

ORIGINAL RESEARCH

PROFILE OF DIABETIC KETOACIDOSIS PATIENTS AT REGIONAL PUBLIC HOSPITAL DR. SOETOMO IN 2017

Profil Pasien Ketoasidosis Diabetikum di Rumah Sakit Umum Daerah Dr. Soetomo Tahun 2017

Desak Gde Ushadi Bulan Dewata¹, Hermina Novida², Aryati Aryati³

¹Faculty of Medicine, Universitas Airlangga, <u>bulandewata@gmail.com</u>

² Departement of Internal Medicine, Faculty of Medicine, Universitas Airlangga/ RSUD Dr. Soetomo, <u>herminanovida@ymail.com</u>

³ Departement of Clinical Pathology, Faculty of Medicine, Universitas Airlangga/ RSUD Dr. Soetomo, dr_aryati@yahoo.com

Correspondence Author: Desak Gde Ushadi Bulan Dewata, <u>bulandewata@gmail.com</u>, Faculty of Medicine, Universitas Airlangga, Jalan Prof. Dr. Moestopo 6-8, Surabaya City, East Java, 60286, Indonesia

ARTICLE INFO

Article History: Received June, 5th, 2020 Revised form August, 26th, 2020 Accepted September, 11th, 2020 Published online September, 20th, 2020

Keywords:

diabetic ketoacidosis; type 1 diabetes mellitus; type 2 diabetes mellitus; regional public hospital dr. soetomo

Kata Kunci:

ketoasidosis diabetikum; diabetes melitus tipe 1; diabetes melitus tipe 2; rumah sakit umum daerah dr. soetomo

ABSTRACT

Background: Diabetic ketoacidosis (DKA) is one of many lifethreatening complications of diabetes mellitus (DM), which is characterized by severe hyperglycemia, metabolic acidosis and ketonemia. This complication can eventually lead to coma and death if not treated properly. Purpose: The aim of this study is to describe the profile of the DKA patients who were at Regional Public Hospital (RSUD) Dr. Soetomo in 2017. Methods: This study was a descriptive study that used the medical record data of DKA patients who were at RSUD Dr. Soetomo in 2017. The study's total sample size was 63 patients. The study's variables were gender, age, type of DM, severity of DKA, precipitating factors, main complaints, vital signs, random plasma glucose level, electrolyte level, and blood gas analysis. The frequency, mean, and standard deviation were analyzed. Results: Most of the 63 DKA patients were female (66.67%), aged from 50-59 years (38.10%). The DKA cases being handled by the Dr. Soetomo Hospital were overwhelmingly of type 2 DM patients (88.89%). More than half the patients (58.73%) experienced severe DKA. Altered states of consciousness (46.03%) and shortness of breath (26.98%) were the most common main complains made by the DKA patients. Almost all patients experienced infection (88.89%) as the precipitating factor; the most common infections were sepsis (92.86%), pneumonia (30.36%), and urinary tract infections (23.21%). Two thirds of the patients (66.67%) had a length of stay of 0-7 days. About 57.14% of the DKA patients died while undergoing treatment. Conclusion: The number of severe DKA patients and the mortality rate in our study were higher than in other studies. Females and the elderly were more prone to DKA, and the most common precipitating factor was infection.

©2020 Jurnal Berkala Epidemiologi. Published by Universitas Airlangga. This is an open access article under CC-BY-SA license (https://creativecommons.org/licenses/by-sa/4.0/) How to Cite: Dewata, D. G. U. B., Novida, H., & Aryati, A. (2020). The overview of dengue haemorrhagic fever cases and environmental factors in Sumenep District in 2018. *Jurnal Berkala Epidemiologi*, 8(3), 301–309. https://dx.doi.org/10.20473/jbe.v8i320 20. 301–309

ABSTRAK

Latar Belakang: Ketoasidosis Diabetikum (KAD) merupakan salah satu komplikasi Diabetes Melitus (DM) yang berbahaya, yang ditandai oleh hiperglikemia berat, asidosis metabolik dan ketonemia. Komplikasi ini dapat berakibat koma hingga kematian apabila tidak ditangani dengan baik. Tujuan: Penelitian ini bertujuan untuk mengetahui profil pasien KAD di RSUD Dr. Soetomo tahun 2017. Metode: Penelitian ini adalah penelitian deskriptif menggunakan data dari rekam medis pasien KAD di RSUD Dr. Soetomo tahun 2017. Total sampel pada penelitian ini adalah 63 pasien. Variabel yang diteliti adalah jenis kelamin, usia, tipe DM, derajat keparahan KAD, faktor pencetus, keluhan utama, tanda vital, kadar glukosa darah acak, kadar elektrolit, dan analisis gas darah. Kami menganalisis frekuensi, rata-rata, dan standar deviasi. Hasil: Mayoritas pasien berjenis kelamin perempuan (66,67%) dan berada pada kelompok usia 50-59 tahun (38,10%). Pasien DM Tipe 2 (88,89%) mendominasi jumlah kasus KAD di RSUD Dr. Soetomo. Lebih dari setengah total pasien (58,73%) menderita KAD derajat berat. Penurunan kesadaran (46,03%) dan sesak (26,98%) merupakan keluhan utama yang paling umum didapatkan pada pasien KAD. Hampir seluruh pasien memiliki faktor pencetus infeksi (88,89%) dengan jenis infeksi yang paling banyak dialami adalah Sepsis (92.86%), Pneumonia (30.36%), dan Infeksi Saluran Kemih (23.21%). Dua pertiga dari jumlah pasien (66,67%) dirawat dengan durasi 0-7 hari. Sebanyak 57,14% pasien KAD meninggal saat menjalani perawatan. Conclusion: Jumlah pasien KAD derajat berat dan kematian pada penelitian ini lebih tinggi dibanding penelitian lain. Perempuan dan usia lanjut lebih rentan terhadap KAD dengan infeksi sebagai faktor pencetus paling итит.

©2020 Jurnal Berkala Epidemiologi. Penerbit Universitas Airlangga. Jurnal ini dapat diakses secara terbuka dan memiliki lisensi CC-BY-SA (https://creativecommons.org/licenses/by-sa/4.0/)

INTRODUCTION

Diabetic ketoacidosis (DKA) is an acute metabolic disorder characterized by severe hyperglycemia, metabolic acidosis and ketonemia. DKA can affect patients with type 1 or type 2 diabetes mellitus (DM), in which the most common precipitating factors are infection and non-compliance insulin therapy. The underlying pathophysiologies are insulin deficiency, increased insulin counter-regulation hormones, and peripheral insulin resistance. These processes then manifest as the signs of DKA, such as dehydration, hyperglycemia, ketosis, and electrolyte imbalance. In recent years, the number of DKA cases has dramatically increased. In the United States, the number of patients hospitalized with DKA increased from 140,000 cases in 2009

to 168,000 cases in 2014 (Gosmanov, Gosmanova, & Kitabchi, 2000).

In Indonesia, DKA is still rarely studied. According to a study conducted in Jakarta, 60% of DKA patients who were treated in the emergency room of Cipto Mangunkusumo Hospital from 2007 to 2008 were women. About 58% of patients' precipitating factors were infection, and more than half (51%) of those were respiratory infections. Furthermore, the mortality rate of DKA patients with infection (57%) is higher than patients without infection (16%) (Suwarto, Sutrisna, Waspadji, & Pohan, 2014). However, until now, no studies have been conducted that specifically discuss DKA patients at Regional Public Hospital (RSUD) Dr. Soetomo, Surabaya.

DKA is extremely life-threatening because it can lead to diabetic coma and death; therefore, prompt and effective treatment must be encouraged. DM patients also need to maintain blood glucose levels within normal limits and remain aware of precipitating factors in order to prevent DKA. Therefore, this study aims to describe the profiles of DKA patients so such complications can be prevented and treated, and patients can be educated about them.

METHODS

This was a descriptive study undertaken to describe the profiles of DKA patients on the internal medicine ward of Dr. Soetomo Hospital from January 1 to December 31, 2017. We reviewed every medical record of patients with ICD 10-code acidosis and diabetic coma (because these codes include DKA). The total population was 316 patients (11 type 1 DM and 305 type 2 DM patients). The inclusion criterion was patient diagnosis with DKA; there were no exclusion criteria. We also considered patients with a random plasma glucose level >250 mg/dL, HCO3- \leq 18 mmol/L, and urine ketone-positive as having DKA. The total sampling technique was used, vielding 63 patients (seven patients with type 1 DM and 56 patients with type 2 DM) as the sample of this study. Many patients were excluded due to their medical records, whose ICD 10 codes falsely indicated DKA.

The variables for our study were gender, age, type of DM, severity of DKA, precipitating factors, main complaints, vital signs (i.e., blood pressure, heart rate, respiratory rate, temperature), random plasma glucose level, electrolyte level (sodium, potassium, chloride), and blood gas analysis (arterial pH, pCO2, pO2, HCO3-, anion gap). Data regarding all variables were obtained from medical records. We used the results of laboratory tests and vital sign examinations on the first day of admission. Table 1 outlines the classification of DKA by Gosmanov & Kitabchi

Table 1

```
Classification of DKA
```

(2000) and is divided into mild, moderate, and severe DKA.

The anion gap is calculated by converting the levels of sodium, chloride, and bicarbonate into units of mEq/L and then calculating using the formula:

Anion
$$gap = (Na^{+}) - [(Cl^{-}) + (HCO_{3}^{-})]$$

We analyzed the data using Microsoft Excel 2010. The data from all the variables were then expressed as a number and a frequency (%). The data from the random plasma glucose levels, electrolyte levels, and blood gas analysis were also expressed as mean \pm standard deviation (SD). This study was declared as ethical and was approved by the Ethical Committee of Health Research at RSUD Dr. Soetomo, certificate number 0555/KEPK/VIII/2018.

RESULTS

A total of 2,073 type 1 and type 2 DM patients were treated at Dr. Soetomo Hospital. Out of these, 63 admissions were diagnosed with DKA, thus meeting the inclusion criteria. Most of the DKA patients were female (66.67%), predominately aged 50–59 years (38.10%). Their demographic characteristics can be seen in Table 2.

Patients predominantly had type 2 DM (88.89%) with severe DKA (58.73%). Infection was the most common precipitating factor in the DKA patients (88.89%). When elaborated, the most common types of infections were sepsis (92.86%), pneumonia (30.36%), and urinary tract infections (23.21%). Patients' main complaints were altered states of consciousness (46.03%) and shortness of breath (26.98%) The clinical characteristics can be seen in Table 3.

	Mild DKA	Moderate DKA	Severe DKA
Plasma Glucose	> 250 mg/dl	> 250 mg/dl	> 250 mg/dl
Arterial pH	7.25 - 7.30	7.00 - < 7.24	<7.00
Serum Bicarbonate (mEq/l)	15 - 18	10 - < 15	<10
Urine ketone*	+	+	+
Serum ketone <mark>*</mark>	+	+	+
Effective serum osmolality †	Variable	Variable	Variable
Anion gap ‡	>10	>12	>12
Mental status	Alert	Alert / drowsy	Stupor / coma

*Nitroprusside reaction method; †Effective serum osmolality: 2[measured Na+ (mEq/l)] + glucose (mg/dl)/18. ‡Anion gap: (Na+) – [(Cl- + HCO3- (mEq/l)].

Table 2	
Demographic Characteristics of DKA Patients	

Variable	n	%
Gender		
Female	42	66.67
Male	21	33.33
Age group (years)		
< 20	1	1.59
20-29	7	11.11
30-39	5	7.94
40-49	14	22.22
50-59	24	38.10
60-69	10	15.87
≥ 70	2	3.17
Mean \pm (SD)	49.51	± 13.88

The DKA patients' vital signs predominantly displayed normotension (66.67%), tachycardia (73.02%), increased respiratory rate (93.65%), and increased body temperature (44.44%). Patients predominantly had type 2 DM (88.89%) with severe DKA (58.73%). Infection was the most common precipitating factor in the DKA patients (88.89%). When elaborated, the most common types of infections were sepsis (92.86%), pneumonia (30.36%), and urinary tract infections (23.21%). Patients' main complaints were altered states of consciousness (46.03%) and shortness of breath (26.98%). The DKA patients' vital signs predominantly displayed normotension (66.67%), tachycardia (73.02%), increased respiratory rate (93.65%), and increased body temperature (44.44%) The clinical characteristics can be seen in Table 3.

About 61.91% of the patients had random plasma glucose levels of 250–600 mg/dL, but we also found that 3.17% of patients had random plasma glucose levels of less than 250 mg/dL. The patients' electrolyte examinations were dominated by hyponatremia (39.68%), normokalemia (42.86%), and hyperchloremia (47.62%). From blood gas analysis, we found that most patients had an arterial pH of more than 7.30 (50.79%), low PCO2 (92.06%), high PO2 (74.60%), bicarbonate of less than 10 mmol/L (58.73%), and an anion gap of more than 12 mEq/L (98.41%). The laboratory profile can be seen in Table 4.

The length of stay for the majority of the DKA patients (66.67%) was from 0–7 days (mean 6.6 \pm 5.25 days). More than half of the patients (57.14%) died while receiving treatment at Dr. Soetomo Hospital (see Figures 1 and 2).

Tabel 3	
Clinical Characteristics of DKA Patients	

	Jitts	
Variable	n	%
Type of DM		
Type 1 DM	7	11.00
Type 2 DM	56	89.00
Severity of DKA		
Mild DKA	10	15.87
Moderate DKA	16	25.40
Severe DKA	37	58.73
Precipitating Factor		
Infection	56	88.89
Non infection	1	1.59
Both	4	6.34
Unknown	2	3 17
Infection*	-	2.17
Sensis	52	92.86
Pneumonia	17	30.36
Uringry Tract Infection	13	23 21
Ulcor	0	16.07
Cangrana	5	8.03
	1	0.93
	4	7.14 5.26
Luig I D Others	2	5.50
Others M: C I: +	3	5.50
	20	16.02
Altered state of consciousness	29	46.03
Shortness of breath	1/	26.98
Nausea vomiting	5	7.94
Fever	5	7.94
Wound on foot	3	4.76
Lethargy	2	3.17
Abdominal Pain	2	3.17
Others	5	7.94
Blood Pressure (mmHg)		
Hypotension ($< 90/60$)	7	11.11
Normotension (90/60 - <140/90)	42	66.67
Hypertension ($\geq 140/90$)	14	22.22
Heart Rate (x/minute)		
Bradycardia (< 60)	0	0.00
Normal (60-100)	17	26.98
Tachycardia (> 100)	46	73.02
Respiratory Rate (x/minute)		
Decreased (<12)	0	0.00
Normal (12-20)	4	6.35
Increased (>20)	59	93.65
Temperature (°C)		
Decreased (< 36.1)	8	12.70
Normal (36.1-37.2)	27	42.86
Increased (> 37.2)	28	44.44

* Each patient could have more than one type of infection † Each patient could have had more than one type of main complaint

Table	4
-------	---

Laboratorium Profiles of	DKA	Patients
--------------------------	-----	----------

Variable	n	%
Random Plasma Glucose (mg/dL	<i>.</i>)	
< 250	2	3.17
250-600	39	61.91
> 600	22	34.92
Mean \pm (SD)	550.79	± 203.85
Sodium (mmol/L)		
Hyponatremia (< 136)	25	39.68
Normonatremia (136-144)	23	36.51
Hypernatremia (> 144)	15	23.81
Mean \pm (SD)	137.87	' ± 10.79
Potassium (mmol/L)		
Hypokalemia (< 3.8)	20	31.75
Normokalemia (3.8-5.0)	27	42.86
Hyperkalemia (> 5.0)	16	25.39
Mean \pm (SD)	4.	3 ± 1.35
Chloride (mmol/L)		
Hypochloremia (< 97)	15	23.81
Normochloremia (97-103)	18	28.57
Hyperchloremia (> 103)	30	47.62
Mean \pm (SD)	104.06	5 ± 11.74
Arterial pH		
> 7.30	32	50.79
7.25-7.30	6	9.52
7.00-7.24	23	36.51
< 7.00	2	3.18
Mean \pm (SD)	7.2	27 ± 0.13
PCO ₂ (mmHg)		
Low (< 35)	58	92.06
Normal (35-45)	3	4.76
High (> 45)	2	3.18
Mean + (SD)	21.31	+10.12
$PO_2 (mmHg)$	21101	_ 10112
$L_{0} = (< 80)$	8	12.70
Normal (80-100)	8	12.70
High (> 100)	47	74.60
Mean + (SD)	138.81	+58.03
HCO_{2}^{-} (mmol/L)	100.01	_ 00.00
> 18	8	12.70
15 - 18	5	7.94
10 - < 15	13	20.63
< 10	37	58 73
Mean + (SD)	10.4	13 + 5.28
Anion Gan (mE α/L)	10.1	0 _ 0.20
> 12	62	98.41
10-12	1	1.59
< 10	Ô	0.00
Mean \pm (SD)	23.3	57 ± 5.43



Figure 1. Distribution of Length of Stay for DKA Patients



Figure 2. Distribution of Outcome in DKA Patients

*DAMA: Discharge against Medical Advice

DISCUSSION

Diabetic ketoacidosis (DKA) is a dangerous acute complication that can occur in type 1 and type 2 DM. From 2009 to 2014, the age-adjusted rate of DKA hospitalization among DM patients in United States increased by 54.9%, from 19.5 to 30.2 per 1,000 persons, with an average annual rate of 6.3%. This complication is characterized by hyperglycemia, ketonemia, and metabolic acidosis (Benoit, Zhang, Geiss, Gregg, & Albright, 2018).

Of the total 63 DKA patients, two thirds were female (66.67%). This proportion is in accordance with Thewjitcharoen et al (2019) and Usman, Syed Sulaiman, Khan, & Adnan (2015); females are prone to a greater risk of obesity because they tend to store fat. Females primarily gain fat in subcutaneous regions; after menopause, adiposity shifts to visceral areas, which increases the risk of metabolic syndrome. Additionally, menopausal women suffer from estrogen deficiency, which can lead to insulin resistance. This state makes female more prone to DKA (Gupte, Pownall, & Hamilton, 2015). In addition, females are also at a 30-times higher risk of urinary tract infections (UTI) than males (Tan & Chlebicki, 2016); UTIs were one of the most common infections in our study.

DKA patients are mostly aged from 50-59 years (38.10%), with the mean age being 49.51 ± 13.88 years. This result is in accordance with George, Mishra, & Iyadurai (2018), Thewjitcharoen et al., (2019), and Usman, Syed Sulaiman, Khan, & Adnan (2015). Factors that make the elderly more susceptible to DKA are decreased pancreatic beta cells' regenerative capabilities and insulin secretion with a sedentary lifestyle (Lee & Halter, 2017).

The DKA patients in this study consisted of 7 patients of type 1 DM (11.11%) and 56 patients with type 2 DM (88.89%). This result is in accordance with George, Mishra, & Iyadurai (2018), Thewjitcharoen et al., (2019), and Usman, Syed Sulaiman, Khan, & Adnan (2015). DKA is always associated with type 1 DM but, lately, the prevalence of DKA in patients with type 2 DM has been increasing. As Zhong, Juhaeri, & Mayer-Davis (2018) state, the incidence of DKA hospitalization for type 2 DM patients was lower than that of patients with type 1 DM, but the incidence increased about 4.2% from 1998 to 2013. So many type 2 DM patients have DKA in this study because the type 2 DM patients dominate the DM cases in the internal medicine ward of RSUD Dr. Soetomo. Xu et al (2018) state that, among adults diagnosed with DM, about 91.2% were type 2 DM, which supports the results of this study, because most of the DM patients on the internal medicine ward were adults and young patients often treated in the pediatric ward.

Most patients in this study had severe DKA (58.73%). One possible cause for this was the lack of awareness on behalf of the DM patients regarding DKA. This possibility is supported by a study in Saudi Arabia that found that most DM patients (54%) possessed very little knowledge about DKA. This lack of knowledge causes patients to be slow to recognize symptoms and delay seeking treatment (Alanazi et al., 2018). In addition, RSUD Dr. Soetomo is a tertiary hospital that is a referral center from another health facility, so most of its patients are severe DKA patients who need further treatment.

Altered states of consciousness (46.03%) and shortness of breath (26.98%) were the most common complaints experienced by DKA patients. DKA and altered consciousness are often related, but the etiology is still unclear. One study stated that acidosis was the main cause of altered consciousness, but hyperosmolarity also played a synergistic role in patients with severe acidosis (Nyenwe & Kitabchi, 2016). Another common complaint, shortness of breath, is caused by compensation from the respiratory system due to metabolic acidosis. Decreased bicarbonate and pH levels cause hyperventilation and decreased carbon dioxide levels (de Moraes & Surani, 2019).

Infection was the most precipitating factor (88.89%) in DKA patients. This is in accordance with Hamed, Gawaly, Abbas, & El Ahwal (2017) and Seth, Kaur, & Kaur (2015). The most common types of infection experienced by DKA patients in RSUD Dr. Soetomo were sepsis (92.86%), pneumonia (30.36%), and UTI (23.21%). These results are consistent with Hamed, Gawaly, Abbas, & El Ahwal (2017) and Seth, Kaur, & Kaur (2015). In a study conducted at Cipto Mangunkusumo Hospital, Jakarta, approximately 58% of the DKA patients had infection as a precipitating factor, and more than half (51%) were respiratory tract infections (Suwarto, Sutrisna, Waspadji, & Pohan, 2014).

In this study, the majority of patients displayed normotension (66.67%), tachycardia (73.02%), increased respiratory rate (93.65%), and increased body temperature (44.44%). Common signs in DKA patients include hypotension, tachycardia and Kussmaul's breathing (fast, deep breaths). Patients could have a normal or slightly decreased body temperature even if they had an infection (Gosmanov, Gosmanova, & Kitabchi 2000). This is likely due to the shock process, which is still in the non-progressive phase. In general, shock is divided into three phases: nonprogressive, progressive, and irreversible. At the beginning of shock, the non-progressive phase, the compensatory reflex is activated, maintaining perfusion to the vital organs. In this phase, various mechanisms operate to maintain cardiac output and blood pressure. The mechanisms involved are baroreceptor the reflex, the release of catecholamines and ADH, the activation of the renin-angiotensin-aldosterone system, and the stimulation of the sympathetic nervous system. The effects of this are tachycardia, peripheral vascular vasoconstriction (in septic shock, arterial vasodilation can occur initially in the skin, so the patient can experience warm and reddish skin) and fluid conservation by the kidneys (this causes decreased urine production). Peripheral blood flow decreases and is focused on vital organs such as the heart and brain. If the underlying cause is not corrected, the process will advance to the progressive phase, which is characterized by extensive tissue hypoxia (Kumar, Abbas, & Aster, 2015).

About 3.17% of DKA patients had random plasma glucose levels of <250 mg/dL. This condition is called euglycemic diabetic ketoacidosis. A study conducted in Thailand reported that 6.4% of DKA cases also had euglycemia (Thewjitcharoen et al., 2019). The mechanism underlying this is a decrease in hepatic glucose production (in a fasting state) or an increase in glucose excretion in urine induced by excessive levels of contraregulator hormones-the first mechanism is more common. Some of the most common causes of euglycemic DKA are low calorie intake, fasting, pregnancy, pancreatitis, cocaine intoxication, prolonged vomiting or diarrhea, use of insulin pumps, and new use of SGLT-2 inhibitors (empagliflozin and canagliflozin) and others (Rawla, Vellipuram, Bandaru, & Raj, 2017).

In this study, it was found that most DKA patients had hyponatremia (39.68%). In DKA, insulinopenia results in hyperglycemia because glucose cannot enter the cell. Increased plasma glucose levels will increase serum osmolality, causing water transfer from the intracellular to the extracellular space. This condition promotes a decreased plasma sodium concentration due to dilution. Furthermore, hyperglycemia and the formation of ketone bodies causes osmotic diuresis, during which sodium ions are also excreted in the urine. Concurrent conditions, such as vomiting and diarrhea, can worsen this loss. Eventually, this will lead to hyponatremia (Gosmanov, Gosmanova, & Kitabchi 2000)

Most DKA patients (42.86%)had normokalemia. Insulin is the main cause of potassium imbalance between intracellular and extracellular. A lack of insulin causes disruption in intracellular potassium uptake via the Na-K ATPase pump. These conditions, aggravated by stress, induce cellular insensitivity to insulin, which leads to an intracellular decrease in potassium and an increase in serum potassium. Hyperglycemia results in hyperosmolarity, which causes potassium to move from the inside to the outside of cells. Then, due to osmotic diuresis, potassium is excreted through the kidneys. All these processes lead to a total body potassium deficit. Although the amount of potassium in the body is decreasing, DKA patients can have normal or increased plasma potassium levels. Normal plasma potassium levels still indicate that the amount of potassium in the body is greatly reduced (Konstantinov et al., 2015; Usman, 2018).

In this study, it was found that most DKA patients had hyperchloremia (47.62%).

Hyperchloremia in DKA can occur because of intensive administration of chloride-containing fluids, such as normal saline. The other cause is due to the body's compensation to low bicarbonate levels. Chloride is displaced to outside of cells to maintain the electroneutral state (Sharma, Hashmi, & Aggarwal, 2020; Toledo et al., 2018).

From the results of blood gas analysis, the majority of patients had arterial pH > 7.30 (50.79%), low PCO2 (92.06%), high PO2 (74.60%), bicarbonate > 10 mmol/L (58.73%), and anion gap > 12 mEq/L (98.41%). Blood gas analysis may help doctors determine the severity of acidosis and decide the appropriate treatment for the patient. In DKA, insulin resistance and increased levels of counter-regulatory hormones lead to the release of free fatty acids via lipolysis. This results in the excessive production of β hydroxybutyrate and acetoacetate. Overproduction of these ketoacids causes excess hydrogen ion production and decreases the amount of stored bicarbonate. Following this process, the patient would have lower pH, lower bicarbonate levels, and higher anion gaps in blood gas analysis results. Moreover, the PCO2 may help with assessing the respiratory compensation for metabolic acidosis and deciding when to use a mechanic ventilator (Patel, Ahmed, Gunapalan, & Hesselbacher, 2018).

Two thirds of the patients (66.67%) had a length of stay from 0–7 days (mean 6.60 \pm 5.25 days). This is consistent with Almalki, Buhary, Khan, Almaghamsi, & Alshahrani, 2016 and Thewjitcharoen et al (2019). Some aspects that could affect the length of stay are the severity of the DKA, the severity of the metabolic acidosis, and any underlying comorbidities. About 94.45% of the deceased patients in this study had a 0–7day length of stay. This may also explain why many patients had short hospitalization durations.

The majority of DKA patients died while receiving treatment in hospital (57.14%). This result was much higher than in the studies conducted by Seth, Syed Sulaiman, Khan, & Adnan (2015) and Usman, Kaur, & Kaur (2015), with the number of DKA patient deaths in those studies reaching only 10% and 11.30%, respectively. Several possible causes are a small sample size compared to other studies, low awareness of DKA in diabetic patients, severity of acidosis, and the presence of infection. To prevent fatal outcomes, it is of paramount importance that a proper diagnosis is made and prompt treatment is initiated. The education program for medical personnel must be strengthened, and guidelines need to be updated regularly to improve the quality of patient care (Thewjitcharoen et al., 2019). Medical personnel also need to educate their patients about the importance of controlling plasma glucose levels and raise their levels of awareness regarding the complications of DM (such as DKA).

Research Limitation

This study has several limitations that need to be considered. First, this study only used data on DKA patients from 2017, so we were unable to describe any trends in DKA cases from year to year. Secondly, this study was conducted at Dr. Soetomo Hospital, so it was not representative of all DKA patients.

CONCLUSION

The number of patients with severe DKA and the mortality rates were higher in this study than in others. We also found that women and the elderly were more prone to DKA. In addition, the DKA cases in this study were predominantly in type 2 DM patients, with infection as the most common precipitating factor. Therefore, early detection, accurate diagnosis, and effective and aggressive management must be encouraged to reduce the number of patients with severe DKA, as well as the mortality rates associated with DKA in RSUD Dr. Soetomo.

CONFLICT OF INTEREST

The authors has declared no conflicts of interest in this study..

AUTHOR CONTRIBUTION

DGUBD and HN participated in the conception and design of this study and literature search. DGUBD, HN, and A reviewed the proposal, discussed the data analysis, and reviewed and revised the manuscript. DGUBD prepared the manuscript for publication. All authors read and approved the final manuscript.

ACKNOWLEDGMENTS

This study is part of bachelor's degree program. The authors would like to thank Dr. Sony Wibisono, Dr. SpPD, K-EMD, and FINASIM for the critiques given, as well as all staff members of RSUD Dr. Soetomo who helped with data collection and the ethics process.

REFERENCES

- Alanazi, A. M., Alotaibi, A. J., Albakheit, H. A., Aldewish, S. N., Alenzi, M. K. A., & Salim, A. A. (2018). Awareness of risk factors of DKA among diabetic adults in KSA. *The Egyptian Journal of Hospital Medicine*, *71*(1), 2304–2309. https://doi.org/10.12816/0045307
- Almalki, M. H., Buhary, B. M., Khan, S. A., Almaghamsi, A., & Alshahrani, F. (2016). Clinical and biochemical characteristics of diabetes ketoacidosis in a tertiary hospital in Riyadh. *Clinical Medicine Insights: Endocrinology and Diabetes*, 9, 7–11. https://doi.org/10.4137/CMED.S39639
- Benoit, S. R., Zhang, Y., Geiss, L. S., Gregg, E.
 W., & Albright, A. (2018). Trends in diabetic ketoacidosis hospitalizations and in-hospital mortality United States, 2000-2014. *Morbidity and Mortality Weekly Report*, 67(12), 362–365. https://doi.org/10.15585/mmwr.mm6712a3
- de Moraes, A. G., & Surani, S. (2019). Effects of
- diabetic ketoacidosis in the respiratory system. World Journal of Diabetes, 10(1), 16–22. https://doi.org/10.4239/wjd.v10.i1.16
- George, J. T., Mishra, A. K., & Iyadurai, R. (2018). Correlation between the outcomes and severity of diabetic ketoacidosis: a retrospective pilot study. *Journal of Family Medicine and Primary Care*, 7(4), 787–790. https://doi.org/10.4103/jfmpc.jfmpc 116 18
- Gosmanov, A. R., Gosmanova, E. O., & Kitabchi,
 A. E. (2000). Hyperglycemic crises: diabetic ketoacidosis (DKA), and hyperglycemic hyperosmolar state (HHS). In K. R. Feingold,
 B. Anawalt, A. Boyce, G. Chrousos, K. Dungan, A. Grossman, ... D. P. Wilson (Eds.), *Endotext [Internet]*. Retrieved from https://www.ncbi.nlm.nih.gov/books/NBK27 9052/
- Gosmanov, A. R., & Kitabchi, A. E. (2000). Diabetic ketoacidosis. In K. R. Feingold, B. Anawalt, A. Boyce, G. Chrousos, K. Dungan, A. Grossman, ... D. P. Wilson (Eds.), *Endotext [Internet]*. Retrieved from https://www.ncbi.nlm.nih.gov/books/NBK27 9146/
- Gupte, A. A., Pownall, H. J., & Hamilton, D. J. (2015). Estrogen: an emerging regulator of insulin action and mitochondrial function.

Journal of Diabetes Research, 2015, 1–9. https://doi.org/10.1155/2015/916585

- Hamed, Z. S. S., Gawaly, A. M., Abbas, K. M., & El Ahwal, L. M. (2017). Epidemiology of infection as a precipitating factor for diabetic ketoacidosis at Tanta University Hospital. Tanta Medical Journal, 45. 68–72. https://doi.org/10.4103/tmj.tmj
- Konstantinov, N. K., Rohrscheib, M., Agaba, E. I., Dorin, R. I., Murata, G. H., & Tzamaloukas, A. H. (2015). Respiratory failure in diabetic ketoacidosis. World Journal of Diabetes, 6(8). 1009-1023. https://doi.org/10.4239/wjd.v6.i8.1009
- Kumar, V., Abbas, A. K., & Aster, J. C. (2015). Robbins and cotran pathologic basis of disease (9th ed.). Philadelphia: Elsevier/Saunders.
- Lee, P. G., & Halter, J. B. (2017). The pathophysiology of hyperglycemia in older adults: clinical considerations. Diabetes Care. 40(4), 444-452. https://doi.org/10.2337/dc16-1732
- Nyenwe, E. A., & Kitabchi, A. E. (2016). The evolution of diabetic ketoacidosis: an update etiology, pathogenesis of its and management. Metabolism: Clinical and Experimental, 65(4),507-521. https://doi.org/10.1016/j.metabol.2015.12.00 7
- Patel, M. P., Ahmed, A., Gunapalan, T., & Hesselbacher, S. E. (2018). Use of sodium bicarbonate and blood gas monitoring in diabetic ketoacidosis: a review. World Journal of Diabetes, 9(11), 199–205. https://doi.org/10.4239/wjd.v9.i11.199
- Rawla, P., Vellipuram, A. R., Bandaru, S. S., & Raj, J. P. (2017). Euglycemic diabetic ketoacidosis: a diagnostic and therapeutic Endocrinology, dilemma. Diabetes å Metabolism Case Reports, 2017(September), 15-18. https://doi.org/10.1530/edm-17-0081
- Seth, P., Kaur, H., & Kaur, M. (2015). Clinical profile of diabetic ketoacidosis: a prospective study in a tertiary care hospital. Journal of Clinical and Diagnostic Research, 9(6), OC01-OC04. https://doi.org/10.7860/JCDR/2015/8586.599 5
- Sharma, S., Hashmi, M., & Aggarwal, S. (2020). Hyperchloremic Acidosis. In StatPearls [Internet]. Retrieved from https://www.ncbi.nlm.nih.gov/books/NBK48 2340/
- Suwarto, S., Sutrisna, B., Waspadji, S., & Pohan,

H. T. (2014). Predictors of five days mortality in diabetic ketoacidosis patients: a prospective cohort study. Acta Medica Indonesiana, 46(1), 18-23.

- Tan, C. W., & Chlebicki, M. P. (2016). Urinary tract infections in adults. Singapore Medical Journal. 57(9), 485-490. https://doi.org/10.11622/smedj.2016153
- Thewjitcharoen, Y., Plianpan, P., Chotjirat, A., Nakasatien, Chotwanvirat, S., Ρ., Wanothayaroj, E., ... Himathongkam, T. (2019). Clinical characteristics and outcomes of care in adult patients with diabetic ketoacidosis: a retrospective study from a tertiary diabetes center in Thailand. Journal of Clinical and Translational Endocrinology, 16. 1 - 5.

https://doi.org/10.1016/j.jcte.2019.100188

- Toledo, I., Wainsztein, R., Mannucci, C., Ferraro, M., Ferreira, J., & Balestracci, A. (2018). Impact of the hyperchloremic component of metabolic acidosis on the patient's hydration status and the treatment of diabetic ketoacidosis. Argentinos Archivos de Pediatria. 116(3). e365-e370. https://doi.org/10.5546/aap.2018.eng.e365
- Usman, A. (2018). Initial potassium replacement in diabetic ketoacidosis: the unnoticed area of gap. Frontiers in Endocrinology, 9, 1–3. https://doi.org/10.3389/fendo.2018.00109
- Usman, A., Syed Sulaiman, S. A., Khan, A. H., & Adnan, A. S. (2015). Profiles of diabetic ketoacidosis in multiethnic diabetic population of Malaysia. Tropical Journal of Pharmaceutical Research, 14(1), 179–185. https://doi.org/10.4314/tjpr.v14i1.25
- Xu, G., Liu, B., Sun, Y., Du, Y., Snetselaar, L. G., Hu, F. B., & Bao, W. (2018). Prevalence of diagnosed type 1 and type 2 diabetes among US adults in 2016 and 2017: population study. BMJ, 362. based The 1 - 7. https://doi.org/10.1136/bmj.k1497
- Zhong, V. W., Juhaeri, J., & Mayer-Davis, E. J. (2018). Trends in hospital admission for diabetic ketoacidosis in adults with type 1 and type 2 diabetes in England, 1998-2013: a retrospective cohort study. Diabetes Care, 41(9), 1870-1877.

https://doi.org/10.2337/dc17-1583