

Survival analysis of the recovery rate of typhoid fever using the Kaplan-Meier and Nelson-Aalen methods

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Abstract

Typhoid fever remains a health problem with a high incidence in Indonesia. This study analyzes the recovery rate and identifies factors influencing the recovery of typhoid fever patients using the Kaplan-Meier, Nelson-Aalen, and Cox Proportional Hazard models. This quantitative study was based on data from 400 inpatients at Medan Haji General Hospital from January to December 2024. The variables studied included age, gender, type of antibiotic, and comorbidities. The results showed a median recovery time of five days, with a sharp decline after the fourth day. Patients without comorbidities had a higher chance of recovery, and comorbidities were shown to significantly influence the recovery rate ($p < 0.001$; HR = 1.626), while other variables were insignificant.

Keywords: Typhoid Fever; Survival Analysis; Kaplan-Meier; Nelson-Aalen; Cox Proportional Hazards

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INTRODUCTION

Typhoid fever (*Typhus*), commonly known as typhoid, is a life-threatening infection caused by the bacteria *Salmonella typhi* (Manesh et al., 2021). Typhoid fever is generally transmitted through the consumption of contaminated food or water (Kim et al., 2023). Effective treatment for typhoid caused by *Salmonella typhi* is with antibiotics (Shaikh et al., 2023). However, increasing resistance to antibiotics makes the disease more easily spread, especially in areas without access to clean water and proper sanitation (Jani et al., 2021). Typhoid fever can be confirmed through a blood test. The main risk factors contributing to the high incidence of typhoid fever in Indonesia include the relationship between personal hygiene and hand washing habits (Saini et al., 2024).

This disease is included in the top ten types of diseases that most often require hospital treatment (Kaunang et al., 2022). In Indonesia, typhoid is ranked third among ten diseases with the highest number of hospitalizations, with 55,098 cases (Indonesian Health Profile, 2011). The incidence of typhoid fever in Indonesia tends to increase every year, with an average incidence of 500 per 100,000 population and an estimated mortality

rate of between 0.6% and 5% (Marchello et al., 2020). The factor that influences health problems is the level of knowledge, which means that if knowledge about Typhoid Fever is still low, then the possibility of this disease occurring will be higher (Garrett et al., 2022).

Survival analysis is a statistical method that examines the time until a specific event or incident occurs (Lee, 2023). The probability that an object is said to have resilience is that it can function without experiencing an event (such as death or recovery) within a specific predetermined time period and under specific predetermined conditions (Mulu et al., 2021). In resilience analysis, three terms must be understood. First, the time an individual survives the observation period (Widyasari et al., 2022). Second, the event or variable that serves as the focal point of a study. The third term is censoring, which occurs when the survival time of an individual as a subject cannot be fully observed (Masten et al., 2021).

The Kaplan-Meier method, introduced by Kaplan and Meier in 1958, is a non-parametric method used to estimate survival functions. Kaplan and Meier considered non-parametric estimation of survival functions from incomplete or censored data in 1958 (Saranya and Karthikeyan, 2015). They solved the problem of estimating survival curves straightforwardly while properly accounting for censoring. The Kaplan-Meier method is suitable for use when there are no assumptions about the functional distribution of the hazard rate with time (Baek et al., 2021). Survival probabilities can be estimated non-parametrically from observed failure times; this method can be applied to both censored and uncensored data (Saranya and Karthikeyan, 2015). On the other hand, the Nelson-Aalen estimator, developed by Aalen in 1978, offers an alternative approach to survival analysis by focusing on estimating the cumulative hazard function (Ditzhaus et al., 2023). This method has the advantage of providing a better understanding of the risk of an event at each time point (Chen et al., 2021).

A study conducted by Dianti et al. (2023), entitled "Analysis of the Nelson-Aalen Curve Using the Weighted Log Rank Test," concluded that the test results showed no difference in survival rates based on age, hypertension, random blood sugar levels, and diabetic foot conditions. However, there were differences in survival rates based on gender and a balanced diet, meaning that both factors influence the survival rate of Type II Diabetes Mellitus patients at Sayang Regional Hospital, Cianjur Regency. In line with

research (Ananda et al., 2024), the results of the Kaplan-Meier analysis revealed that 94.3% of patients experienced peak events or incidents on the second day. Of all patients, only three people were called due to improved health conditions. On the second day, the probability of survival was recorded at 0.943. The results of the Log Rank test showed a significant difference in the probability of survival based on age groups and different comorbidities. It can be concluded that only variables based on age and comorbidities have a substantial difference in the length of hospitalization of patients with Type II Diabetes Mellitus at Kuala Pembuang Regional Hospital. However, most studies use only one analytical method. Therefore, similar research is needed in typhoid fever patients to determine differences in recovery rates. Fever occurs when the body temperature exceeds 37.5°C, a natural response to infection (Syuhefti et al., 2021). This study aims to analyze the recovery rate of typhoid fever patients using the Kaplan-Meier and Nelson-Aalen methods and identify the factors that influence it. The results are expected to benefit agencies and the community in their efforts to prevent typhoid.

METHODS

This research is quantitative. According to Sugiyono (2023), quantitative research is a method based on the philosophy of positivism, meaning data are collected in numerical form and analyzed using statistical techniques to determine the relationship between variables. The study was conducted at the Haji General Hospital in Medan, located at Jl. Haji Hospital No. 47, Baru Percut Sei Tuan Village, Deli Serdang Regency, North Sumatra. Secondary data were obtained from the medical records of existing inpatients, including age, gender, type of antibiotic, history of comorbidities, and the patient's recovery time.

Kaplan-Meier

The Kaplan-Meier method is one of the most effective statistical methods for estimating the probability of survival of observed objects within a specified time interval immediately after treatment initiation. Despite all the challenges associated with the research object, the Kaplan-Meier approach is the most straightforward statistical process for estimating the survival of an object over time. The Kaplan-Meier curve can be used to identify events, censored data, and calculate the probability of (Darmawan & Lubis, 2023).

$$S(t) = \begin{cases} 1 & \text{if } t < t_i \\ \prod_{t_{(i)} \leq t} \left(1 - \frac{d_i}{n_i}\right) & \text{if } t_i \leq t \end{cases}$$

Where:

$S(t)$ = probability of survival

t_i = survival time of an object experiencing an event

d_i = number of observations that experience an event in time t_i

n_i = the number of observations that survive or have not experienced the event at time t_i

Nelson-Aalen

The Nelson-Aalen method is a technique in survival analysis that calculates estimates of unknown quantities at the time an event occurs. The unknown quantity is the hazard function, or the probability conditional on the conditions that existed before the event occurred (Madani, 2023). Nelson-Aalen is a non-parametric statistical method for calculating the cumulative hazard function estimate as follows.

$$H(t) = \begin{cases} 0 & \text{if } t < t_1 \\ \sum_{t_i \leq t} \frac{d_i}{n_i} & \text{if } t_i \leq t \end{cases}$$

Where:

$h(t)$ = hazard function at time t_i

t_i = time of occurrence of an object experiencing an event

d_i = many objects experience an event in time t_i

n_i = the number of objects that are at risk of experiencing an event at time t_i

Cox Proportional Hazard Model

The Cox Proportional Hazards model is used to determine whether there is a relationship between independent and dependent variables. In Cox-PH regression, the data used is survival duration data for one person or another individual. The following is a Cox Proportional Hazards regression model (Alya et al., 2025).

$$h(t, x) = h_0(t) \exp(\beta_1 X_1 + \beta_2 X_2 + \dots + \beta_p X_p)$$

Where:

$h_0(t)$ = basic hazard function

$\beta_1, \beta_2, \dots, \beta_p$ = parameter values in regression

$x_1, x_2, x_3, \dots, x_p$ = value of the independent variable X_1, X_2, \dots, X_p

Data Analysis Techniques

1. Collect medical record data.
2. Identify research variables.
3. Analysis of survival using the Kaplan-Meier method includes.
 - a. Calculating the chances of survival or recovery time for typhoid fever.

$$S(t) = \begin{cases} 1 & \text{if } t < t_i \\ \prod_{t_i \leq t} \left(1 - \frac{d_i}{n_i}\right) & \text{if } t_i \leq t \end{cases}$$

- b. Creating a survival curve for the probability of survival in typhoid fever patients.
4. Conducting survival analysis using the Nelson-Aalen method, among others.
 - a. Calculating the cumulative hazard function for each time in typhoid fever

$$H(t) = \begin{cases} 0 & \text{if } t < t_1 \\ \sum_{t_i \leq t} \frac{d_i}{n_i} & \text{if } t_i \leq t \end{cases}$$

- b. Create a survival curve from the cumulative hazard probability to show the cumulative risk associated with time to recovery.
5. Comparing the results of the survival rate of typhoid fever patients using the Kaplan-Meier and Nelson-Aalen methods.
6. Conducting a Cox Proportional Hazard model analysis.
7. Concluding.

RESULTS AND DISCUSSION

The study utilized data from inpatients with typhoid fever at Medan Haji Hospital, which comprised four factors: age, gender, type of antibiotic, and comorbidities, collected from 400 patients. The study period was from January 1 to December 31, 2024. The graph of the percentage of research variables is depicted in Figure 1.

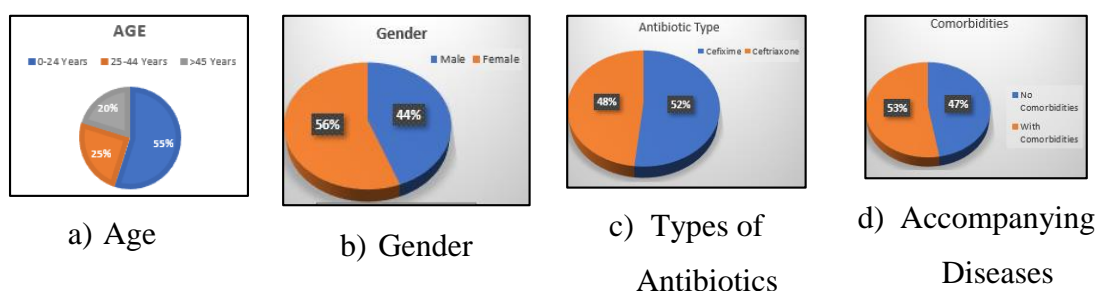


Figure 1. Graph of the percentage of research variables

The data presented included age variables, with 220 adolescents aged 0-24 years experiencing typhoid fever, 99 adults aged 25-44 years, and 81 patients aged 45 years or older. The gender variable included 223 female patients and 177 male patients. The antibiotic type variable included 207 patients with Cefixime and 193 patients with Ceftriaxone. The comorbidity variable included 211 patients with comorbidities and 189 patients without comorbidities.

Survival Analysis of Typhus Patients Using the Kaplan-Meier Method

To analyze the survival of typhoid patients, Kaplan-Meier analysis was employed to estimate the probability of patient survival. From the 400 patient data sets treated, the analysis results are presented in Figure 2. The overall Kaplan-Meier curve graph shows that the probability of survival for typhoid fever patients experienced a sharp decline between the 3rd day, with a survival rate of 0.9450, and the 6th day, with a survival rate of 0.1575. The median recovery time was 5 days, and the survival rate was 0.3100. This condition typically indicates that most patients recover within a week or less. The Kaplan-Meier survival curve for typhus patients is depicted in Figure 2.

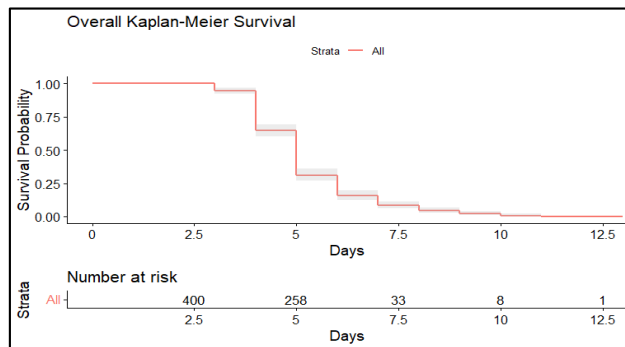


Figure 2. Kaplan-Meier survival curve of typhus patients

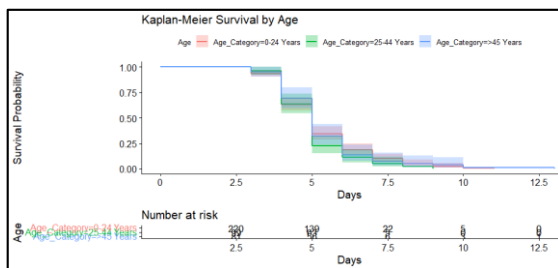


Figure 3. Kaplan-Meier survival curve by age

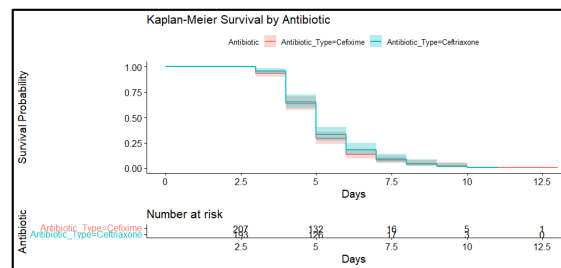


Figure 4. Kaplan-Meier survival curves by sex

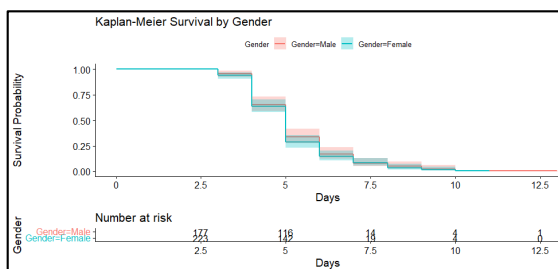


Figure 5. Kaplan-Meier survival curve based on antibiotic type

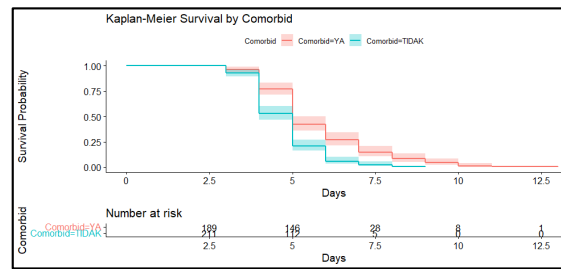


Figure 6. Kaplan-Meier survival curve based on comorbidities

Patient Survival Analysis with the Kaplan-Meier Method Based on Age

Based on age, the survival of typhoid patients can be analyzed using the Kaplan-Meier method. The analysis is categorized into three age groups: children and adolescents aged 0-24 years, adults aged 25-45 years, and elderly patients aged 45 years and older. In Figure 3, the red curve represents the recovery time for children and adolescents aged 0-24 years, the green curve represents the recovery time for adult patients aged 25-45 years, and the blue curve represents the recovery time for elderly patients aged 45 years and older. As shown in Figure 3.3, the green curve tends to decline more rapidly and is lower than the other curves. The green curve ends on day 9 or 2 days earlier than the red curve.

Meanwhile, the blue curve is always at the top and ends later than the other two curves. It can be said that, during the initial observation period and the first 7 days of treatment, adult patients have a faster chance of recovery than other patients. This is because the curve graph for patients aged 25-44 years ends on day 9, while for children and adolescents aged 0-24 years, it ends on day 11. Elderly patients aged > 45 years have the longest recovery time, which ends on day 13.

Survival Analysis of Typhus Patients Using the Kaplan-Meier Method Based on Gender

Survival analysis was conducted based on gender, which was divided into two categories: female and male patients. In Figure 4, the red curve represents the survival curve representing the recovery time for male patients, and the blue curve represents the recovery time for female patients. Based on these curves, female patients have a relatively faster recovery time than male patients. This can be seen from the curve graph for female patients, which is below the curve for male patients, indicating that they experience the event sooner.

Survival Analysis of Typhus Patients Using the Kaplan-Meier Method Based on Antibiotic Type

Survival analysis based on antibiotic use in typhoid fever patients is divided into two categories: Cefixime and Ceftriaxone. Figure 5 shows that the red curve represents the recovery time for patients receiving Cefixime, while the blue curve represents the recovery time for patients receiving Ceftriaxone. Based on the curve, patients receiving Ceftriaxone have a relatively faster recovery time compared to patients receiving Cefixime. This can be seen from the curve graph for patients receiving Ceftriaxone, which means they experience a faster recovery event.

Survival analysis of typhoid patients using the Kaplan-Meier method based on comorbidities

The survival analysis using the Kaplan-Meier method based on the history of comorbidities in typhoid fever patients was divided into two categories: those with a history of comorbidities and those without. In Figure 6, the red curve represents the recovery time for patients with a history of comorbidities, and the blue curve represents the recovery time for patients without a history of comorbidities. Based on the curve,

patients without a history of comorbidities tend to have a faster recovery time compared to those with a history of comorbidities.

This can be seen from the curve graph for patients without a history of comorbidities, which is lower and ends sooner than the curve for patients with a history of comorbidities. The curve graph for patients with a history of comorbidities ends on day 9, while the curve for patients with a history of comorbidities ends on day 13.

Survival Analysis of Typhus Patients Using the Nelson-Aalen Method

In addition to using the Kaplan-Meier analysis method, researchers also calculated the probability of surviving treatment for inpatients with typhoid fever using the Nelson-Aalen analysis method.

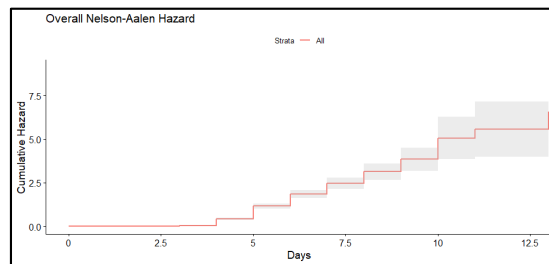


Figure 7. Survival curves using the Nelson-Aalen method for typhus patients

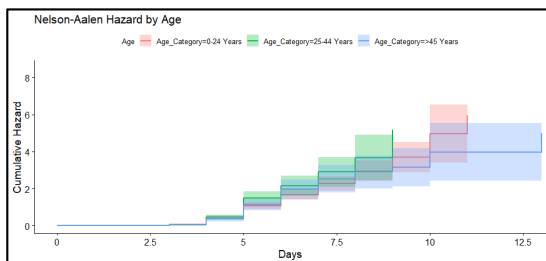


Figure 8. Nelson-Aalen survival curve method based on age

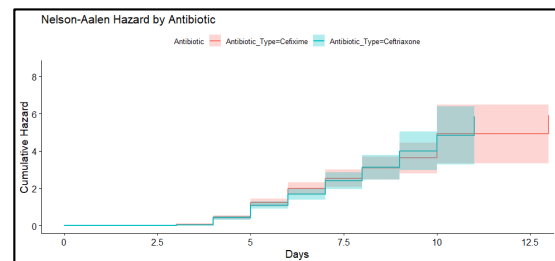


Figure 10. Nelson-Aalen method survival curve based on antibiotic type

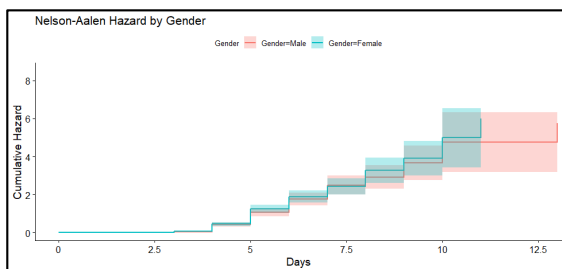


Figure 9. Nelson-Aalen survival curve method based on gender

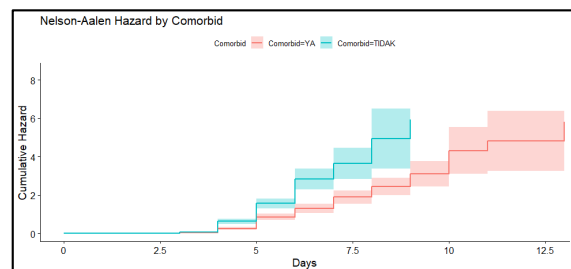


Figure 11. Nelson-Aalen survival curve based on comorbidities

The graph in Figure 7 shows a progressive increase from day 3 to day 12, with a significant rise, particularly from day 4 to day 10. This condition indicates that the longer the treatment time, the higher the accumulated risk of the patient experiencing recovery. Clinically, this means that the majority of patients experience gradual recovery in a relatively short time.

Survival Analysis of Typhus Patients Using the Nelson-Aalen Method Based on Age

Survival analysis of the Nelson Aalen method based on the age of typhoid fever patients (typhus) The study was carried out based on age, which was divided into 3 age categories, namely the age category of children and adolescents 0-24 years, adults 25-45 years, and the category of elderly patients over 45 years. The survival curve shown in Figure 8 illustrates the Nelson-Aalen method for patients aged 0-24 years, adults aged 25-45 years, and elderly patients over 45 years. Patients aged 25-44 years have a faster chance of recovery compared to patients aged 0-24 years and elderly patients over 45 years. This is evident in Figure 4.8, where the curve for children and adolescents aged 0-24 years terminates on day 11. Meanwhile, for adult patients aged 25-45 years, treatment ends on day 9, and for elderly patients aged > 45 years, it ends on day 13.

Survival Analysis of Typhus Patients Using the Nelson-Aalen Method Based on Gender

The analysis was conducted based on gender, which was divided into two categories: female patients and male patients. The Nelson-Aalen method survival curve for patients, based on gender, is shown in Figure 9. The Nelson-Aalen method survival curve for male patients ended on day 13, whereas the female patient's curve ended on day 11. This shows that female patients have a faster chance of recovery compared to male patients.

Survival analysis of typhoid patients using the Nelson-Aalen method based on antibiotic type

The Nelson-Aalen survival analysis method based on antibiotic use in typhoid patients is divided into two categories: Cefixime and Ceftriaxone. In Figure 10, the red curve represents the recovery time for patients receiving Cefixime, and the blue curve represents the recovery time for patients receiving Ceftriaxone. Patients receiving

Ceftriaxone have a relatively faster recovery time compared to patients receiving Cefixime. This is evident from the curve graph for patients receiving Ceftriaxone, indicating that they experience an event more quickly. This is evident from the curve graph for patients receiving Ceftriaxone, which ends on day 11, while the curve for patients receiving Cefixime ends on day 13.

Survival analysis using the Nelson-Aalen method based on comorbidities

The analysis was divided into two categories: patients with and without a history of comorbidities. In Figure 11, the red curve indicates patients with comorbidities, while the blue curve indicates patients without comorbidities. The graph shows that patients without comorbidities recovered more quickly, as evidenced by their higher curve and earlier end (day 9) compared to the curve for patients with comorbidities, which ended on day 13.

Comparison of the Kaplan-Meier and Nelson-Aalen methods based on age

In calculating survival analysis based on age using the Kaplan-Meier and Nelson-Aalen methods, consistent results were obtained. Based on the Kaplan-Meier analysis, it was seen that patients in the 25-44 age group had a faster recovery time compared to other age groups. This result was confirmed by the analysis using the Nelson-Aalen method, which showed that the cumulative hazard function in the 25-44 age group increased more rapidly than in other age groups. This indicates a higher risk of recovery in a shorter time in those aged 25-44.

Comparison of the Kaplan-Meier and Nelson-Aalen methods by gender

In a survival analysis of survival based on gender factors using the Kaplan-Meier and Nelson-Aalen methods, results showed a similar trend. According to the Kaplan-Meier method, female patients experienced a faster recovery rate than male patients. This result was supported by an analysis using the Nelson-Aalen method, which showed that the cumulative hazard function in the female group increased more rapidly than in the male group. The results of this analysis indicate that the risk of recovery in female patients is higher and achieved in a shorter time than in male patients.

Comparison of the Kaplan-Meier and Nelson-Aalen methods based on antibiotic type

In calculating survival analysis based on antibiotic type using the Kaplan-Meier and Nelson-Aalen methods, results showed a consistent trend. Based on the Kaplan-Meier analysis, patients receiving ceftriaxone antibiotic therapy showed a faster recovery rate than patients receiving Cefixime. Similar results were confirmed by the Nelson-Aalen method, where the cumulative hazard function for the ceftriaxone group increased more rapidly than for the cefixime group. This indicates a higher risk of recovery for those receiving Ceftriaxone, which is achieved in a shorter period of time.

Comparison of the Kaplan-Meier and Nelson-Aalen methods based on comorbidities

Survival analysis based on comorbidities was performed using the Kaplan-Meier and Nelson-Aalen methods. Both methods yielded consistent results: patients without comorbidities tended to recover more quickly than those with comorbidities. Kaplan-Meier showed a shorter recovery time in the non-comorbid group, while Nelson-Aalen showed a faster increase in cumulative hazard in that group. Because the two methods provide different perspectives, Kaplan-Meier analysis for survival probability and Nelson-Aalen analysis for accumulated risk were used to test the model and assess significance. To this end, Cox proportional hazards regression was used to obtain the hazard ratio.

Cox proportional hazards model

The Cox proportional hazards model is a method that can be used to model survival data if all studied variables meet the model's assumptions. Using SPSS software calculations, the following analysis results were obtained.

Table 3.1 Cox proportional hazard model estimation results

Variabel	Estimasi Parameter	Standard error	wald	p-value	Exp (B)
Gender	0.112	0.111	1.015	0.314	1.119
Age	0.002	0.003	0.418	0.518	1.002
Antibiotic Type	0.038	0.111	0.116	0.733	1.039

Comorbidities	0.486	0.106	20.909	< 0.001	1.626
Variabel	Chi-square	df	p-value		
Likelihood Ratio	21.674	4	< 0.001		

Source: SPSS Data Processing 2025

In Table 3.1, the simultaneous test yields a Likelihood Ratio of 21.674 with a df of 4 and a p-value <0.001. This p-value is less than α , thus a decision to reject α . This means that at least one independent variable has a significant influence on the model. The partial test, or one-to-one test, reveals that one variable has a p-value less than $\alpha(0.05)$ 0.001, meaning $\alpha < 0.001$, which indicates a decision to reject H_0 . It can be concluded that comorbidities have a significant influence on the recovery rate of typhoid fever patients. The analysis table shows that gender, age, and antibiotic type were not significantly affected by the recovery rate of typhoid fever. Therefore, the best Cox proportional hazards model was obtained.

$$h(t) = h_0(t) \exp(0.486 \text{ concomitant diseases})$$

In this model, a positive sign for comorbidities indicates that the presence of comorbidities increases the risk of an event compared to patients without comorbidities.

Based on the Cox proportional hazards model, the hazard ratio for comorbidities was $\exp(0.486) = 1.6257$. This indicates that patients with typhoid fever and comorbidities have a 1.6257-fold higher instantaneous probability of recovery at any given time compared to patients without comorbidities. The p-value (< 0.0001) indicates that this effect is statistically significant at the 5% significance level.

CONCLUSION

The results of this study, which analyzed the recovery rate of typhoid fever (typhus) using the Kaplan-Meier and Nelson-Aalen methods, showed that the age variable: patients aged 25-44 years have a higher chance of recovering faster than those aged 0-24 years and those over 45 years. The gender variable shows that female patients have a higher chance of recovering faster than male patients. The antibiotic type variable indicates that the use of ceftriaxone antibiotics results in faster recovery than cefixime antibiotics. The comorbidity variable suggests that patients without comorbidities recover faster than those with comorbidities. So it was found that the factors that influence the

recovery rate of typhoid fever using the Kaplan-Meier and Nelson-Aalen methods, with a significant level test of the Cox Proportional Hazard regression model, are comorbidities with an exp value (0.486), which is 1.6257 times slower to recover than those without a history of comorbidities. It is hoped that further research can utilize other methods for survival analysis in similar studies and, in subsequent research, employ more varied data in the analysis to obtain different survival results.

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