

# Morbimortality Analysis of Diabetic Ketoacidosis in a Second Level Hospital in Mexico

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## ABSTRACT

Background: Diabetic ketoacidosis (DKA) is a very frequent entity that presents as an acute complication of diabetes mellitus, in which there is a state of hyperglycemia, metabolic acidosis and ketosis. Acute complications of diabetes represent a high percentage of admissions to the emergency department of second level hospitals in Mexico.

Methods: This is a retrospective, observational, comparative, cohort and descriptive study with documented analysis technique. We obtained information from a diary of records of the intensive care unit of our hospital and included all patients older than 14 years with a diagnosis of diabetic ketoacidosis. Patients younger than 14 years were excluded as well as hyperosmolar states.

Results: Of the 1725 patients admitted to the ICU only 134 had diabetic ketoacidosis; 91% of which were of metabolic origin; 3 patients had acute pancreatitis, and complications were equal to 0.7%, being acute renal injury, urosepsis, preeclampsia and pneumonia. The most frequent age group was between 20 and 30 years old, while mortality was 10%. The incidence of diabetic ketoacidosis was more frequent in the male sex in contrast with the study of Li *et al* who report a predominance in the female sex. In the age group we agree with Ramphul *et al*. who determine an average age of 18 to 44 years in the U.S. population. Therefore, we take into account that our casuistry in Mexico is partially similar and that the tendency of diabetic ketoacidosis has been greater in the male population, as well as an increased mortality.

Conclusions: In this study involving patients with diabetic ketoacidosis, the incidence and mortality tend to be increasing in our hospital and is that related to economic and sociocultural factors given the fact that our country and hospital of origin is in the means of development.

**Keywords:** Ketoacidosis, Diabetes, Incidence, Acute Complications, Mortality

## Background

Diabetic ketoacidosis, a very frequent entity that presents as an acute complication of diabetes mellitus, in which there is a state of hyperglycemia, metabolic acidosis and ketosis. It occurs commonly in patients diagnosed with type 1 diabetes mellitus and type 2 diabetes mellitus (Guerra *et al.*, 2019).

According to the ADA, diabetes mellitus is a metabolic disease that is characterized by a state of hyperglycemia secondary to inappropriate insulin secretion, insulin action, or both. The chronic state of hyperglycemia results in long-term damage, dysfunction, and failure of several organs and tissues like the eyes, blood vessels, nerves, kidneys, and heart (American Diabetes Association, 2004). Ketoacidosis is usually the debut of diabetes in almost half of children with DM 1 and approximately 20% of adults, being the leading cause of mortality in those patients with DM 1. Knowing the pathophysiology behind diabetes mellitus, insulin deficiency in ketoacidosis can be absolute as in DM 1 or relative as in DM 2 (Guerra *et al.*, 2019). There are different causes of an absolute insulin deficit, among them DM 1 or the lack of exogenous insulin application. The causes of a relative deficit of this hormone are an inadequate dose of exogenous insulin, infections, trauma, or stress that elevate counter-regulatory hormones. On the other hand, certain drugs such as corticosteroids, antipsychotics and immunosuppressants can cause hyperglycemia (Olivieri and Chasm, 2013). Insulin is the primary source of glucose regulation in the body. It increases peripheral glucose uptake as well as decreases gluconeogenesis. As serum insulin levels increase, counter-regulatory hormones play a reciprocal role in maintaining glucose homeostasis, including cortisol, glucagon, growth hormone and catecholamines that promote ketogenesis (Olivieri and Chasm, 2013). The activity of counter-regulatory hormones leads to catabolic alterations that collectively culminate in the two cardinal features of diabetic ketoacidosis, hyperglycemia and ketogenesis (Charfen and Fernández-Frackelton, 2005). Hyperglycemia leads to glycosuria, osmotic diuresis, and dehydration. As a result of osmotic diuresis, large amounts of sodium, chloride, and potassium are lost in the urine, resulting in dehydration and electrolyte abnormalities commonly seen in DKA (Charfen and Fernández-Frackelton, 2005). Insulin deficiency and increased counterregulatory hormones lead to the liberation of free fatty acids into blood circulation from adipose tissue and uncontrolled oxidation of free fatty acids to ketone bodies ( $\beta$ -hydroxybutyrate [ $\beta$ -OHB] and acetoacetate), with subsequent ketonemia and metabolic acidosis (American Diabetes Association, 2001). There are multiple precipitating factors of DKA, among the most frequent of which are the omission or inadequate dosing of insulin, as well as infections (Nyenwe and Kitabchi, 2016). Other causes include stroke, myocardial infarction, pancreatitis, trauma and drugs that alter carbohydrate metabolism such, thiazide diuretics, sympathomimetic agents or corticosteroids (Nyenwe and Kitabchi, 2016). The clinical picture includes, polydipsia, polyuria polyphagia, vomiting, abdominal pain, weight loss dehydration, weakness and eventually coma. Physical findings may involve Kussmaul respirations, tachycardia, hypotension, poor skin turgor, altered mental status, shock, lastly ultimately coma (American Diabetes Association, 2001). According to the ADA, management aim should be resolution of hyperglycemia, ketosis, and correction of electrolyte imbalance along with the restoration of circulatory volume and tissue perfusion (American Diabetes Association, 2019). Another frequent and the most severe complication of diabetes mellitus with an estimated mortality of 20% is hyperosmolar

hyperglycemic state, which is characterized by elevation of serum glucose greater than 600 mg/dl, an effective plasma osmolarity greater than 320 mOsm/kg in the absence of ketoacidosis (Pasquel and Umpierrez, 2014).

According to the CDC, the prevalence of diabetes has increased over the past 10 years, both in Texas as well as nationally. It further refers that, in 2017, an estimated 2,323,220 people in Texas had diabetes, which represented 11.4 % of the adult population (Johnson *et al.*, 2019). In 2021 in a study by Lin Li, *et al.* (2021) on the incidence of diabetic ketoacidosis in patients with DM 1 in the United States, the incidence was determined to be 55.5 per 1000 person/years, as well as higher frequency in women and children. In another study conducted in 2017, with a total population of 220,340 patients with a primary diagnosis of DKA (61.6 cases of DKA per 10,000 admissions), the incidence of DKA per 10,000 hospital admissions were higher in males (71.2) than females (54.1). Of all patients with, 53.3% were aged 18 to 44 years. However, a higher incidence per 10,000 admissions was observed in patients aged 1 to 17 years (Ramphul and Joynauth, 2020). A total of 835 deaths were found among patients with DKA, with a mortality rate of 0.38%. The overall mortality rate was higher among males than females admitted with DKA, (40.5 deaths per 10,000 DKA cases) and (35.3 deaths per 10,000 DKA cases) respectively. In addition to an average length of stay of 3.22 days (Ramphul and Joynauth, 2020). Comparing the two previously mentioned studies, the incidence rose from 32.04 in 2003 to 61.6 in 2017 (Ramphul and Joynauth, 2020). In contrast with Mexico, according to ENSANUT in 2018, 10.3 % of the population, 8,542,718 people, reported having diabetes mellitus, being more frequent in women than in men. Several studies mention that among the causes of the increase in the incidence of hospitalizations for diabetes complications in the USA are the increase in the prevalence of diabetes, as well as economic and socio-cultural factors that limit access to medical care and treatment (Karslioglu *et al.*, 2019). Another study mentions that the average cost of managing DKA is \$17,500 dollars per patient, which represents an annual hospital cost of \$2.4 billion dollars (Umpierrez and Korytkowski, 2016). In Mexico, acute complications of diabetes represent approximately 20-30% of adult patients hospitalized in the emergency departments of second level hospitals, which demonstrates an important and above all preventable economic expense (Domínguez Ruiz *et al.*, 2013). Given this, we ought on comparing the incidence of local DKA in a second level hospital in Mexico and correlating it with national and international ones. For the above mentioned, the general objective of this study is to determine how many patients were admitted to the ICU from 2013 to 2021 with a diagnosis of diabetic ketoacidosis and what the outcome was. Specific objectives: To know the predominant gender of DKA; To know the mortality casuistry in our second level hospital in Mexico; To determine how many patients will end with ventilatory support management; To compare the incidence of local DKA and correlate it with the national and international ones. To deduce that diabetic ketoacidosis is preponderantly high in

morbidity and mortality in our hospital and that there is statistical probability with the states of the northern part of Mexico and the southern part of the USA, especially the state of Texas.

## Methods

This is a retrospective, observational, comparative, cohort, and descriptive study with documented analysis technique. We obtained information from a diary of records of the intensive care unit of our hospital and included all patients older than 14 years with a diagnosis of diabetic ketoacidosis. Patients younger than 14 years were excluded as well as hyperosmolar states.

## Results

From November 2013 to December 2021 with a total of 1725 patients admitted to the ICU, only 134 patients met the diagnosis of diabetic ketoacidosis (Table 1). The results obtained show that the lowest number of patients admitted with a diagnosis of diabetic ketoacidosis was in 2013 with 4 patients and the maximum peak was in 2021 with 35 patients (Fig. 1). Likewise, the predominance of gender was male giving a subtotal of 75 patients out of 134 studied, taking a valid percentage of 56% (Table 1). We found that diabetic ketoacidosis was only metabolic; with a total of 123 cases, representing 91%; and associated with other non-specific damage was 3%, and finally only 3 patients presented acute pancreatitis. Although pneumonia, renal lesions, urosepsis and acute obstetric complications were also seen (Table 2). Among the reasons for discharge, clinical improvement was almost 86%, while more than 10% were discharges due to death (Table 3). In addition, the average hospital stay was almost 3 days, and the most frequent age group was between 20 and 30 years of age, followed by the group between 31 and 40 years of age, which together represent 60%. Finally, almost 20% of the patients studied were subjected to the use of ventilatory support, as well as the use of barbiturate coma induction (Table 5).

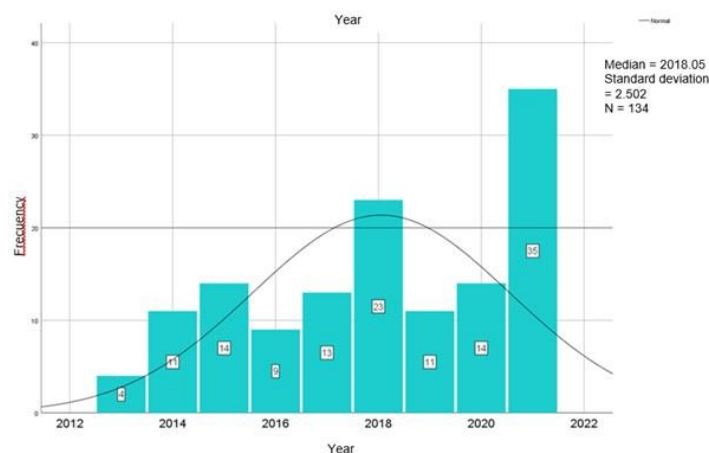


Figure 1: Year Studied.

**Table 1:** Gender.

		Frequency	Percentage	Valid percentage	Accumulated percentage
<b>Valid</b>	Males	75	56.0	56.0	56.0
	Females	59	44.0	44.0	100.0
	Total	134	100.0	100.0	

**Table 2:** Diagnostics.

		Frequency	Percentage	Valid percentage	Accumulated percentage
<b>Valid</b>	Diabetic Ketoacidosis (DKA)	123	91.8	91.8	91.8
	DKA + Acute Pancreatitis	3	2.2	2.2	94.0
	DKA + Pneumonia	1	.7	.7	94.8
	DKA + Acute Kidney Injury	1	.7	.7	95.5
	DKA + Preeclampsia	1	.7	.7	96.3
	DKA + Urosepsis	1	.7	.7	97.0
	DKA + Miscellaneous	4	3.0	3.0	100.0
	Total	134	100.0	100.0	

**Table 3:** Discharge Reasons.

		Frequency	Percentage	Valid percentage	Accumulated percentage
<b>Valid</b>	Death	14	10.4	10.4	10.4
	Referral to another center	4	3.0	3.0	13.4
	Clinical improvement	115	85.8	85.8	99.3
	Maximum Benefit discharge	1	.7	.7	100.0
	Total	134	100.0	100.0	

**Table 4:** One sample T- test (Test value = 95).

	t	gl	Sig. (bilateral)	Mean difference	95% confidence Interval	
					Lower	Upper
<b>Age</b>	45.344	133	.000	+21.940	+14.00	+65.00
<b>days</b>	16.064	133	.000	+12.366	-0.85	+23.89

**Table 5:** Mechanical Ventilation Use.

		Frequency	Percentage	Valid percentage	Accumulated percentage
<b>Valid</b>	YES	26	19.4	19.4	19.4
	NO	108	80.6	80.6	100.0
	Total	134	100.0	100.0	

## Conclusions

The present study shows that the tendency of diabetic ketoacidosis in our hospital is increasing as well as its mortality. The latter is due to the correlation with international statistics, as proposed by Hamdy *et al.* mortality in developing countries is 0.2-2% (Osama Hamdy, 2022). However, in our study it was determined that mortality tends to be higher, reaching approximately 10%; this could be explained by the fact that our hospital of origin is a second level in Mexico, which is a country in the

process of development. The DKA incidence was more frequent in the male sex in comparison with the study of Li, *et al.* (2021) in which a difference is appreciated and the tendency of them is greater in the female sex, but; we coincide in an average of approximately 3 to 4 days of hospital stay with ours. The most common age group was between 20 and 40 years, as reported by Ramphul *et al.* who also determined an average age of 18 to 44 years in the U.S. population. Ebenezer *et al.* report that its main complications have been the inadequate use of insulin, infections, cerebrovascular accidents, myocardial infarction, trauma, pancreatitis and drug use; in comparison with our study, we agree that the diabetic ketoacidosis studied is mainly manifested by abandonment or suboptimal doses of insulin therapy management; and we also found complications associated in 3 and 4 % of the cases with acute pancreatitis and miscellaneous. We consider that the tendency of DKA in male population can be explained as proposed by French *et al.* that the increase in prevalence is related to economic and sociocultural factors; and our casuistry predominates in a highly productive population, which due to the situations mentioned before limits access or early attention to complicated diabetes mellitus. It is very common that in second level hospitals in Mexico we have study limitations due to the absence of diagnostic elements and in this case we found limitations that allow us to cover comprehensively the answers in their entirety, such as the comparison with the incidence of the state of Texas and other southern states of the USA.

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