SSRG International Journal of Medical Science
ISSN: 2393 – 9117 /doi:10.14445/23939117/IJMS-V8I2P101

Volume 8 Issue 2, 1-9, February 2021

Clinical Outcomes of Diabetic Ketoacidosis in Adult patients in Bahrain

Aysha Asif Sarwani[1*], Husain Taha Radhi[2*], Fatema Husain Mandeel[3*], Rawdha Al Fardan[4*], Mahmood Al Saeed[5*]

[1]*Internal Medicine Specialist, Department of Endocrinology, Salmaniya Medical Complex, Bahrain*
[2]*Consultant Endocrinologist, Chairperson Internal Medicine Department, Salmaniya Medical Complex, Bahrain.*
[3]*Internal Medicine Specialist, Salmaniya Medical Complex, Bahrain.*
[4]*Internal Medicine Specialist, Department of Endocrinology, Salmaniya Medical Complex, Bahrain.*
[5]*Department of Internal Medicine, Salmaniya Medical Complex, Bahrain.*

Abstract

Introduction:

Diabetic ketoacidosis (DKA) is among the most significant and regularly seen condition in hospitals among diabetic patients. It is on the top of the list of Endocrine emergencies, and many studies done in many countries and in different hospitals are focusing on the management and outcomes of the DKA.

Objective:

The aim of the study is to observe the causes, length of hospitalization, need for ICU care, the number of admissions, and general outcomes among 154 adult patients with diabetic ketoacidosis, either with type 1 or type 2 Diabetes Mellitus (DM), in a tertiary care hospital in Bahrain.

Methods:

The data was collected from the Endocrine unit in Salmaniya Medical Complex from diabetes patients who presented with Diabetic Ketoacidosis, including both type 1 or typed 2 diabetic patients. Furthermore, the data collected depends on the demographic variables, which were age, gender, type of DM, newly diagnosed or a known diabetic, clinical presentation, plus any precipitating factors if present, for example, infection or myocardial infarction. Laboratory data were used to identify the severity of DKA that depends on the pH and degree of acidosis.

Data includes the need for the use of antibiotics among these patients plus the mortality rate.

Results

A total of 224 admissions with recorded among DKA patients over a two-year period. A high admission rate was noted in type 1 Diabetes Mellitus patients (94%). Another observation was that the younger age group of patients (14 to 30 years) was more inclined towards developing DKA.

A comparison of the biochemical values between DM type 1, type 2, and the newly diagnosed was conducted. Anion gap was found to be low in newly diagnosed DM (26.03) in comparison to the other subgroups.

Antibiotic initiation was high in DM type 2 (66.7), and DM type 1 had the lowest hospital length of stay.

The mortality rate was reportedly 2.2% among all the DKA admissions.

Conclusion

The finding of our study highlighted an association between higher mortality and type 2 DM, with older age and multiple comorbidities.

The study demonstrates that mortality may be predicted by various clinical and biochemical parameters. Therefore, a global social system needed to predict mortality in DKA.

Abbreviations

DKA – Diabetic ketoacidosis

ICU – intensive care unit

DM – Diabetes mellitus

KCL – Potassium chloride

Keywords - *Diabetic ketoacidosis, Outcome, Diabetes Mellitus*

Introduction

DKA is a complex Endocrinological disease with blood glucose metabolism derangement. It is a long-standing disorder with long- and short-term complications [1].

DKA is characterized by massive hyperglycemia, acidosis, and ketosis. It is most commonly precipitated by non-compliance to insulin and infections, and as many as 33% of undiagnosed DM cases presented with DKA at the first instance [2,3]. The most common presenting features are nausea, vomiting, abdominal pain, fatigue, acetone breath, and Kussmaul breath pattern [4].

DKA can be successfully managed within 12-36 hours with the intensive treatment protocol, including early hydration therapy and intravenous insulin administration, with electrolyte replacement and treatment of any underlying precipitating factors. This is to be followed by careful monitoring to prevent the occurrence of iatrogenic complications, such as hypoglycemia, hypokalemia, and cerebral edema. Thus, the clinical outcome is largely dependent on the patient's response to initial medical interventions, with which the complications and mortality rate can be reduced effectively [5,6,7].

To address this, very limited literature reviews were conducted previously regarding DKA outcomes in Bahrain, and this study aims to assess the DKA outcomes in adult patients at Salmaniya Medical Complex, Bahrain.

Material and methods

- **Design:** The study design was a retrospective, descriptive study.

- **Setting**: It was conducted in the department of medicine at the largest tertiary care hospital in Manama, Bahrain. The study duration was January 2017 until December 2018. The study was approved by the Secondary health Care Research Committee, Salmaniya Medical Complex.

- **Eligibility and exclusion criteria:** The inclusion criteria comprised patients 14 years of age and above with diabetes mellitus or undiagnosed cases (first presentation) presenting with DKA. DKA was defined as a biochemical triad of hyperglycemia, acidemia, and ketonemia.

- **Data collection:** All patients were followed during their hospital stay to evaluate their clinical presentation, precipitating risk factors, clinical and laboratory parameters, length of hospital stay, ICU admission, mortality rate, and their outcome.

- **Statistical methods used in the analysis:** Data were processed through and analyzed using IBM SPSS 25 and R studio 1.1.4. The descriptive statistics were performed to all categorical variables using the Chi-square test for independence and ANOVA test. P-value < 0.05 was taken as significant.

Results

Our study sample consisted of 224 admissions with DKA during a two-year period between 2017 – 2018. There were multiple admissions in the same patients as well, and the total number of patients included in the study was 154. This was after excluding the patients with missing data.

One of the clinical outcomes observed was a high readmission rate (Table 1). Many patients were readmitted over the two-year period as much as up to 8 times. The high readmission rate was especially noticed in type 1 DM patients. All in all, 33 patients contributed to readmissions, and 94% were contributed by those with type 1 DM, a statistically significant difference from the other groups (93.5% vs. 0%, 6.5%) as confirmed with the Chi-square test (X^2=6.3, df=1, p=0.011).

The patients were divided into three subgroups for comparison of outcomes, those being patients with newly diagnosed DM with DKA, type 1 DM patients, and type 2 DM patients.

While assessing the effect of demographical variables on clinical outcomes, no gender inequality was observed. Both genders showed a statistically similar incidence of development of DKA. Patients of various nationalities were present in the study group, and again this had no significant impact on the occurrence of DKA.

However, it was noticed that the younger age group of patients was more inclined towards developing DKA, precisely the age group 14 to 30 years (Table 2).

It was seen that after the resolution of DKA, the most common regimen that the patient was discharged on was insulin treatment (87.5%) (Table 3).

No relationship of statistical significance was seen between the patient's hematological profile except for a lower hemoglobin level in type 2 DM patients as compared to newly diagnosed and type 1 DM patients (12.5 vs. 14.4 and 13 respectively) (Table 4).

The patient's electrolyte profile demonstrated reduced sodium and chloride levels in type 2 DM patients. In contrast, the potassium levels were found to be low in newly diagnosed DM patients compared to the other two subgroups (Table 4).

Noticeably increased levels of blood urea were seen (11.4 vs. 6.7 and 7.3) in type 2 DM patients upon admission compared to other subgroups. Despite variations in the serum creatinine levels, no statistically significant difference was seen (Table 4).

We compared the level of severity of DKA by comparing the pH, HCO3, ketone levels, and calculated anion gap. We divided the patients into those with mild, moderate, and severe DKA (Table 5, Figure 1). No significant difference was seen between the subgroups while assessing the severity of acidosis. However, the anion gap was found to be lower in newly diagnosed DM patients in comparison to type 1 and 2 DM patients 2 (26.03 vs. 29.02 and 29.38), respectively (Table 5, Figure 1).

Another clinical outcome that was observed was the initiation of antibiotics in type 2 DM more than the other subgroups (66.7% vs. 30.6% and 40.6%) (Table 6, Figure 2).

Type 1 DM group had a significantly lower hospital length of stay (Table 7, Figure 3).

In terms of ICU admission, there was no significant difference among the three groups in the rate or length of stay (Table 7, Figure 4). The mean ICU length of stay was the least in type 1 DM patients as compared to other groups (2.7 vs. 5.3 and 5.0 days) (Table 7. Figure 5).

Mortality was reported in 2.2% of the DKA admissions. Mainly the type 2 DM patients subgroup had the higher rate (6.7%) compared to type 1 DM patients (0.7%) (Table 7, Figure 6).

Discussion

Diabetic ketoacidosis (DKA) is most commonly present and causes complications among diabetic patients. Although it is a life-threatening metabolic condition, especially among the elderly and those with multiple comorbidities, its diagnosis is made by the presence of uncontrolled hyperglycemia (blood glucose >250 mg/dL), metabolic acidosis (pH <7.3), and ketosis (increase ketone level in the body). DKA is either classified as mild, moderate, or severe according to ADA guidelines [8].

Classic symptoms of DKA are polyuria, polydipsia, abdominal pain, nausea, and vomiting, which were the most common presenting complaints in most cases of this study cohort.

The primary goals in the treatment of these patients include dehydration treatment with isotonic saline to expand the extracellular volume, but it also depends on the sodium concentration if its less than 135 mEq/L, isotonic saline should be continued at a rate of approximately 250 to 500 mL/hour and if it's normal or elevated, the IV fluid is generally switched to one-half isotonic saline at a rate of 250 to 500 mL/hour. The next step is potassium replacement is initiated immediately if the serum potassium is <5.3 mEq/L as long as there is adequate urine output (approximately >50 mL/hour), and replacement depends on the initial potassium level. If the initial serum potassium is below 3.3 mEq/L, IV potassium chloride (KCl; 20 to 40 mEq/hour, which usually requires 20 to 40 mEq/L added to saline) should be given, patients with marked hypokalemia require aggressive potassium replacement (40 mEq/hour plus the extra blouses needed to raise the serum potassium concentration above 3.3 mEq/L). If the initial serum potassium is between 3.3 and 5.3 mEq/L, IV KCl (20 to 30 mEq) is added to each liter of IV replacement fluid to maintain a level between 4 to 5 mEq/L [9,10,11]. But If the initial serum potassium concentration is greater than 5.3 mEq/L, then potassium replacement should be delayed until it falls subsequently to insulin infusion therapy [12].

The next step is the starting intravenous regular insulin, after being certain that the potassium is normal with the rate of (0.1 units/kg body weight) followed by an infusion of 0.1 units/kg per hour until the serum glucose was less than 250 mg/dL (13.9 mmol/L). The insulin dose is then decreased to 0.05 to 0.1 units/kg per hour until resolution of the ketoacidosis [9]. Bicarbonate therapy is needed only when arterial pH ≤6.9 [10]. Finally, effective treatment of any other underlying factors should be sought [12].

The most common precipitating factors found in our study were infections and poor compliance, including skipped/missed doses or taking less than the therapeutic dose by the patients. DKA precipitated by non-compliance was demonstrated to have the highest economic burden in the study [4,9].

Our study also demonstrated that the number of patients with severe DKA requiring ICU care equaled 9.1%, and among all patients who are newly diagnosed with diabetes with DKA have longer hospital stays than previously known diabetics. Plus, severe DKA was occurring more frequently than moderate and mild forms.

There are many studies done in many centers worldwide discussing one of the most common emergency conditions among diabetic adults and pediatrics, and we will present and compare some of them. Most of them agreed on the same net result regarding the cause of the DKA, hospitalization period, and general outcome, whether it is pure DKA or associated with other conditions.

First study: Outcome of Patients with Diabetic Ketoacidosis in South of Iran. The outcome showed that the mortality of DKA in Nemaazi hospital in the south of Iran is more than those reported from countries such as the USA and Sweden (developed countries) [13].

Second study: Diabetic Ketoacidosis: Demographic Data, Clinical Profile and Outcome in a Tertiary Care Hospital, among children with diabetes type 1, the conclusion was that all patients had a good prognosis and no deaths were reported. Awareness of diabetes symptoms, particularly in girls, needs more attention [14].

Third study: Precipitating Risk Factors, Clinical Presentation, and Outcome of Diabetic Ketoacidosis in Patients with Type 1 Diabetes, the conclusion of the study was that the outcome of DKA depends on the protocol and management during the first 24 hours [15].

Fourth study: Treatment Outcome of Diabetic Ketoacidosis Among Patients Attending General Hospital in North-West Ethiopia: Hospital-Based Study. The net result was that the mean length of hospital stay was around five days. About

twenty percent of patients had long hospital stays. Nearly ninety-five percent of patients improved and were discharged. The presence of infection is the main cause of hospital longer stays [16].

Fifth study: Clinical characteristics and outcomes of care in adult patients with diabetic ketoacidosis: A retrospective study from a tertiary diabetes center in Thailand. The outcome demonstrated median length of stay was 3 days, and 76.3% of patients were discharged within 5 days after admission. No deaths due to complications from DKA management were found [17].

Limitation of study

A limitation of our study is the limited time period of the study, the study itself being restricted to one hospital and not generalized to other hospitals in Bahrain. Further studies are needed to better understand the clinical outcome and mentality of DKA.

Conclusion

DKA is not an infrequent endocrinological emergency. The finding of our study highlight that young patients aged 14 – 30 years are more vulnerable to develop DKA. A lower anion gap was found in newly diagnosed DM patients. DM type 1 patients had a high readmission rate and lowest hospital length of stay compared to other subgroups. The majority of DKA patients showed clinical improvement and were discharged with a very low mortality rate (2.2%). In addition, the study demonstrated an association between higher mortality and type 2 DM, with older age and multiple comorbidities. Studies from different countries quoted different clinical and biochemical variables as mortality predictors.

Therefore, we recommend the development of the global scoring system to predict mortality in DKA.

Acknowledgment

We would like to thank Mr. Ridha Al – Hammam for his valuable contribution in this study.

Disclaimer

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References:

[1] Umpierrez G, Korytkowski M. Diabetic emergencies — ketoacidosis, hyperglycaemic hyperosmolar state, and hypoglycemia. Nature Reviews Endocrinology. 12(4)(2016) 222-232. doi:10.1038/nrendo.2016.15

[2] 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. 29(12)(2006) 2739-2748. doi:10.2337/dc06-9916

[3] Shaltout AA, Channanath AM, Thanaraj TA, et al. Ketoacidosis at first presentation of type 1 diabetes mellitus among children: a study from Kuwait. Scientific Reports. 6(1) (2016) doi:10.1038/srep27519

[4] Gosmanov AR, Gosmanova EO, Kitabchi AE. Hyperglycemic Crises: Diabetic Ketoacidosis (DKA), And Hyperglycemic Hyperosmolar State (HHS). In: Feingold KR, Anawalt B, Boyce A, et al., eds. End text. South Dartmouth (MA): MDText.com, Inc.; 17 (2018).

[5] Hifumi T, Kiriu N, Kato H, Inoue J, Koido Y. Survival after prolonged resuscitation from cardiac arrest due to diabetic ketoacidosis using extracorporeal life support. Am J Emerg Med. 31(5) (2013) 892.e1-2. doi: 10.1016/j.ajem.2012.12.041. Epub 2013 Mar 1. PMID: 23453834.

[6] Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN. Hyperglycemic Crises in Adult Patients With Diabetes. Diabetes Care. 32(7)(2009) 1335-1343. doi:10.2337/dc09-9032

[7] Alotaibi A, Aldoukhi A, Albdah B, Alonazi JA, Alseraya AS, Alrasheed N. Diabetic Ketoacidosis Treatment Outcome and Associated Factors Among Adult Patients Admitted to the Emergency Department and Medical Wards at King Abdulaziz Medical City, Riyadh, Saudi Arabia. Cureus. (2020). doi:10.7759/cureus.10067

[8] Kitabchi AE, Umpierrez GE, Murphy MB, et al. Management of hyperglycemic crises in patients with diabetes. Diabetes Care. 24(1)(2001) 131-153. doi:10.2337/diacare.24.1.131

[9] Barrett EJ, Defronzo RA. Diabetic Ketoacidosis: Diagnosis and Treatment. Hospital Practice. 19(4)(1984) 89-104. doi:10.1080/21548331.1984.11702796

[10] DeFronzo RA, Matsuda M. Diabetic ketoacidosis. A combined metabolic-nephrologic approach to therapy. Diabetes Reviews. 1994 Jan 1;2(2):209-238

[11] Maldonado MR, Chong ER, Oehl MA, Balasubramanyam A. Economic impact of diabetic ketoacidosis in a multiethnic indigent population: analysis of costs based on the precipitating cause. Diabetes Care. 26(4)(2003) 1265-1269. doi:10.2337/diacare.26.4.1265

[12] Maletkovic J, Drexler A. Diabetic ketoacidosis and hyperglycemic hyperosmolar state. Endocrinol Metab Clin North Am. 42(4)(2013) 677-695. doi:10.1016/j.ecl.2013.07.001

[13] Ilkhanipour H. Outcome of Patients with Diabetic Ketoacidosis in South of Iran. Journal of Endocrinology and Diabetes. 4(2)(2017) 1-6. doi:10.15226/2374-6890/4/2/00177.

[14] Razavi Z, Hamidi F. Diabetic Ketoacidosis: Demographic Data, Clinical Profile and Outcome in a Tertiary Care Hospital, Iran J Pediatr. 27(3)(2017) e7649. doi: 10.5812/ijp.7649.

[15] Ahuja W, Kumar N, Kumar S, Rizwan A. Precipitating Risk Factors, Clinical Presentation, and Outcome of Diabetic Ketoacidosis in Patients with Type 1 Diabetes. Cureus. 11(5)(2019) e4789. Published 2019 May 31. doi:10.7759/cureus.4789

[16] Abegaz TM, Mekonnen GA, Gebreyohannes EA, Gelaye KA. Treatment Outcome of Diabetic Ketoacidosis Among Patients Attending General Hospital in North-West Ethiopia: Hospital-Based Study. 2018. doi:10.1101/441964

[17] Thewjitcharoen Y, Plianpan P, Chotjirat A, et al. Clinical characteristics and outcomes of care in adult patients with diabetic ketoacidosis: A retrospective study from a tertiary diabetes center in Thailand. J Clin Transl Endocrinol. 2019;16:100188. Published 2019 Apr 10. doi:10.1016/j.jcte.2019.100188

	Number of patients with readmissions	
DM type	**N**	**%**
New	**0**	**0%**
Type 1	**29**	**93.5%**
Type 2	**2**	**6.5%**
p-value	***0.011***	

Table 1: Readmission rate according to DM type.

Variable	**Categories**	**New**	**Type 1**	**Type 2**	**Total**
Age group					
	14 - 30	**17(14.4%)**	**100(84.7%)**	**1(0.8%)**	**118(52.7%)**
	31 - 45	**12(16.9%)**	**41(57.7%)**	**18(25.4%)**	**71(31.7%)**
	46 - 60	**3(12%)**	**6(24%)**	**16(64%)**	**25(11.2%)**
	61 - 75	**0%**	**0%**	**9(100%)**	**9(4.0%)**
	76 and more	**0%**	**0%**	**1(100%)**	**1(0.4%)**
p-value		**< 0.0001**	**< 0.0001**	**< 0.0001**	

Table 2: Age groups of patients with DKA according to newly diagnosed, type 1 DM and type 2 DM.

	Insulin	**Insulin + OHA**	**OHA**
New	**22(75.8%)**	**6(20.7%)**	**1(3.4%)**
Type 1	**136(100%)**	**0**	**0**
Type 2	**24(55.8%)**	**17(39.5%)**	**2(4.7%)**
Total	**182(87.5%)**	**23(11.1%)**	**3(1.4%)**
P-value	**<0.0001**		

Table 3: Insulin was the most commonly prescribed medication to patients with DKA upon discharge.

Type of DM	**WBC Mean(±SD)**	**Hb Mean(±SD)**	**Platelets Mean(±SD)**	**Na+ Mean(±SD)**	**K+ Mean(±SD)**	**Cl- Mean(±SD)**	**Serum Urea Mean(±SD)**	**Serum Creatinine Mean(±SD)**
New	**11.2(±5.8)**	**14.4(±2.4)**	**316.6(±221.4)**	**132.9(±6.7)**	**4.3(±0.9)**	**99.6(±7.5)**	**6.5(±3.8)**	**75.5(±34.8)**
Type 1	**11.6(±5.5)**	**13.5(±1.8)**	**336(±98.7)**	**134.1(±4.6)**	**5.1(±0.7)**	**98.6(±5.8)**	**7.3(±4.6)**	**77.0(±73.9)**
Type 2	**11.8(±7.1)**	**12.5(±2.6)**	**307.8(±127.4)**	**131.6(±5.8)**	**5.1(±0.8)**	**96.0(±6.6)**	**11.4(±9)**	**100.6(±85.3)**
Total	**11.5(±5.9)**	**13.4(±2.1)**	**327.5(±128.6)**	**133.4(±5.3)**	**5.0(±0.8)**	**98.2(±6.3)**	**8.0(±5.9)**	**81.6(±72.6)**
p-value	***0.931***	***<0.004***	***0.384***	**0.017**	**<0.0001**	**0.026**	***0.001***	***0.144***

Table 4: Comparison of the hematologic, serum electrolyte, and renal profile in all the subgroups presenting with DKA.

Type of DM	**pH Mean(±SD)**	**HCO3 Mean(±SD)**	**Anion gap Mean(±SD)**	**Serum Ketone Mean(±SD)**	**Urine Ketone Mean(±SD)**
New	7.17(±0.15)	11.6(±4.4)	26.03(±5.8)	2.8(±0.42)	2.9(±0.49)
Type 1	7.16(±0.14)	11.5(±4.4)	29.02(±6)	2.6(±0.62)	2.9(±0.44)
Type 2	7.14(±0.17)	11.2(±4.3)	29.38(±5.6)	2.7(±0.65)	2.5(±1)
Total	7.15(±0.14)	11.5(±4.4)	28.67(±5.9)	2.7(±0.60)	2.8(±0.64)
p-value	***0.771***	***0.903***	***0.024***	***0.201***	***0.004***

Table 5: DM type and their acid-base control profile on admission.

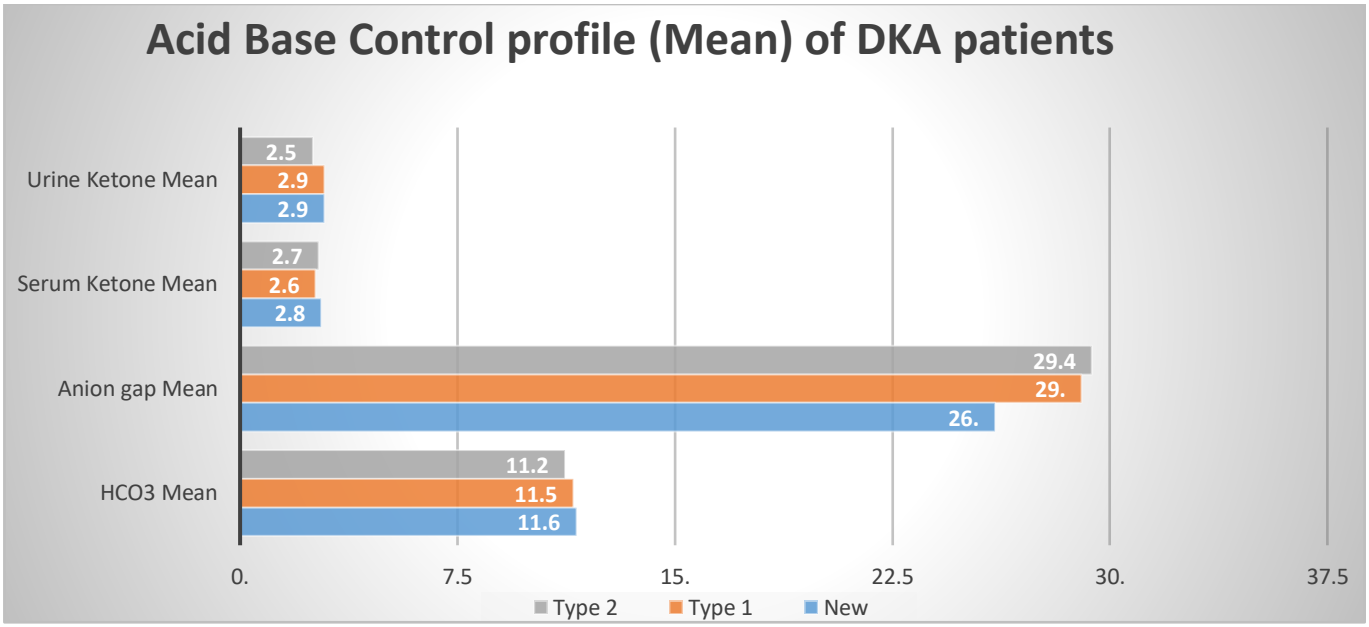

Figure 1: A bar graph representing DM type and their mean acid-base control profile on admission.

Type of DM	***Use of Antibiotics*** *n(%)*
New	13(40.6%)
Type 1	45(30.6%)
Type 2	30(66.7%)
Total	88(39.3%)
p-value	***<0.0001***

Table 6: The usage of antibiotics in DKA patients.

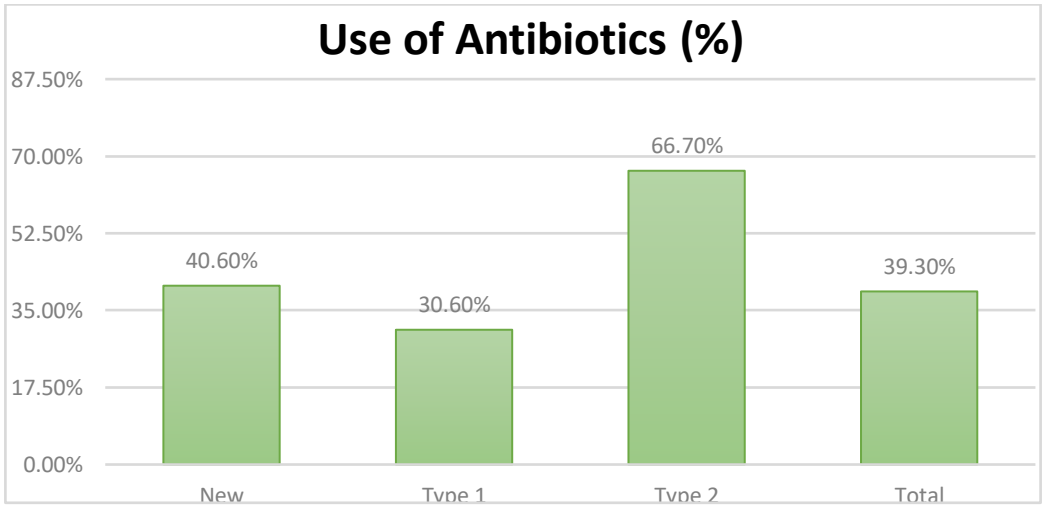

Figure 2: A bar graph representing the % of the usage of antibiotics in DKA patients.

Type of DM	**Hospital Length of stay Mean(±SD)**	**ICU admission n (%)**	***Length of stay in ICU** Mean(±SD)*	***Mortality n(%)***
New	5.3(±4.7)	5(15.6%)	5.4(±5.6)	1(3.1%)
Type 1	2.7(±1.4)	13(8.8%)	2.4(±0.96)	1(0.7%)
Type 2	5.0(±3.7)	4(8.9%)	3.7(±3.1)	3(6.7%)
Total	3.5(±2.9)	22(9.8%)	3.3(±3.1)	5(2.2%)
p-value	***<0.0001***	***0.533***	***0.425***	0.055

Table 7: Mean hospital length of stay, ICU admission, mean length of ICU admission, and the mortality rate in patients with DKA.

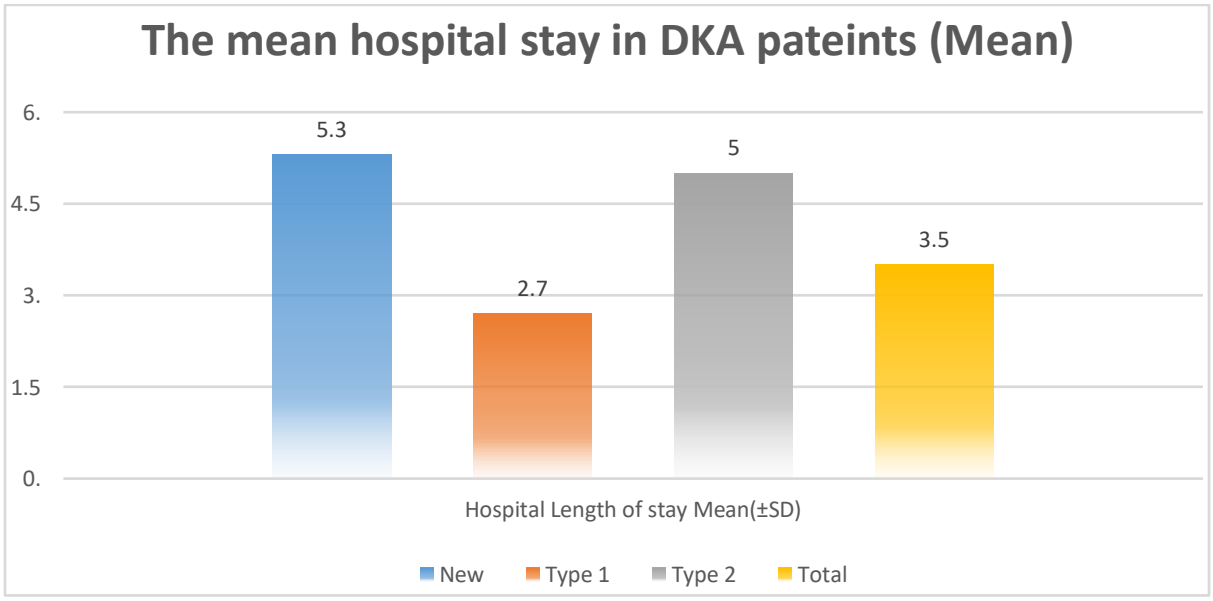

Figure 3: A bar graph representing DM type and the mean length of hospital stay.

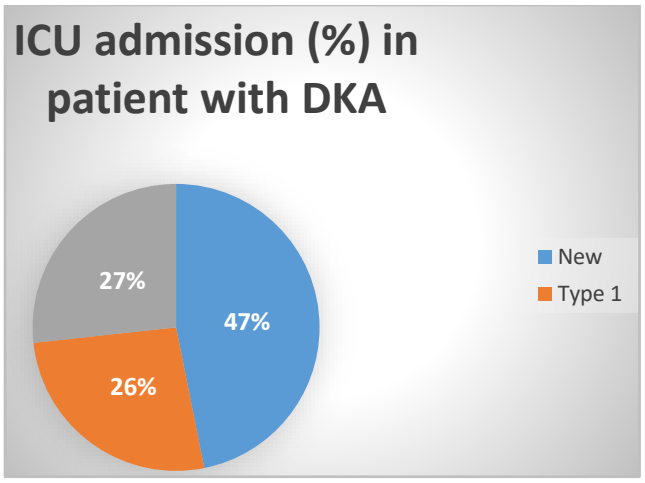

Figure 4: ICU admission rate (%) in patients with DKA.

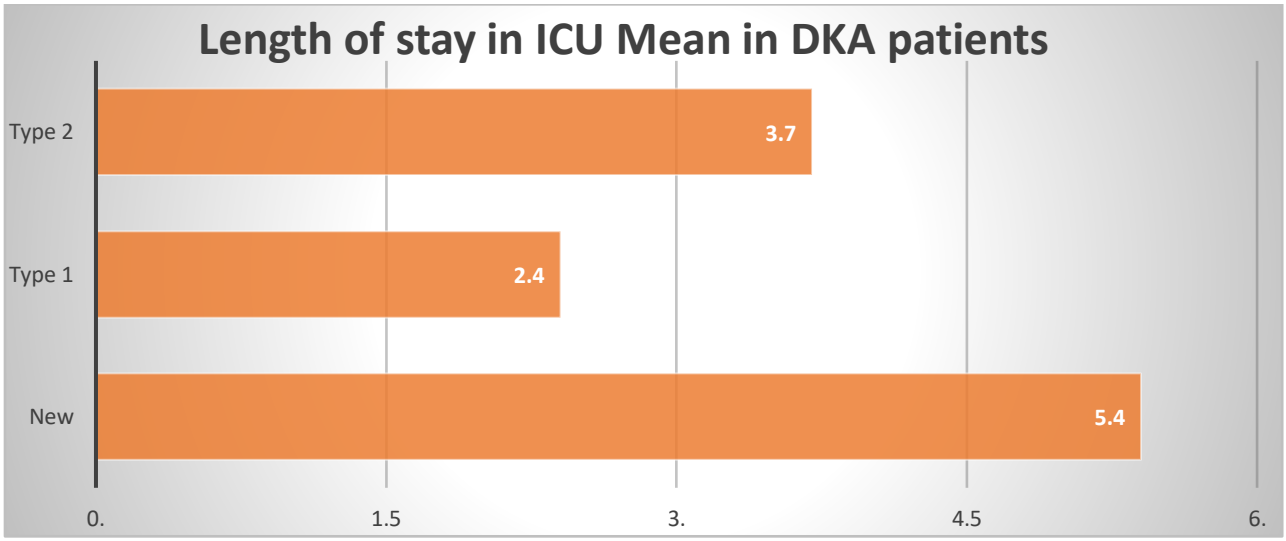

Figure 5: The mean length of ICU admission in DKA patients.

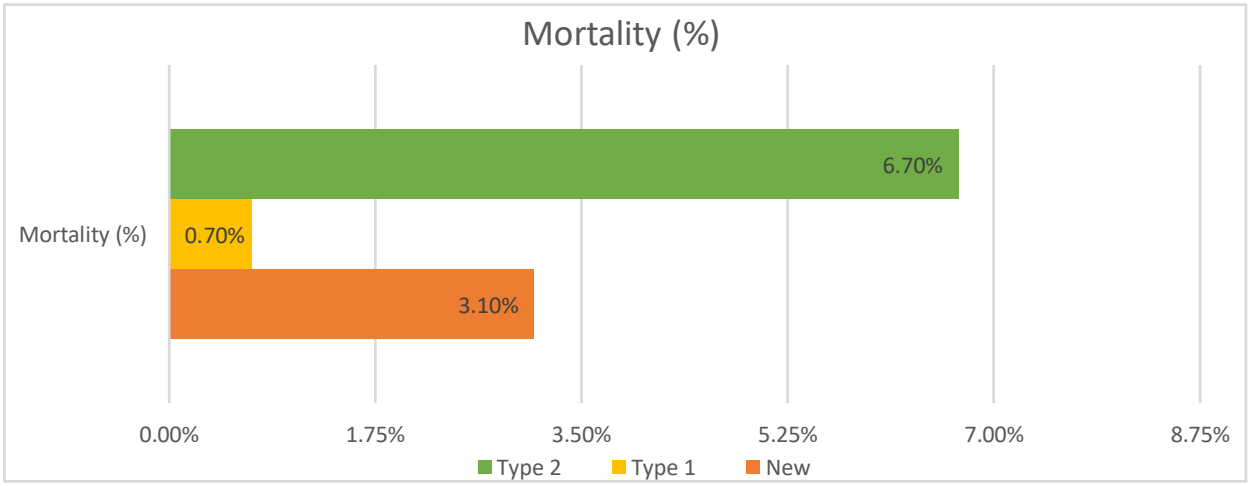

Figure 6: Mortality rates (%) in DKA patients.