EDUMATSAINS
JURNAL PENDIDIKAN MATEMATIKA DAN SAINS
E-ISSN:2527-7235
Volume 9 Issue. 2 January, 2025, pp 119-131
http://ejournal.uki.ac.id/index.php/edumatsains

Survival Analysis with Weibull Regression on The Rate of Healing of Diabetes Mellitus Patients

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Article Info
Article history:
Received : December 24, 2024
Revised : January 15, 2025
Accepted : January 21, 2025
Available online : January 31, 2025

https://doi.org/10.33541/edumatsains.v9i2.6490

Abstract
Survival analysis is a statistical technique used to study survival related to time, starting from the initial time of the study that has been determined until the end time of the study, therefore the purpose of this study was to determine the equation of the Weibull regression model of the clinical condition of patients with diabetes mellitus at the Malahayati Islamic Hospital Medan and what factors affect the rate of recovery of the clinical condition of patients with diabetes mellitus. The type of research used in this paper is Applied Research, from data collection and analysis, the results are obtained based on the Kaplan-Meier curve, visually it can be seen that the longer the coronary heart disease patient recovers (t). the less likely they are not to recover until time t. The Kolmogorov-Smirnov test was used to test the Weibull distribution, which describes the survival time of patients with diabetes mellitus. The partial test results indicate that the variables of gender, age, hyperglycemia, hypertension, and complications significantly impact the model. The following is how the Weibull regression model for the recovery time data of patients with diabetes mellitus was acquired for this study:

$$S(t|x) = exp(-exp(1.42219 + (-0.01018)x1 + 0.03942x2 + (-0.02976)x3 + (-0.01887)x4)\, t)\, \alpha$$

Keywords: Survival Analysis, Diabetes Mellitus, Weibull Regression

1. Introduction

Diabetes mellitus, also known as diabetes, is a long-term condition that can last a lifetime. Increased blood sugar or hyperglycemia caused by decreased pancreatic insulin levels is a sign of metabolic disorders that cause Diabetes Mellitus (DM) (Amalliah et al., 2024). Diabetes mellitus can cause various complications, both macrovascular and microvascular. DM can cause cardiovascular disorders, which if not treated immediately, can increase the risk of hypertension and heart infarction (Lestari et al., 2021).

The International Diabetes Federation (IDF) estimates that 537 million people globally have diabetes in 2021, and that figure is projected to rise to 643 million in 2030 and 783 million in 2045. With 19.5 million diabetics in 2021 and an estimated 28.6 million in 2045, Indonesia is seventh in the world for the highest number of diabetics. The Ministry of Health is paying attention to this

problem because diabetes mellitus is the mother of all diseases. Like a mother, diabetes can "give birth" to various other diseases (Adli, 2021).

Data from the 2018 Basic Health Research (Riskesdas) shows that, based on districts and cities in North Sumatra Province, there are diabetes mellitus patients diagnosed by health services or have the highest symptoms in Pakpakbarat (1.6%), Medan City (1.2%), Tebing Tinggi City (1.5%), Padang Sidempuan City (1.3%), Mandailing Natal (1.3%), and the lowest in Samosir (0.2%) (Tambunan et al., 2024).

There are two types of DM risk factors: modifiable and non-modifiable ones. Factors like age, gender, and genetics are unchangeable. Most frequently, these risk factors manifest themselves after the age of 45 or older (Nurhayani, 2022). Diet, smoking, obesity, high blood pressure, stress, physical exercise, and alcohol use are other modifiable risk factors. If BMI is more than 23 can cause higher blood glucose, obesity is related to blood glucose levels (Nasution et al., 2021).

As organisations involved in the provision of health services, hospitals have changed. Hospitals served as social institutions when they first started out, but today they are more well-known as health care sectors with management modelled after that of commercial entities. Malahayati Islamic Hospital Medan is a type C Private General Hospital with excellent cardiac catheterization laboratory services. The doctor on duty is always in the ER or in the room needed by patients who need medical care at the Malahayati Islamic Hospital (RSIM). To help people who need immediate hospital services, this facility is provided for 24 hours (Harahap, 2021). Malahayati Hospital continues to show its commitment by developing and improving its services and updating hospital facilities and infrastructure to provide comfort and safety for both patients and employees. Malahayati Hospital has a VISION of "*becoming a hospital that can provide health services for everyone*", and has a MISSION of "*improving employee welfare and satisfaction*" (Meutia, 2021).

Survival analysis is a statistical technique used to study survival related to time, starting from the initial time of the study that has been determined until the end time of the study (Mukaromah, 2020). Therefore, survival analysis requires the amount of time a person spends to survive. Death, illness, recurrence of a disease, birth, graduation from school, recovery from a disease, or response to an experiment conducted in a study can be included in the category of failure events (Widyawati & Bekti, 2020). One of the distributions of continuous random variables that is frequently used to examine environmental and failure time data is the Weibull distribution. In the univariate Weibull distribution, there are three parameters: shape, scale, and location. The scale-shape version, or scale version, includes shape and scale parameters. In many cases, external factors, such as independent variables or covariates, affect the response data in the field, so distribution modeling is needed. Only determining the parameters of the response data distribution, such as the probability density function, survival function, and hazard function, is covered in the discussion of the Weibull distribution (Faisal et al., 2020). A Weibull distribution with independent variables makes up the Weibull regression model (Akbar et al., 2020). Weibull regression is an evolution of the Weibull distribution, which contains covariates or independent variables, so that the scale parameters or shape of the Weibull distribution can be represented in the regression model (Panduwinata et al., 2022).

By applying the Weibull regression method as an analytical tool, this study makes a significant contribution to the development of the theory of diabetes mellitus. The scientific novelty of this study lies in the application of this method in the context of diabetes mellitus disease which has never been used before. Readers are encouraged to read this study as it provides new insights into how the Weibull Regression model can be applied to predict and understand the pattern of Diabetes Mellitus disease progression in a more effective and efficient manner. This method also allows for more accurate modeling compared to existing traditional methods.Based on this background, the research conducted by the author is related to **"Survival Analysis Using Weibull Regression on the Healing Rate of Diabetes Mellitus Patients."**

2. Methods

Applied research is a type of research used to address problems in society, industry, or government, and is a continuation of basic research. The purpose of this research is to implement, test, and evaluate the effectiveness of theories in solving real problems. In this study, a quantitative approach was applied to measure research results, from data collection to analysis and interpretation of the results.

This research was conducted at the Malahayati Islamic Hospital, Jl. Pangeran Diponegoro No.2-4 Medan. The time of this research was conducted from May 2024 until completion. The population used in this study utilized all inpatients registered with Diabetes Mellitus at the Malahayati Islamic Hospital, Medan.

Descriptive Analysis of Each Independent Variable

Analysis of variables that affect the survival time of coronary heart patients, including censored and uncensored patients, and the proportion of each category for each variable.

1. Kaplan Meier Estimation

One of the best statistical methods for calculating the probability of a person's survival in a certain period of time, which is generally used to summarize survival experiences. Creating, testing, and analyzing Kaplan Meier curves based on independent variables. Kaplan Meier estimation is carried out to calculate the survival curve based on survival time data. The Kaplan Meier model equation (Ramadhani, 2020) is written as follows:

$$\hat{S}(t) = \prod_{i:\, t_i < t} \left(1 - \frac{d_i}{n_i}\right)$$

2. Conducting a Log-Rank Test

A method for comparing the relationship between two groups under various conditions. The results of the log rank test can show whether the two groups affect the survival time and survival function the same or not. The Kaplan Meier curve formed in each category shows a statistically

significant difference, which is indicated by the log rank test. For its analysis, the log rank test uses the hypothesis:

$H_0 = S_1 (t) = S_2 (t)$, meaning that there is no significant difference between the 2 survival functions.
$H_1 = S_1 (t) \neq S_2 (t)$, meaning that there is a significant difference between the 2 survival functions.
The test results are determined by the p-value at a significance of 0.05 as follows:

a) If the calculated p-value> 0.05 then there is no difference in the 2 survival functions, so accept H_0 and reject H_1
b) If the calculated p-value <0.05 then there is a difference in the 2 survival functions., so accept H_0 and reject H_1 (Sukarma & Anggraini, 2023).

3. Distribution fit test

The test of data distribution, or distribution, is performed to determine the appropriate distribution during survival time. The Kolmogorov-Smirnov test, a chi-square goodness-of-fit test that relies on adequate sample size to verify the validity of the method, is used to determine whether the sample variables come from a population with a specific distribution. The hypothesis $h(t) = \beta\gamma t^{\gamma-1}$ (Harnikayani Hasa & Nadjib Bustan, 2022) used is as follows:

H_1 : The dependent variable (survival time) follows the Weibull distribution
H_0 : The dependent variable (survival time) does not follow the Weibull distribution

4. Parameter significance test

The scale (β) and shape (Y) parameters of the survival model that follows the Weibull distribution have Accelerated Failure Time (AFT). The AFT formula of the Weibull distribution is as follows.

$$S(t) = 1 - F(t)$$
$$= 1 - \left(1 - \exp\left(-\left(\frac{t}{\beta}\right)^{\gamma}\right)\right)$$
$$S(t) = \exp(-\beta t^{\gamma})$$

Accelerated Failure Time (AFT) can be calculated by plotting survival time (t) for each independent variable, which produces a parallel pattern. The equation shows the Weibull regression hazard function

Where: $\beta = \exp(a_0 + a_1x_1 + a_2x_2 ..... a_j x_j)$ with t is the survival time, X is the independent variable.

3. Result and Discussion

Typically, descriptive statistics are employed to characterise the properties of the data that will be examined. Descriptive statistical analysis was used in this study to give a summary of the features of the data pertaining to the rate of recovery of patients with diabetes mellitus and the variables thought to affect it. Table 1 displays information on age and survival time.

Table 1. Descriptive Statistics

Descriptive Statistics					
	N	**Minimum**	**Maximum**	**Mean**	**Std. Deviation**
Time	470	0	367	4.94	17.454
Age	470	20	90	60.76	10.848
Valid N	470				

According to Table 1's data, patients with diabetes mellitus spent an average of 5 days in the hospital, with a standard deviation of 17.454. The longest hospital stay was 367 days, while the shortest was 0 days. Furthermore, the data indicates that individuals with diabetes mellitus are 60 years old on average, with a standard deviation of 10.848. The oldest patient with diabetes mellitus is 90 years old, and the youngest is 20. These quantitative variables are presented in the descriptive statistical analysis above (Tuanaya et al., 2024).

According to the Weibull regression model, the data follows a Weibull distribution. This may not always hold true, but can also be affected by errors in handling categorical data, outliers, and large amounts of truncated data, which can reduce the accuracy of the estimates. In addition, this model is not suitable for long-term predictions and is not suitable for continuous or ordered data. As a result, to improve the validity and accuracy of the analysis results, it is necessary to apply additional methods or alternative models.

3.1. Kaplan-Meier Curve Analysis and Log Rank Test

3.1.1. Gender Factor

Gender is one of the factors suspected to affect the recovery rate of diabetes mellitus patients. *Kaplan-Meier survival* curves based on gender are shown in Figure 1 below.

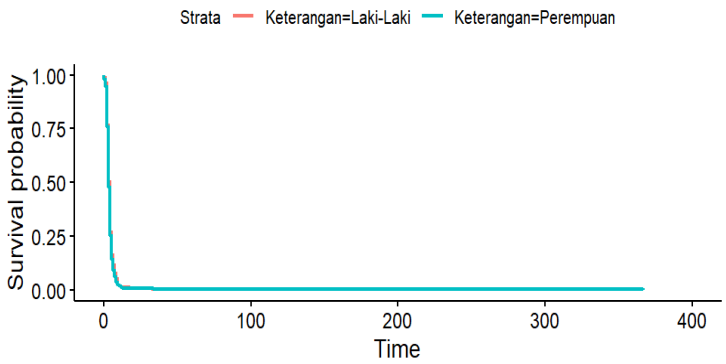

Figure 1. Survival Curve of Gender Factor

According to the statistics in Figure 1, individuals with diabetes mellitus who are female have a higher likelihood of surviving than those who are male. This is because the average curve of female diabetes mellitus patients is lower than that of male patients. However, because the visual meaning of the difference is considered statistically insignificant, it is necessary to test the significance using the *Log Rank test*. As a result, the X2 Table value of 3.841 is more than the *Log Rank* value of 0.5. Therefore, the conclusion that can be made is that patients with diabetes mellitus who are male and female do not significantly differ in their recovery times.

3.1.2. Age Factor

In addition to gender factors, age factors are also thought to affect the rate of recovery of diabetes mellitus patients. Figure 2 below displays the *Kaplan-Meier survival curve* based on age factors in diabetes mellitus patients.

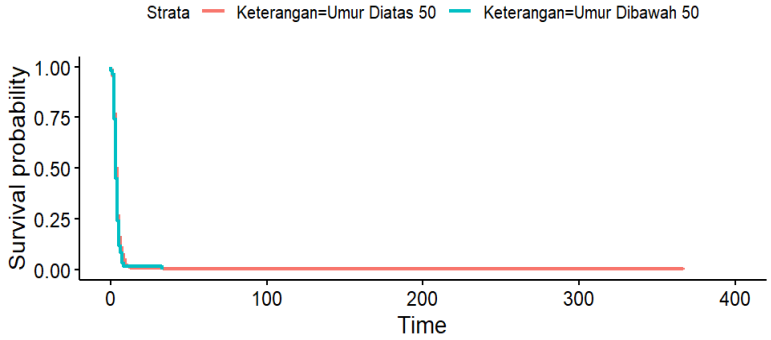

Figure 2 Age Factor Survival Curve

According to the data in Figure 2, individuals with diabetes mellitus before 50 years of age had a higher likelihood of surviving than those over 50. This is due to the fact that patients with diabetes mellitus under 50 have a lower average curve than patients over 50. However, because the visual meaning of the difference is considered statistically insignificant, it is necessary to test the significance using the *Log Rank test.* The result is a *Log Rank* value of 0.4, which is less than the

X^2 Table value of 3.841. Therefore, it may be concluded that there is no discernible difference in the recovery time between those with diabetes mellitus who are under 50 and those who are over 50.

3.1.3. Hyperglycemia Factors

The pace of recovery for people with diabetes mellitus is believed to be influenced by age, gender, and hyperglycemia variables. The Kaplan-Meier survival curve for patients with diabetes mellitus based on age variables is displayed in Figure 3 below.

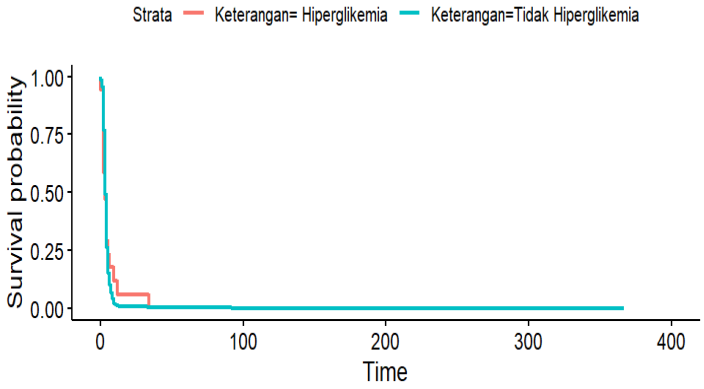

Figure 3. Hyperglycemia Factor Survival Curve

Non-hyperglycemic diabetes mellitus patients have a higher chance of survival than hyperglycemic diabetes mellitus patients, as shown by the data in Figure 3. This is because the average curve of non-hyperglycemic diabetes mellitus patients is lower than the curve of hyperglycemic patients. However, because the visual meaning of the difference is considered statistically insignificant, it is necessary to test the significance using the *Log Rank test.* The result is a *Log Rank* value of 0.4, which is less than the X^2 Table value of 3.841. Therefore, it may be concluded that patients with diabetes mellitus who are hyperglycaemic and those who are not have no appreciable variation in recovery times.

3.1.4. Hypertension Factors

Other characteristics that are believed to influence the rate of recovery for patients with diabetes mellitus include age, gender, hyperglycemia, and hypertension. The Kaplan-Meier survival curve for patients with diabetes mellitus based on age variables is displayed in Figure 4 below.

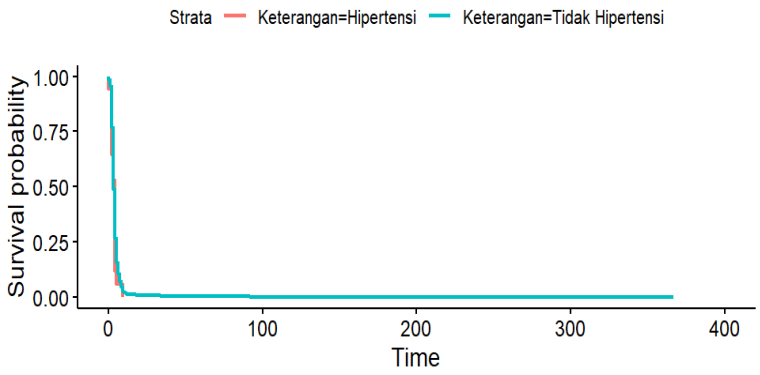

Figure 4. Hypertension Factor Survival Curve

Non-hypertensive diabetes mellitus patients have a higher chance of survival than hypertensive diabetes mellitus patients, as shown by the data in Figure 4. This is because the average curve of non-hypertensive diabetes mellitus patients is lower than the curve of hypertensive patients. However, because the visual meaning of the difference is considered statistically insignificant, it is necessary to test the significance using the *Log Rank test.* The result is a *Log Rank* value of 0.4, which is less than the value of 3.841. Therefore, it may be concluded that patients with diabetes mellitus who have hypertension and those who do not have it do not significantly differ in their recovery times.

3.1.5. Complication Factors

In addition to gender factors, age factors, hyperglycemia factors, hypertension factors, complication factors are also thought to affect the rate of recovery of diabetes mellitus patients. Figure 5 below displays the *Kaplan-Meier survival curve* based on age factors in diabetes mellitus patients.

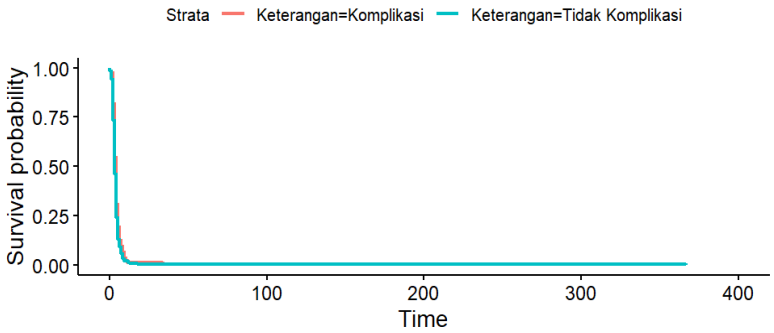

Figure 5 Survival Curve Complication Factors

According to the statistics in Figure 3, patients with uncomplicated diabetes mellitus had a higher likelihood of surviving than those with severe diabetes mellitus. This is due to the fact that persons with uncomplicated diabetes mellitus typically have a lower curve than those with problems. However, the significance must be tested using the Log Rank test because the difference's visual meaning is deemed statistically unimportant. As a result, the Log Rank value is

smaller than the value of 3.841, at 0.03. Therefore, it may be concluded that individuals with difficulties and those with uncomplicated diabetes mellitus do not significantly differ in their recovery times.

3.2. Data Distribution Testing

The data distribution test was conducted using Kolmogorov-Smirnov to determine the distribution followed by the survival time data. The hypotheses used in this test are as follows:

H_0: Survival time follows the Weibull distribution

H_1: Survival time does not follow the Weibull distribution

Table 2. Kolmogorov Smirnov Output Results

Kolmogorov Smirnov	
Sample Size	470
Test Statistic	0,062

Because $D_{hitung} < D_{tabel}$` H_0 is accepted, which means that the coronary heart patient data follows the Weibull distribution. The Dhitung value is 0.062 and Dtabel is 0.086 with a value of α = 0.05. (Mukaromah, 2020)

3.3. Weibull Regression Modeling

3.3.1. Weibull Regression Test Results

By using the following function of Weibull regression analysis, the medical records of diabetes mellitus patients at Malahayati Islamic Hospital in 2023 showed an increase.

```
Weibull distribution
Loglik(model)= -736   Loglik(intercept only)= -752.2
      Chisq= 32.4 on 4 degrees of freedom, p= 1.6e-06
Number of Newton-Raphson Iterations: 6
n= 470
```

Figure 6. Overall Test of Weibull Regression Model

It can be seen from the output in Figure 1 above that with a significance level of $\propto$5% = 0.05, p - value = 1.6e - 06 = 0.0000033 < 0.05. However, the variable X^5 is not significant, as shown by the results of the dropterm() function in Figure 4.8. Therefore, the regression test must be repeated to eliminate these variables.

Table 3. Partial Test Results of Weibull Regression Model 1

	Nilai Value	Nilai Std. Error	Nilai Z_{hitung}	Nilai p
(Intercept)	1.43761	0.04856	29.61	< 2e – 16
x1	-0,00096	0.00364	-2.73	0.0063
x2	0.03948	0.01017	3.88	0.0001

x3	-0.02958	0.00695	-4.26	2.1e – 05
x4	-0.01877	0.00772	-2.43	0.0151
x5	-0.00430	0.00444	-0.97	0.3331
Scale = 0.312				

Table 4. Results of the dropterm() Test for the Weibull Regression Model 1

	Df	AIC	LRT	Pr (Chi)
< none >		4832.8		
x1	1	4835.0	4.1705	0.041133*
x2	1	4847.3	16.5031	4.857e - 05*
x3	1	4841.1	10.2945	0.001334*
x4	1	4835.7	4.8619	0.027616*
x5	1	4831.5	0.7285	0.393385

Table 5. Weibull Regression Model 1

AIC	L. Model	L. Intercept	Chi Square	p – value
4832.8	-735.6	-752.2	33.27	3.3e – 06

After the variable X^5 was removed, the following results were obtained.

```
Weibull distribution
Loglik(model)= -736   Loglik(intercept only)= -752.2
      Chisq= 32.4 on 4 degrees of freedom, p= 1.6e-06
Number of Newton-Raphson Iterations: 6
n= 470
```

Figure 7. Overall Test of Weibull Regression Model 2

The output of Figure 1 shows that p - value = 1.6e - 06 = 0.0000016 < 0.05 with a significance level of α(= 5%.

Table 6. Uji Parsial Model Regresi Weibull 2

	Value	Value Std. Error	Value Z_{hitung}	P- Value
(Intercept)	1.42219	0.4577	**31.07**	< 2e – 16
x1	-0,01018	0.00360	-2.83	0.00472
x2	0.03942	0.01017	3.88	0.00011
x3	-0.02976	0.00692	-4.30	1.7e – 05
x4	-0.01887	0.00771	-2.45	0.01444
Scale = 0.312				

Table 7. Results of the Dropterm Test of the Weibull Regression Model 2

	Df	AIC	LRT	Pr (Chi)
< none >		4831.5		
x1	1	4834.0	4.4283	0.035348*
x2	1	4845.9	16.3222	4.343e - 05*
x3	1	4840.0	10.4528	0.001225*
x4	1	4834.4	4.8801	0.027164*

The following is a summary table of the Weibull regression results for the second model:

Table 8. Weibull Regression Model 2

AIC	L Model	L. Intercept	Chi Square	p – value
4831.5	-736	-752.2	32.4	1.6e – 06

The independent variables, x1, x2, x3, x4 and x5, shown in Figure 6, have been shown to be significant to the model. The *p-value* is also less than 0.05. However, the Weibull regression model 2 is the best to show how long it takes to recover from diabetes mellitus patients, because the AIC value between the Weibull model 2 and 1 is greater. This model is described as follows in the summary.

Table 9. Weibull Regression Model Summary

Model Regresi	Coeficient	Z hitung	p-value	Information
Intercept	1.42219	31.07	< 2e - 16	Reject H_0
x1 (Gender)	-0.01018	-2.83	0.00472	Reject H_0
x2 (Age)	0.03942	3.88	0.00011	Reject H_0
x3 (Hyperglycemia)	-0.02976	-4.30	1.7e - 05	Reject H_0
x4 (Hypertension)	-0.011887	-2.45	0.01444	Reject H_0

With an intercept value = 1.42219, scale value = 0.312, and shape = 1/0.312 = 3.205, the Weibull regression model that can be formed based on equation 2.11 is as follows:

$$S\,(t|x) \;=\; exp\,(-exp\,(1.42219 + \;(-0.01018)x1 \;+\; 0.03942x2 \;+\; (-0.02976)x3$$

$$+\,(-0.01887)x4\,)\;t\,)\alpha$$

In addition, the hazard function for the Weibull regression model can be constructed based on equation 2.12 as follows:

$$h\,(t|x) \;= \propto (\,(\,\exp\,(-\exp\,(1.42219 + \;(-0.01018)x1 \;+\; 0.03942x2 \;+\; (-0.02976)x3$$

$$+ (-0.01887)x4))$$

$$(exp ((1.42219 + (-0.01018)x1 + 0.03942x2 + (-0.02976)x3 + (-0.01887)x4))t)\alpha - 1$$

4. Conclusion

Based on the *Kaplan-Meier curve,* it can be seen visually that the longer the coronary heart disease patients experience recovery (t), the less likely they are not to recover until time t. According to the Kolmogorov-Smirnov test, the Weibull distribution describes the survival time of individuals with diabetes mellitus.

Gender, age, diabetes, hypertension, and complications all significantly impact the model, according to the partial test results. The Weibull regression model for the recovery time data of individuals with diabetes mellitus is derived as follows in this study.

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