Type 1(n=106)	Type 2 (n=128)	*p*-value	Total
Severity of DKA				
Mild	25.5(27)	39.1 (50)	0.017	32.9 (77)
Moderate	56.6(60)	53.1 (68)		54.7 (128)
Sever	17.9(19)	7.8(10)		12.4 (29)
Amount of Insulin (units per hour)	152.4±224.9	141.3±159.8	0.252	146.5±192.8
Length of stay (days)	5.92±8.8	5.92±5.3	0.106	5.92±7.08
Admission in ICU	24.5 (26)	30.5 (39)	0.313	27.8 (65)
Ventilator support	20.8 (22)	28.1 (36)	0.194	24.8 (58)
Precipitating factors				
Infection	20.8 (22)	49.2 (63)	<0.0001	36.3 (85)
Non-compliance	25.5 (27)	10.2 (13)		17.1 (40)
Myocardial Infarction	0.9 (1)	7.8 (10)		4.7 (11)
Stroke	0.9 (1)	3.1 (4)		2.1 (5)
Other	51.9 (55)	29.7 (38)		39.7 (93)
Mortality	5.7 (6)	12.5 (16)	0.013	9.4 (22)

DISCUSSION

As highlighted earlier the aim of this study was to determine the prevalence, mortality and morbidity associated with DKA. The finding of this study has revealed that all diabetic patients irrespective of type of diabetes are at risk of being hospitalized with DKA. This finding is supported by similar previous study as well.[8]

In our study, T1DM was predominantly higher among middle aged patients whereas T2DM was highly prevalent in older patients (mostly above fifty-five years of age). This finding is also supported by other studies.[8–10] Studies also reported that atypical diabetes with ketosis also widely exist worldwide.[10,11]

The average length of stay in our study was 6 days. Moreover, there was insignificant difference in length of stay of among patients with T1DM and T2DM. This finding was found higher when compared with a study conducted in USA but lower when compared with a study conducted in China.[8,12]

Overall mortality was found to be considerably higher in our cohort as compared to various studies conducted in different regions of the world.[8,9,13–15] In particular, mortality was predominantly higher in patients with T2DM. The higher mortality rate in T2DM may be due the reason that T2DM is highly prevalent in our region. Most of the patients with T2DM presented with multiple complications which is supported by the evidence that precipitating factors like infections, myocardial infection and stroke was significantly higher among patients with T2DM.

It is reported that DKA can be caused when patients forget or knowingly do not take diabetic medications or they may have developed a secondary condition such as infection, myocardial infarction, stroke, pancreatitis etc. which results in increased demand or insufficient levels of insulin in the body. It can also occur when diabetic patients take medications such as corticosteroids.[1,2] Several complications also occurred during the treatment of DKA.[3,16–21]

CONCLUSION

Majority of the patients had moderate to severe DKA at presentation. Mortality and morbidity related with DKA was found considerably higher among patients with T2DM while infection, myocardial infarction and stroke found as triggering factors in these patients.

AUTHORS' CONTRIBUTION

MO and AS conceived the study. AS and SF helped in data collection and data analysis. MO and SF were involved in drafting of manuscript. NUI and ZK were involved in critical revision of manuscript. All authors read and approved the final manuscript.

REFERENCES

1. Kamata Y, Takano K, Kishihara E, Watanabe M, Ichikawa R, Shichiri M. Distinct clinical characteristics and therapeutic modalities for diabetic ketoacidosis in type 1 and type 2 diabetes mellitus. J Diabetes Complications 2017;31(2):468–72.
2. Huri HZ, Foong GT, Pendek R, Widodo RT. Different characteristics of diabetic ketoacidosis between type 1 and type 2 diabetes patients in Malaysia. Asian Biomed 2009;3(2):201–5.
3. Kitabchi AE, Hirsch IB, Emmett M. Diabetic ketoacidosis and hyperosmolar hyperglycemic state in adults: Treatment. [Internet]. Uptodate.com. 2016 [cited 2016 Aug 16]. Available from: http://www.uptodate.com/contents/diabetic-ketoacidosis-and-hyperosmolar-hyperglycemic-state-in-adults-treatment
4. Newton CA, Raskin P. Diabetic Ketoacidosis in Type 1 and Type 2 Diabetes Mellitus Clinical and Biochemical Differences. Arch Intern Med 2004;164(17):1925–31.
5. Yamada K, Nonaka K. Diabetic Ketoacidosis in Young Obese Japanese Men. Diabetes Care 1996;19(6):671.
6. Maldonado M, Hampe CS, Gaur LK, D'Amico S, Iyer D, Hammerle LP, *et al*. Ketosis-Prone Diabetes: Dissection of a Heterogeneous Syndrome Using an Immunogenetic and β-Cell Functional Classification, Prospective Analysis, and Clinical Outcomes. J Clin Endocrinol Metab 2003;88(11):5090–8.

7. Balasubramanyum A, Zern JW, Hyman DJ, Pavlik V. New profiles of diabetic ketoacidosis type 1 vs type 2 diabetes and the effect of ethnicity. Arch Int Med 1999;159(19):2317–22.
8. Xu Y, Bai J, Wang G, Zhong S, Su X, Huang Z, *et al*. Clinical profile of diabetic ketoacidosis in tertiary hospitals in China: a multicentre, clinic-based study. Diabet Med 2015;33(2):261–8.
9. Henriksen OM, Roder ME, Prahl JB, Svendsen OL. Diabetic ketoacidosis in Denmark. Incidence and mortality estimated from public health registries. Diabetes Res Clin Pract 2007;76(1):51–6.
10. Tan H, Zhou Y, Yu Y. Characteristics of diabetic ketoacidosis in Chinese adults and adolescents – a teaching hospital-based analysis. Diabetes Res Clin Pract 2012;97(2):306–12.
11. Smiley D, Chandra P, Umpierrez GE. Update on diagnosis, pathogenesis and management of ketosis-prone Type 2 diabetes mellitus. Diabetes Manag (Lond) 2011;1(6):589–600.
12. McGuire S. Centers for Disease Control and Prevention. 2013. Strategies to Prevent Obesity and Other Chronic Diseases: The CDC Guide to Strategies to Support Breastfeeding Mothers and Babies. Atlanta, GA: U.S. Department of Health and Human Services, 2013. Adv Nutr 2014;5(3):291–2.
13. Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN. Hyperglycemic crises in adult patients with diabetes. Diabetes Care 2009;32(7):1335–43.
14. Savage MW, Dhatariya KK, Kilvert A, Rayman G, Rees JA, Courtney CH, *et al*. Joint British Diabetes Societies guideline for the management of diabetic ketoacidosis. Diabet Med 2011;28(5):508–15.
15. Lin SF, Lin JD, Huang YY. Diabetic ketoacidosis: comparisons of patient characteristics, clinical presentations and outcomes today and 20 years ago. Chang Gung Med J 2005;28(1):24–30.
16. Jabbar A, Farooqui K, Habib A, Islam N, Haque N, Akhter J. Clinical characteristics and outcomes of diabetic ketoacidosis in Pakistani adults with Type 2 diabetes mellitus. Diabet Med 2004;21(8):920–3.
17. Qari F. Clinical Characteristics of Patients with Diabetic Ketoacidosis at the Intensive Care Unit of a University Hospital. Pak J Med Sci 2015;31(6):1463–6.
18. Barski L, Nevzorov R, Rabaev E, Jotkowitz A, Harman-Boehm I, Zektser M, *et al*. Diabetic ketoacidosis: clinical characteristics, precipitating factors and outcomes of care. Isr Med Assoc J 2012;14(5):299–303.
19. Kitabchi AE, Umpierrez GE, Murphy MB, Kreisberg RA. Hyperglycemic Crises in Adult Patients with Diabetes: A consensus statement from the American Diabetes Association. Diabetes Care 2006;29(12):2739–48.
20. Venkatesh B, Pilcher D, Prins J, Bellomo R, Morgan TJ, Bailey M. Incidence and outcome of adults with diabetic ketoacidosis admitted to ICUs in Australia and New Zealand. Critical Care 2015;19:451.
21. MacIsaac RJ, Lee LY, McNeil KJ, Tsalamandris C, Jerums G. Influence of age on the presentation and outcome of acidotic and hyperosmolar diabetic emergencies. Int Med J 2002;32(8):379–85.

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