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Risk Factor Related to Mortality of Diabetic Ketoacidosis Patients in Dr. Soetomo General Hospital Surabaya

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A B S T R A C T

Introduction: Diabetic ketoacidosis (DKA) is a complication of diabetes mellitus which has a high risk of mortality. Mortality in DKA patients in developed countries is less than 5%, some other sources mention 5-10%, 2-10%, or 9-10%. Mortality events at clinics with simple facilities and elderly patients can reach 25-50%. The mortality rate of DKA patients is generally higher in infection conditions, especially in developing countries and in septic patients. Several factors such as age, sex, and high blood glucose can increase mortality risk of DKA patients. Other risk factors such as history of discontinued insulin therapy, impaired bicarbonate levels, pH, and increased leukocytes of DKA patients due to infection, abnormal albumin levels, electrolyte disturbances, and Serum Creatinine (SK) were thought to affect mortality of DKA patients. The purpose of this study was to determine the risk factors associated with mortality of DKA patients in Dr. Soetomo General Hospital Surabaya.

Methods: The method used in this study was observational analytic involving 63 adult patients diagnosed with DKA with analysis using Chi-Square test.

Results: From 63 patients included in this study, 37 patients diagnosed with DKA died and 26 patients lived. In a multivariate analysis, DKA severity with $p = 0.001$ ($p < 0.005$) was identified as having a relationship with mortality of DKA patients Dr. Soetomo General Hospital Surabaya.

Conclusion: Severity is the only risk factor associated with mortality of DKA patients in Dr. Soetomo General Hospital Surabaya.

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Introduction

Diabetic ketoacidosis (DKA) is a metabolic decomposition and is characterized by hyperglycemia, ketosis, and acidosis. DKA is a severe acute complication of diabetes type 1 and type 2 with 8/1000 prevalence of all age group of DM patients from the United States community. The US also reported that DKA is also responsible for more than 100,000 patients each year. DKA community data have not been found yet in Indonesia, but DKA incidences are suspected not as high as western countries because of the low DM type 1 prevalence. The report is commonly collected from hospital data and DM type 2 patients.[1,2]

Several factors such as age, gender, and high blood glucose can increase the risk of mortality in DKA patients. Other risk factors such as discontinued insulin therapy, disturbance of bicarbonate level, pH, and increased leukocyte DKA patients caused by infection, abnormal albumin level, electrolyte disturbance, and creatinine serum are suspected to influence mortality of DKA patients.[3]

Inaccuracy in doing therapy and risk factors of DKA patients can increase death risk. The death of DKA patients in developed countries are less than 5%, other references mentioned 5-10%, 2-10%, and 9-10%. Mortality events in a clinic with simple facilities and elderly patients could reach 25-50%[1]. Generally, mortality number of DKA patients is higher than infection, especially in developing countries and sepsis patients. Data from Cipto Mangunkusumo Hospital showed that DKA patient's death tends to be higher because of the low income, comorbidity, delayed medical treatment, and higher infection risk. From more than 60 treated patients, 24 (40%) of them died in day 5 of treatment.[4]

The specific purpose of this study was to determine the prevalence of mortality incident and the relation between age, sex, initial glucose level, severity, leukocyte levels, electrolyte disturbances, serum creatinine levels, history of insulin therapy in DKA mortality in Dr. Soetomo General Hospital Surabaya. These factors are expected to affect mortality of DKA patients through several pathophysiologies that have been explained previously. By knowing and identifying risk factors, it is expected mortality of DKA patients can be prevented. On the other hand, it also needs accurate diagnosis and treatment planning to prevent the death of DKA patients. This research is expected to fix the management of DKA patients in Indonesia.

Methods

This was a cross-sectional research using analytic observational approach. This research used secondary data in the form of the medical records to identify risk factors related to mortality of DKA patients in Dr. Soetomo General Hospital Surabaya.

The population of this research was all DM type 1 and type 2 patients with diabetic ketoacidosis complications in internal medicine ward of Dr. Soetomo General Hospital in the period of January 17th, 2017 – December 31st, 2017. The sampling method used was a total sampling of patients who met the inclusion criteria, namely patients with DM type 1 and 2 who were more than 18 years of age at hospital admission. Samples were excluded if they did not have complete medical record data.

The independent variables of this study were age, gender, initial glucose levels in the hospital, DKA severity, leukocytes, albumin levels, electrolyte disorders, serum creatinine levels, history of insulin therapy. The criteria of American Diabetic Association (ADA) was used to diagnose and determine DKA severity in DKA patients in Dr. Soetomo General Hospital Surabaya. All independent variables were measured at the time the patient was admitted to the hospital. Whereas the dependent variable of this study was the patient's mortality rate. Data from this study were analyzed by multivariate analysis using Chi-Square statistical test and Mantel-Haenszel test to measure whether there is a significant relationship between the independent variable and the dependent variable. IBM SPSS statistics version 23 was used as the software to measure Chi-Square and Mantel-Haenszel test.

Results

Table 1. Characteristics and correlation between risk factor and mortality.

	Mortality		**Percentage (%)**		**p-value**
	Dead	**Alive**	**Dead**	**Alive**	
Age (years)					
18 - 44	9	9	50	50	0.479
44 - 65	29	16	64	36	
Gender					
Female	24	16	60	40	0.997
Male	13	10	57	43	
Initial Blood Glucose Level (mg/dl)					
< 250	1	2	33.4	66.6	0.470
≥ 250	35	24	59.3	40.7	
Severity					
Mild	6	11	35.2	64.8	
Moderate	9	10	47.3	52.7	0.001
Severe	22	4	84.6	15.4	
Leucocyte Count (cells/mm^3)					
≤10.000	4	4	50	50	
10.000 - 15.000	5	6	45.4	54.6	0.657
15.000 - 25.000	19	10	65.5	34.5	
>25.000	9	6	60	40	
Plasma Albumin Level (g/dl)					
< 2.5 g/dl	2	2	50	50	0.888
2.5 – 3.5 g/dl	18	11	62	38	
> 3.5 g/dl	15	9	62.5	37.5	

Electrolyte Disturbances					
Present	39	23	59	31	0.616
Not present	4	3	57.1	42.9	
Serum Creatinine Level (mg/dl)					
≥ 4	7	4	63.6	36.4	0.642
< 4	29	22	56.8	43.2	
History of Insulin Usage					
Never use insulin	23	13	63.8	36.2	0.286
In use insulin	12	12	50	50	
Ever use insulin	0	1	0	100	

The Relationship between Age and Mortality of DKA Patients in Dr. Soetomo General Hospital Surabaya

This data analysis was done by comparing mortality of DKA patients aged 18-44 years old and 45-65 years old. In patients aged 18-44 years old, 9 (50%) patients died and 9 (50%) patients survived. DKA patients in the age range of 44-65 years old obtained the results of 29 (64%) patients died and 16 (36%) patients survived. The data analysis results above indicate that the significance value between age and mortality of DKA patients is 0.479 ($p < 0.005$). This shows that there is no relationship between age and mortality of DKA patients in Dr. Soetomo General Hospital Surabaya.

The Relationship between Gender and Mortality of DKA Patients in Dr. Soetomo General Hospital Surabaya

This data analysis was done by comparing gender (male and female). The results of the study in female patients showed that 24 (60%) patients died and 16 (40%) patients survived. In male patients, 13 (57%) patients died and 10 (43%) patients survived. The analysis results of the data above show that the significance value between gender and mortality of DKA patients is 0.997 ($p < 0.005$). This shows that there is no relationship between gender and mortality of DKA patients in Dr. Soetomo General Hospital Surabaya.

The Relationship between Initial Blood Glucose Levels in the Hospital with Mortality of DKA Patients in Dr. Soetomo General Hospital Surabaya

This data analysis was performed by comparing the initial blood glucose level in the hospital with mortality of DKA patients. This study compared the difference in blood sugar of patients with GDA levels <250mg/dl and ≥250mg/dl. Data analysis was performed using Chi-Square test. The results of the study in patients with blood sugar levels <250mg/dl obtained as many as 1 (33.4%) died and 2 (66.6%) survived. In patients with blood sugar ≥ 250mg/dl, 35 (59.3%) died and 24 (40.7%) survived. The results of the data analysis above indicate that the significance value between initial blood glucose levels in the hospital and mortality of DKA patients is 0.470 ($p < 0.005$). This shows that there is no relationship between initial blood glucose level in hospital and blood glucose level the first day after treatment with mortality of DKA patients.

The Relationship between Severity and Mortality of DKA Patients in Dr. Soetomo General Hospital Surabaya

This data analysis was performed by comparing the severity and mortality of DKA patients. The study was conducted on DKA patients with mild, moderate, and severe scales. The results of studies on patients with mild severity obtained results as many as 6 (35.2%) died and 11 (64.8%) survived. In patients with moderate severity, 9 (47.3%) died and 10 (52.7%) survived. Whereas in severe patients, 22 (84.6%) died and 4 (15.4%) survived. The results of the data analysis above indicate that the significance value between severity and mortality of patients with DKA is 0.001 ($p < 0.005$). This shows that there is a relationship between the severity and mortality of DKA patients.

The Relationship between Leukocyte Levels and Mortality in DKA Patients in Dr. Soetomo Hospital Surabaya

This data analysis was performed by comparing the levels of leukocytes with mortality of DKA patients. The study was conducted on DKA patients with leukocyte levels ≤10,000/mm^3, 10,000-15,000/mm^3, 15,000-25,000/mm^3, and >25,000/mm^3. The results of this study indicate the death of patients at leukocyte levels ≤10,000/mm^3 as many as 4 (50%) and 4 (50%) patients survived. In patients with leukocyte levels of 10,000-15,000/mm^3, 5 (45.4%) died and 6 (54.6%) survived. The highest number of mortality was found in patients with leukocyte levels of 15,000-25,000/mm^3, which were 19 (65.5%) and 10 (34.5%) survived. In patients with leukocyte levels >25,000/mm^3, 9 (60%) died and 6 (40%) survived. The results of the data analysis above indicate that the significance value between the levels of leukocytes and mortality of DKA patients is 0.657 ($p < 0.005$). This shows that there is no relationship between leukocyte levels and mortality of DKA patients.

The Relationship between Albumin Levels and Mortality in DKA Patients in Dr. Soetomo General Hospital Surabaya

This data analysis was done by comparing albumin levels with mortality of DKA patients. The study was conducted on DKA patients with albumin levels <2.5 g/dl, 2.5-3.5 g/dl, >3.5 g/dl. The results of the study in patients with albumin levels <2.5 g/dl showed that 2 (50%) died and 2 (50%) survived. In patients with albumin levels of 2.5-3.5 g/dl, 18 (62%) died and 11 (38%) survived. Whereas in patients with albumin levels of >3.5 g/dl, 15 (62.5%) died and 9 (37.5%) survived. The results of the data analysis above show that the significance value between albumin levels and mortality of DKA patients is 0.888 ($p < 0.005$). This shows that there is no relationship between albumin levels and mortality of DKA patients.

The Relationship between Electrolyte Disorders and Mortality of DKA Patients in Dr. Soetomo Hospital Surabaya

This data analysis was done by comparing the electrolyte disturbance with mortality of DKA patients. The study was conducted on DKA patients with impaired levels of sodium, potassium, and chloride. Data analysis was performed using Chi-Square test. The results of this study indicate the number of deaths of patients with electrolyte disturbances was 33 (59%) and 23 (31%) patients survived. In patients without electrolyte disturbance, 4 (57.1%) died and 3 (42.9%) patients survived. The results of the data analysis above show that the significance value between

electrolyte disturbances and mortality of DKA patients is 0.616 ($p < 0.005$). This shows that there is no relationship between electrolyte disturbance and mortality of DKA patients.

The Relationship between SK Levels with Mortality of DKA Patients in Dr. Soetomo General Hospital Surabaya

This data analysis was carried out by comparing serum creatinine levels with mortality of DKA patients. The study was conducted on DKA patients with serum creatinine levels ≥4mg/dl and 4mg/dl. Data analysis was performed using Chi-Square Test. The results on the serum creatinine level of patients ≥4mg/dl obtained as many as 7 (63.6%) died and 4 (36.4%) survived. In patients with serum creatinine <4mg/dl, 29 (56.8%) died and 22 (43,2%) survived. The results of the data analysis above show that the significance value between serum creatinine and mortality of DKA patients was 0.642 ($p < 0.005$). This shows that there is no relationship between serum creatinine and mortality of DKA patients.

The Relationship between the History of Insulin Therapy with Mortality of DKA Patients in Dr. Soetomo General Hospital Surabaya

Data analysis was performed by comparing the history of insulin therapy with mortality of DKA patients. The study was conducted on DKA patients with the history of never consumed insulin, consuming insulin, and have used insulin. In this study, there were some patients whose treatment history was unknown. The results of the study in patients who had never used insulin showed that patients died as many as 23 (63.8%) and 13 (36.2%) survived. Patients who are using insulin had the same results. 12 patients (50%) died and 12 (50%) survived. No mortality was found in patients with the history of ever consumed insulin, as many as 1 (100%) patient survived. The results of the data analysis above show that the significance value between the history of insulin therapy and mortality of DKA patients is 0.286 ($p < 0.005$). This shows that there is no relationship between the history of insulin therapy and mortality of DKA patients in Dr. Soetomo General Hospital Surabaya.

Discussion

The results showing the percentage of DKA mortality in Dr. Soetomo General Hospital Surabaya was highest in patients aged 44-65 years old as many as 29 (64%). This is in accordance with the study of Malone, *et al*.[5] which mentioned that patients with older age are more susceptible to mortality and risk factors. For age with mortality of DKA patients in Dr. Soetomo General Hospital Surabaya, it has no significant relationship with the value of 0.479 ($p < 0.005$). This is not consistent with the study of Malone, *et al.* This is due to different number of samples used between this study and the study by Malone, *et al.*[5]

The relationship of gender and DKA mortality in Dr. Soetomo General Hospital Surabaya showed 63.5% were female and 36.5% were male. This is in accordance with the research conducted by Sinaga[6] which stated that patients with diabetes mellitus with complications based on the highest sex are female patients (65%), which are higher than men (35%). Significance value between sex and mortality of DKA patients in Dr. Soetomo General Hospital Surabaya found no significant relationship with a significance value of 0.997 ($p < 0.005$). This is consistent with the study of Goetra, *et al*.[7], that the mortality rate of DKA patients is more influenced by the accompanying disease.

The results of the relationship between initial blood glucose levels in the hospital with DKA patients in Dr. Soetomo General Hospital Surabaya showed conformity with American Diabetic Association[8], which stated hyperglycemia as the main criteria in DKA. The results of this study are in accordance with those conducted by Ullah, *et al*.[9] Analysis of data on initial blood glucose admission to hospital and the first day after treatment did not find a significant relationship with a significance value of 0.470 ($p < 0.005$).

On the relationship between severity and mortality of DKA patients in Dr. Soetomo General Hospital Surabaya, it showed that mild was 27%, moderate was 30.2%, and severe was 41.3%. Moderate and severe severity had higher mortality rates. This is consistent with the study of George, *et al*.[1], who conducted a study in India with 8%, 41%, and 51%, respectively. This study is in line with the significance of severity with the death of DKA patients in Dr. Soetomo General Hospital Surabaya with a significance value of 0.001 ($p < 0.005$).

The results of the relationship between leukocyte levels and mortality in DKA patients in Dr. Soetomo General Hospital Surabaya showed that DKA patients with leukocytes ≤10,000 cells/mm^3 were 8 (12.7%), 10,000-15,000 cells/mm^3 were 11 (17.5%), 15,000 - 25,000 cells/mm^3 were 29 (46%), and ≥25,000 cells/mm^3 were 15 (23.8%). This study is in accordance with the study by Arifin, *et al*.[10], that 20-55% of cases of hyperglycaemic crisis are infections. Leukocyte level ≥25,000 cells/mm^3 could be one of the signs of infection in DKA patients.[11] The highest number of mortality was found in patients with leukocyte levels of 15,000-25,000 cells/mm^3, as many as 19 (65.5%). There is no significant relationship between leukocyte levels with mortality of DKA patients in Dr. Soetomo General Hospital Surabaya. In analysis of the data, it obtained a significance value between the levels of leukocytes with mortality of DKA patients of 0.657 ($p < 0.005$).

The results of the relationship between albumin levels with mortality of DKA patients in Dr. Soetomo General Hospital Surabaya shows concordance with the research of Cheng, *et al*.[2], that serum albumin concentration correlates with the risk of ketosis in individuals. The highest mortality in this study was found in albumin levels of 2.5-3.5 g/dl (62%). The study found no relationship between albumin levels with DKA mortality with a significance value of 0.888 ($p < 0.005$). Decreased albumin levels are thought to affect infection in Diabetes Mellitus patients.[11]

The results of the relationship between electrolyte disturbances with mortality of DKA patients in Dr. Soetomo General Hospital Surabaya showed that DKA patients who experienced electrolyte disturbance were 56 (88.9%), while those without electrolyte disturbance were 7 (11.1%). This is in accordance with the research by Goetra, *et al*.[7], that electrolyte disturbances that occur can be caused by an increase in blood glucose levels. Mortality that occurred in DKA patients with electrolyte disturbances in this study was 59%. However, this is not significantly related to mortality of DKA patients in Dr. Soetomo General Hospital Surabaya with a significance value of 0.616 ($p < 0.005$).

Research results of serum creatinine levels with mortality of DKA patients in Dr. Soetomo General Hospital Surabaya showed that DKA patients with serum creatinine ≥4mg/dl were 11 (17.7%), and serum creatinine <4mg/dl were 51 (82.3%). The average value in this data was 1.27 with a standard deviation of 0.652. This is in accordance with the research conducted by Huang (2018)[12], that DKA

patients often experience an increase in serum creatinine. Increased serum creatinine can occur due to an intravascular fluid deficit. Most mortality was found in patients with serum creatinine levels 4mg/dl (63.6%). However, this value is not significantly related to mortality of DKA patients in Dr. Soetomo General Hospital Surabaya with a significance value of 0.642 ($p < 0.005$). Therefore, this is not in accordance with the research of Elmehdawi, *et al*.[13]

The results of the relationship between the history of insulin therapy with mortality of DKA patients in Dr. Soetomo General Hospital Surabaya showed that the highest mortality occurred in patients with the history of never consumed insulin (63.8%). However, the history of insulin therapy is not significantly related to mortality of DKA patients in Dr. Soetomo General Hospital Surabaya with a significance value of 0.264 ($p < 0.005$). This is not in accordance with the study of Goetra, *et al*.[7], that mortality rates are higher in conditions that accompany DKA, such as sepsis, acute myocardial infarction, high initial blood glucose, uremia, and low blood acidity levels. The results of this study are different from previous studies by Goetra *et al*.[7], because there were very few samples of patients who discontinued insulin therapy while being on treatment.

Conclusion

Some factors can cause high mortality in diabetic patients. In this study, the only risk factor that can be proven to cause an increase in mortality in diabetic patients with DKA, especially diabetes mellitus type 2, is the degree of severity of DKA.

CONFLICT OF INTEREST

The author stated there is no conflict of interest in this study.

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