

Survival Time of Diabetes Mellitus Patients With Hemodialysis: A Study Using Survival Analysis

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Abstract- Diabetes mellitus (DM) is a chronic disease caused by pancreas failure in processing or producing enough insulin in the body. An estimated 20-40% of people with DM will experience complications of kidney failure. DM patients who experience complications of kidney failure should undergo hemodialysis (HD) therapy. This study aims to assess the survival time of DM patients with HD at Rumah Sakit Islam (RSI) Jemursari, Surabaya, Indonesia, in 2016-2019. The study used secondary data in the form of electronic medical records of DM patients with HD who were registered at RSI Jemursari from 2016 to 2019. Survival analysis with the Kaplan Meier and Cox Regression methods is used as data analysis. The data were 126 DM patients with HD. DM patients with the majority of HDs have the following criteria: over than 50-year-old, male, housewives, having previous hypertension and heart disease records, having no previous lung disease records. The average survival time of DM patients with HD is 182 weeks. Subjects with the criteria as follows: male patients, working, having previous hypertension records, having no previous lung and heart disease records, have a higher survival time. Age has a significant effect ($P=0.004$) on the survival of DM patients with HD. The risk of patients' death increases by 1.07 times as the age increase by one year.

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Introduction

Diabetes Mellitus (DM) is a chronic disease that occurs when the pancreas does not produce enough amount of insulin. Insulin is required to regulate blood glucose in the body. An increase in blood glucose is a common effect of DM that causes complications such as cardiovascular disease, neuropathy, nephropathy, and retinopathy (1). Abnormalities occur in the kidneys, starting with the presence of microalbuminuria. Microalbuminuria is albumin excretion of more than 30 mg per day, which causes diabetic nephropathy. Diabetic nephropathy develops into proteinuria, decreases the function of the glomerular filtration rate, and ends with kidney failure (2).

Approximately 30-40% of people with type-1 DM and 20-30% of people with type-2 DM suffer from diabetic nephropathy, which ends in kidney failure (3).

There is a difference in the survival time of patients with chronic kidney disease (CKD) who suffer from DM and those without DM. CKD patients who have DM records have a lower survival time by nine months than those without ones (4).

In 2017 around 425 million adults (20 to 79-year-old) had diabetes, and in 2045 it is estimated that it will increase up to 629 million adults in the world. Health expenditure related to DM is estimated to reach USD 727 billion in 2017 and USD 776 billion in 2045 (5).

The number of DM patients in Indonesia ranked 6th after China, India, the United States, Brazil, and Mexico (5). Based on the 2018 Basic Health Research, the prevalence of DM in Indonesia was 6.9% in 2013 and 8.5% in 2018. DM patients in East Java Province were 2.1% in 2013 and 2.6% in 2018 (6).

Survival time is the period until a particular event occurs. Kaplan Meier and Cox Regression is an analysis

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that can be used on survival data. Kaplan Meier is used to calculate the magnitude of a person's risk of experiencing certain events in the form of hazard functions and person's probability of survival in the form of survival functions. Cox Regression examines survival time with several variables that are considered to influence it (7).

The study aims to assess the survival of DM patients with HD at RSI (Islamic Hospital) Jemursari, Surabaya, East Java, Indonesia. The study used DM patients with HD's medical record data in 2016-2019 at RSI Jemursari, which then were analyzed using Kaplan Meier and Cox Regression survival.

Materials and Methods

The study uses secondary data, obtained from the medical-records data of DM patients with HD at RSI Jemursari in Surabaya, in 2016-2019. The variables in this study were survival time and patient status, patient's disease records, and demographic characteristics. Survival time is the length of time (weeks) of DM patients since they first had HD until they reached the event (death). Patient status is DM patients' at the end of the observation time, which is either reaching the event

(death) or not reaching the event or censored. Patients' records cover the records of hypertension, heart disease, and lung disease. The demographic characteristics of DM patients include age, sex, and occupation.

Data were collected from DM patients who were registered for hemodialysis for the first time at the RSI Jemursari Surabaya in 2016-2019. On March 12, 2020, patients' status was checked, whether they were passed away or not. All of the data were taken from the RSI Jemursari medical record in Surabaya. The data were obtained by doing the editing and cleaning process and censoring with the right sensor to calculate survival time.

By utilizing Kaplan Meier, depicted curve survival to see average survival time based on age, sex, occupation, hypertension records, lung disease records, and heart disease records. Cox regression is used to study the survival model of DM patients with HD by first checking the Proportional Hazard assumption.

Results

There were 126 patients registered as DM patients with HD at RSI Jemursari from 2016 to 2019. Patients' status on March 12, 2020, is served in Figure 1.

The cause of censored data can be seen in Figure 2.

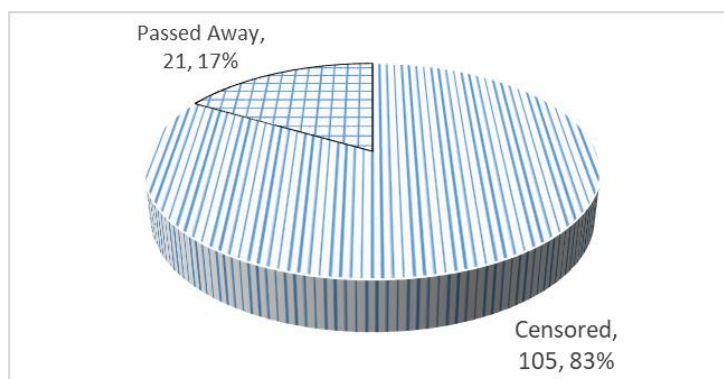


Figure 1. Distribution of DM Patients with HD at RSI Jemursari from 2016 to 2019

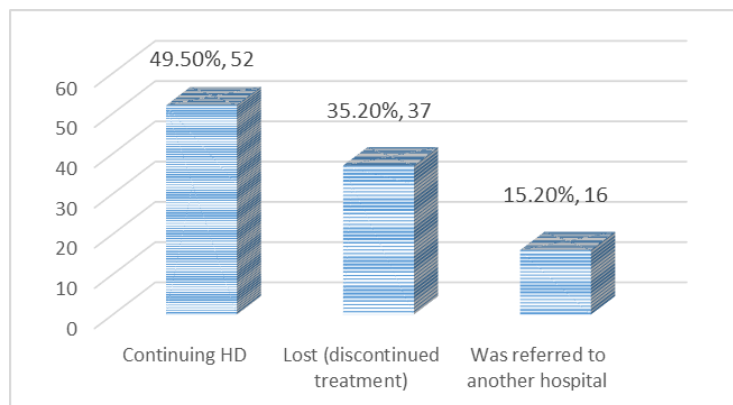


Figure 2. Distribution of Censored Data in DM Patients with HD at RSI Jemursari from 2016 to 2019

The youngest patient is 35 years old, the oldest is 89 years old, and the average data is 58-year-old. A description of sex and occupation and records of the disease can be seen in Table 1.

The patient's survival time is measured in units of

weeks. The Kaplan Meier analysis results obtained an estimate of the DM patients with HD's average survival time at RSI Jemursari in 2016-2019, i.e., 182 weeks, illustrated in Figure 3.

Tabel 1. Distribution of Sex, Occupation, Records of DM Patients with HD at RSI Jemursari from 2016 to 2019

Variable	Category	Frequency	Percentage (%)
Sex	Female	55	43.7
	Male	71	56.3
Occupation	Housewife	48	38.1
	Work	33	26.2
Records of Hypertension	Retired	45	35.7
	Yes	98	77.8
Records of Lung Disease	No	28	22.2
	Yes	40	31.7
Records of Heart Disease	No	86	68.3
	Yes	95	75.4
	No	31	24.6

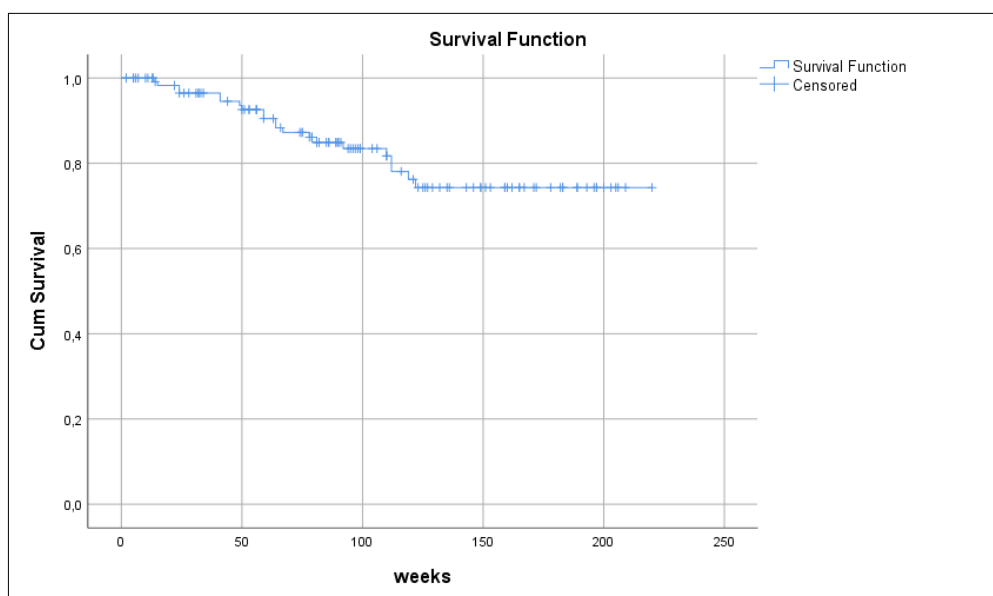


Figure 3. Estimated Curve Probability of Survival of DM Patients with HD at RSI Jemursari in 2016-2019

Male patients have a higher average survival time compared to females. The description of status and the

average survival time of DM patients with HD by sex can be seen in Table 2.

Table 2. Description of Status and Average Survival Time of DM Patients with HD Based on Sex at RSI Jemursari in 2016-2018

Sex	Status		Average survival time
	Passed Away	Censored	
Female	9 (16.4%)	46 (83.6%)	171 weeks
Male	12 (16.9%)	59 (83.1%)	183 weeks

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Patients who work have better survival and the highest average survival time. Description of status and the average survival time of DM patients based on occupation can be seen in Table 3.

Description of status and the average survival time of DM patients with HD based on disease records can be seen in Table 4.

Table 3. Description of Status and Survival Time of DM Patients with HD Based on Occupation at RSI Jemursari in 2016-2018

Profession	Status		Average survival time
	Passed Away	Censored	
Housewife	7 (14.6%)	41 (85.4%)	174 weeks
Working	4 (12.1%)	29 (87.9%)	193 weeks
Retired	10 (22.2%)	35 (77.8%)	164 weeks

Table 4. Description of Status and Survival Time of DM Patients with HD Based on Patients' Disease Records at RSI Jemursari in 2016-2018

Disease Records	Status		Average survival time
	Passed Away	Censored	
Hypertensio Yes	14 (14.3%)	84 (85.7%)	187 weeks
n No	7 (25.0%)	21 (75.0%)	138 weeks
Lungs Yes	7 (17.5%)	33 (82.5%)	169 weeks
No	14 (16.3%)	72 (83.7%)	184 weeks
Heart Yes	18 (18.9%)	77 (81.1%)	169 weeks
No	3 (9.7%)	28 (90.3%)	199 weeks

Table 5. Stages of survival modeling for DM patients with HD at RSI Jemursari in 2016-2018

Step	Variable	P	B	Exp (B)	
1	Sex	0.260	1,950	7,032	
	Profession	housewife vs. retired	0.084	0.032	-2,001
		working vs. retired		0.828	0.142
		Age		.001	0.096
	Records of Hypertension	0.080	0.899	2,458	
	Records of Lung Disease*	0.431	-0.393	0.675	
2	Records of Heart Disease	.334	-0,631	0.532	
	Sex	0.025	1,935	6,925	
	Profession	housewife vs. retired	0.074	0.026	-2,049
		working vs. retired		.901	.81
		Age		0.002	0.090
	Records of Hypertension	.107	0.798	2,221	
Records of Heart Disease*	0.329	-0,636	0.529		
3	Sex	0.033	1,847	6,338	
	Profession*	housewife vs. retired	0.097	0.034	-1,993
		working vs. retired		0.939	-0,51
	Age	0.001	0.090	1,095	
Records of Hypertension	0.069	.887	2,428		
4	Sex*	0.836	0.091	1,096	
	Age	0.002	0.075	1,078	
5	Records of Hypertension	0.088	0.810	2,247	
	Age	0.002	0.075	1,078	
6	Records of Hypertension*	0.090	0.805	2,237	
	Age	0.004	0.068	1,070	

Note : * = eliminated because $P > 0.05$

The dependent variable in this model is patient survival time (weeks). The independent variables used included age (years) and several categories of variables, sex, occupation, records of hypertension, lung, and heart

disease. All variables meet the proportional hazard assumption; therefore, Cox Regression Proportional Hazard was performed. Modeling was done using the backward method.

Records of lung disease have no significant effect on the survival of DM patients with HD. Records of heart disease were also eliminated from the survival model of DM patients with HD. Occupation and sex are the next variables that were eliminated from the model. The final step in forming the model is to eliminate records of heart disease. Table 5 shows that only the patients' age affects the survival of DM patients with HD, with a P of 0.004 and Exp (B)1.07. The survival model of DM patients with HD can be written with the formula:

$$h_{(t)} = ho_{(t)}e^{(0,068*age)}$$

Discussion

The percentage of DM patients with HD that are over 58-year-old is 50%. Research at RS (Hospital) Dr. Moewardi Surakarta showed that 14.7% of DM patients with renal failure complications, aged 40-55 year old, and 11.76% aged 61-65-year-old (8). Research at RS Dr. Soetomo Surabaya stated that the survival time of patients with CKD with HD aged 46-65-year-old is lower than those aged 26-45-year-old (9).

Male are more susceptible to diabetes with complications of kidney failure than female. The results showed that the percentage of males who suffer from DM with HD is 56.3%. Research results at RS Dr. Moewardi Surakarta, male is 1.61 times more likely to get DM, and 61.76% have kidney failure (8). In a study of chronic kidney patients with HD at RS Dr. Soetomo Surabaya, 54.9% were male patients (9). Male have higher survival time than female. The average survival time for male patients was 183 weeks, while for female patients, it was 171 weeks. Male have a survival time of 3 months longer than female. Research at RS Dr. Soetomo Surabaya in chronic kidney patients with HD, the average survival of male patients was 68.84 months, whereas in female patients 66.29 months (9).

DM with HD is more susceptible to housewives (38.1%) and patients whom retired (35.7%). Research at RS Dr. M Djamil Padang showed the percentage of DM patients with chronic kidney disease and were retired by 58.1% (10). Research in Semarang showed that patients with type-2 DM are dominated by housewives (68.3%) and retirees (11.1%). Housewives and retirees tend to have no intense or strenuous physical activity. Older age causes reduced activity, so the activities carried out daily are relatively mild physical activities (11). People with DM who do not work have lower survival time, 22.2% deaths, and average survival time of 164 weeks. DM patients with HD who work have the longest average survival time of 193 weeks, and only 12.1% deaths.

DM patients with HD who had hypertension records were 77.8%. Patients without hypertension records are reaching 25% of deaths. Patients with hypertension records are only by 14.3% deaths. Patients with hypertension records had an average survival time of 49 weeks longer than patients without records. This result is not in line with Yulianto's study, which states that CKD patients with HD and have hypertension records have lower survival times than those without records (9).

Some research results support the results of this research analysis. Research at RS Dr. R. Sosodoro Djatikoesomo showed that the survival time of kidney failure patients undergoing HD does not differ based on hypertension status (12). Ekantri research, on the other hand, showed that there is no relationship between hypertension and CKD patients' deaths undergoing HD (13). Furthermore, research at RS Dr. H. Soewondo showed that there is no relationship between hypertension and the incidence of DM (14).

Hypertension is the effect of many diseases in chronic disease patients. Hypertension can cause strokes, coronary heart disease, impaired kidney function, impaired vision, insulin resistance (14). Hypertension has not been proven to cause death because it can be treated with antihypertensive drugs (13). The mechanism that links hypertension with insulin resistance is also unclear (14). In this study, hypertension records in DM patients with HD at RSI Jemursari could have occurred quickly and recovered with antihypertensive drugs or other measures.

DM patients have decreased immunity, making them susceptible to infections, including respiratory infections. Only 31.7% of DM patients with HD at RSI Jemursari had lung disease records. This result does not follow the Pertiwi statement; 60% of patients with CKD have pulmonary complications (15). The survival time of DM patients with HD who have a history of lung disease is lower than those without records, and 17.5% deaths. DM patients with HD who have lung disease records passed away 20 weeks faster than those who do not have records. The results of this study are in line with Imanina research; there is an influence of respiratory infection on the length of survival of patients with CKD (16). Respiratory infections in people with DM are four times more likely to cause death than in non-DM patients. Lower respiratory tract infections in DM patients are mostly caused by the bacteria *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Streptococcus pneumonia* (17). These bacteria develop and grow in the human body and can cause pneumonia, sinusitis, otitis, bronchitis, bacteremia, meningitis, and

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other infections (18).

Lungs and kidneys have a physiological relationship, namely regulators of electrolyte balance and microenvironment protection for cell function. Disorders in the lungs arise as a direct result of kidney disease or due to a systemic process involving both organ systems simultaneously. The effect of HD on CKD patients is associated with changes in fluid body volume. Dialysis causes a reduction in lung fluid content, which causes a reduction in pulmonary edema and small airway obstruction (15).

DM patients with HD at RSI Jemursari who have heart disease records by 75.4% and 18.9% died. DM patients with HD who have heart disease records passed away 30 weeks sooner than those without records. In a study at RS Kuningan, DM patients were 32 times more at risk of developing acute myocardial infarction than non-DM patients (19). Research at RS Tugurejo Semarang showed a significant relationship between the incidence of type-2 diabetes and the incidence of ischemic heart disease (20). Research at RS Dr. Kariadi Semarang stated that there is a relationship between the severity of chronic kidney failure and the incidence of coronary heart disease (21). Patients diagnosed with heart failure and Coronary Artery Disease tend to have Chronic Kidney disease, with a prevalence rate of 60% (22). The heart and kidneys have an interaction called Cardiorenal Syndrome, which has a strong relationship with heart failure. However, it is caused by a decrease in cardiac output and the activation of the Reticular Activating System, an imbalance between nitric oxide, inflammation, anemia, and increased sympathetic nerve activity (23).

Records of lung disease, heart disease, and hypertension are factors that have no effect on the survival time of DM patients with HD. Occupation and sex also do not affect the resilience of DM patients with HD. This condition is in line with Yulianto's study, which stated that there is no difference in CKD patients' survival time based on sex and hypertension records (9).

Age is the only significant factor in affecting patient survival. Based on the study results, if the age increases by one year, then the risk of patients' deaths also increases by 1.07. This result is supported by Yulianto's research, which showed a significant difference in the survival time of patients with CKD based on age (9).

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