



Determinants of pediatric tuberculosis patient recovery in Semarang City

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Abstract

Background: Tuberculosis is an infectious disease which is the main cause of death worldwide caused by the bacterium *Mycobacterium tuberculosis*. This bacterium can infect children to adults. According to data from the Semarang City Health Office for 2022, Semarang City is one of the regions in Indonesia that has played a role in realizing national tuberculosis cases with a cure rate that is still far from the global target, namely 78,95% in 2020 and 71,72% in 2021. The purpose of this study was to determine the factors that can affect recovery in pediatric tuberculosis patients in Semarang City.

Methods: The type of research used was analytic observational with a retrospective cohort study design. This study used secondary data from the SEMAR BETUL system from January 2021-September 2022.

Results: The results showed that ownership of the supervisor swallowed the drug (PMO) ($p < 0.001$; AOR= 13.997, 95% CI= 8.728-22.446) and house humidity variable ($p = 0.002$; AOR= 2.059, 95% CI= 1.290-3.287) effect on the recovery of pediatric tuberculosis patients in the city of Semarang.

Conclusion: It is known that the supervisor ownership variable for ingesting drugs is the strongest factor influencing the recovery of pediatric tuberculosis patients in Semarang City.

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INTRODUCTION

Tuberculosis is an infectious disease that is the leading cause of death worldwide. (World Health Organization, 2021). The bacterium that causes tuberculosis, *Mycobacterium tuberculosis*, which spreads through the air. (Centers for Disease Control and Prevention, 2016). This disease can infect children to adults (Thomas, 2018). According to the World Health Organization, until the COVID-19 pandemic, tuberculosis ranked above HIV/AIDS. WHO has set a target in 2030 to reduce the number of deaths from tuberculosis by 90% and reduce cases by 80%. (World Health Organization, 2021). However, the fact remains that the global tuberculosis cure rate is still below the target of 85%. (Marlen et al., 2019).

In 2020, the number of tuberculosis cases worldwide was 10.1 million. Then in 2021, the number increased by 4.5% to 10.6 million people (World Health Organization, 2022). The cure rate for tuberculosis treatment in Indonesia in 2019 was 86.51% (Iskandar et al., 2022). Nevertheless, Indonesia is the second largest contributor of tuberculosis cases in the world (9.2%) after India (28%), and in third place is China (7.4%) (World Health Organization, 2022). In 2019, it is estimated that the number of pediatric tuberculosis cases in the world was more than 990,000 cases, much higher than the cases reported by WHO, which amounted to only about 520,000 cases (Yerramsetti et al., 2022). Children under 5 years of age have a lower chance of recovering from tuberculosis than children aged 5-14 years (Ramos et al., 2019). The estimated target number of pediatric tuberculosis cases in Indonesia is 12% of the total number of tuberculosis cases in a region (Dodd et al., 2014). The number of pediatric TB cases in Indonesia is 42,187 cases. About 22/10,000 toddlers in Indonesia suffer from tuberculosis and 12/10,000 children aged 5-14 years suffer from tuberculosis (Ministry of Health of Republic Indonesia, 2021).

Semarang City is one of the regions in Indonesia that contributes to the national tuberculosis cases with a cure rate that is still far from the global target of 78.95% in 2020 and 71.72% in 2021. In 2022 alone, the city has found 2,605 cases of SO (Sensitif Obat/Drug Sensitive) TB and 115 cases of RO (Resistan

Obat/Drug Resistant) TB. As many as 16.58% (432 cases) of the total SO TB cases were children aged 0-4 years. Meanwhile, 7.18% (187 cases) were cases of SO TB in children aged 5-14 years. In 2022, there were no cases of pediatric DR-TB in Semarang City. (Health Department of Semarang City, 2022).

Previous research stated that the presence of a drug swallowing supervisor (Pengawas Menelan Obat/PMO) plays a significant role in the recovery of tuberculosis patients in an effort to improve adherence to tuberculosis treatment (Nezenega et al., 2020). TB patients who have comorbidities can directly affect the recovery process of patients from TB treatment, because comorbidities can worsen the results of TB treatment (Babalik et al., 2013). Based on a study in Brazil, it was found that the proportion of tuberculosis cases in children aged <5 years was more prevalent in female (63.3%) than male. In addition, house environmental factors such as ventilation quality can reduce the risk of new tuberculosis cases for 97% by improving ventilation quality so that indoor CO₂ levels are less than 1000 ppm (Du et al., 2020). According to a study in Brazil, the lowest incidence of tuberculosis was found in areas with good sunlight penetration (F. M. de C. Fernandes et al., 2017). Previous studies have also suggested that the condition of house humidity, which is influenced by temperature and climate, affects the incidence of tuberculosis. An increase in cases occurs when the temperature is low which causes an increase in humidity (Xu et al., 2020).

Based on previous research, geographical barriers including the distance between health facilities and homes also affect the recovery rate of tuberculosis patients because they can cause obstacles to the patient's treatment process and thus patients will often delay treatment and even absent (Robsky et al., 2020). In this study, there is an update from previous studies in the form of calculations to predict the probability of recovery of a pediatric tuberculosis patient with certain criteria. The purpose of this study is to determine the factors that can affect the recovery of pediatric tuberculosis patients in Semarang City.

METHODS

This study used observational analytic

research with a retrospective cohort research design to determine what factors influence the recovery of pediatric tuberculosis patients in Semarang City. One of the retrospective cohort studies with more than one type of exposure

is a study entitled Clinical Characteristics and Mortality Associated with COVID-19 in Jakarta, Indonesia: A Hospital-Based Retrospective Cohort Study (Surendra et al., 2021).

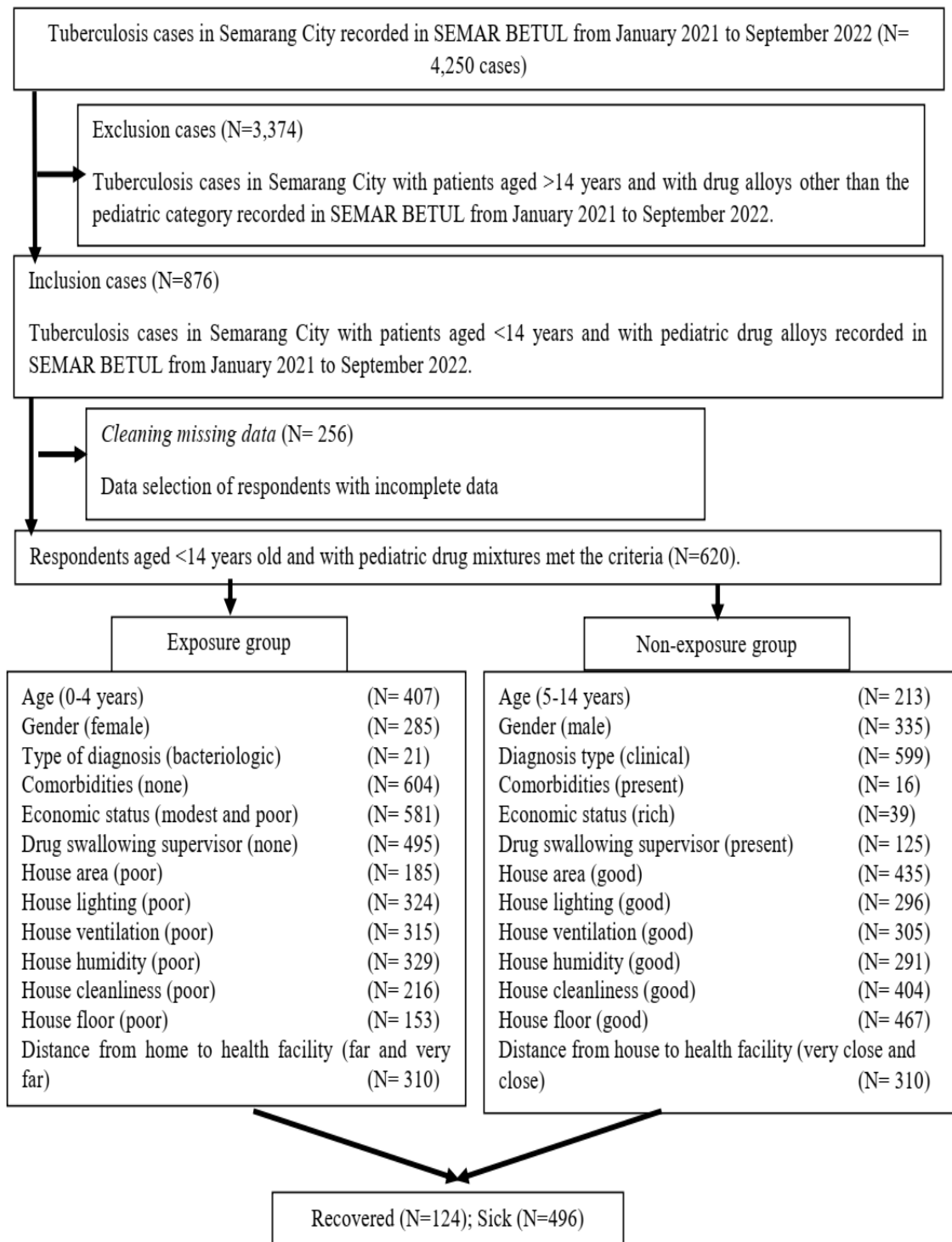


Figure 1. Flowchart of Research Respondents and Completeness of Key Variables

The samples were pediatric patients aged 0-14 years with a primary diagnosis of tuberculosis and a pediatric drug combination recorded in the Surveillance System of Semarang City Health Office called SEMAR BETUL (Semarang Berantas Tuberkulosis) from January 2021 to September 2022. Each healthcare facility in Semarang City has a surveillance officer who is responsible for conducting epidemiologic investigations on each confirmed case through interviews utilizing a form. The contents of the form were then entered into the SEMAR BETUL system to complete the patient data.

The dependent variable in this study was the recovery of pediatric tuberculosis patients. Meanwhile, the independent variables consisted of age, gender, type of TB diagnosis, history of other diseases, distance from home to health facilities, economic status, availability of a drug swallowing supervisor (PMO), and home conditions of patients including lighting, humidity, floor cleanliness, ventilation, and area. Data analysis techniques in this study were conducted using univariate, bivariate, and multivariate analysis. Bivariate analysis used the chi-square test, while multivariate analysis used logistic regression.

Figure 1 is a sample selection flow chart. Based on the figure, it is known that from January 2021 to September 2022, there were 4,250 cases of tuberculosis in Semarang City recorded in the SEMAR BETUL system. Furthermore, identification was carried out according to the exclusion and inclusion criteria of the study. In this case, the inclusion cases were tuberculosis cases in Semarang City with patients aged <14 years old and with pediatric drug alloys recorded in SEMAR BETUL from January 2021 to September 2022. Meanwhile, the exclusion cases in this study were patients aged >14 years and had a drug combination other than the pediatric category recorded in SEMAR BETUL from January 2021 to September 2022. The next stage is data selection of respondents with incomplete variable data as many as 256 cases. A sample size of 620 cases aged <14 years and having a pediatric drug combination that met

the criteria were obtained as samples in this study. This research with the title "Determinants of Pediatric Tuberculosis Patient Recovery in Semarang City" was approved by the UNNES Health Research Ethics Committee (Komite Etik Penelitian Kesehatan/KEPK) with number: 443/KEPK/EC/2022.

RESULTS AND DISCUSSION

Based on the results of univariate analysis in Table 1, out of 620 pediatric tuberculosis patients in Semarang City, the dominant group was 407 patients aged 0-4 years (65.6%) and 213 patients aged 5-14 years (34.4%). Male pediatric patients were more than female pediatric patients, with 335 patients (54%) and 285 patients (46%), respectively. The type of diagnosis was dominated by clinically diagnosed patients with 599 patients (96.6%) and bacteriologically confirmed patients with only 21 patients (3.4%).

There were 16 pediatric patients (2.6%) with not only tuberculosis but also other comorbid diseases. The remaining 604 patients (97.4%) had no comorbidities. The economic status of pediatric tuberculosis patients in Semarang City was classified into 3 categories: rich, modest, and poor. There were 39 patients with rich economic status (6.3%), 540 patients with modest economic status (87.1%), and 41 patients with poor economic status (6.6%). The classification of economic status according to BPS is divided into 3, namely a very high-income group (rich) with an average income of IDR 2,500,000 to more than IDR 3,500,000 per month, a medium-income group with an average income of IDR 1,500,000-Rp2,500,000 per month, and a low-income group (poor) with an average income of less than 1,500,000 per month (Rakasiwi, 2021). There were 125 pediatric tuberculosis patients who had a drug swallowing supervisor (PMO) (20.2%), while the remaining 495 patients (79.8%) did not have a drug swallowing supervisor. PMOs in pediatric tuberculosis patients in Semarang City usually come from health workers with the assistance of the parents of each patient.

Table 1. Univariate Analysis Results

Variable	N	%
Age		
5-14 years old	213	34,4
0-4 years old	407	65,6
Gender		
Male	335	54
Female	285	46
Type of diagnosis		
Clinically diagnosed	599	96,6
Bacteriologically confirmed	21	3,4
Comorbid		
None	604	97,4
Present	16	2,6
Economic status		
Rich	39	6,3
Modest	540	87,1
Poor	41	6,6
Drug swallowing supervisor		
None	125	20,2
Present	495	79,8
House Area		
Good	435	70,2
Poor	185	29,8
House lighting		
Baik	296	47,7
Poor	324	52,3
House ventilation		
Good	305	49,2
Poor	315	50,8
House humidity		
Good	291	46,9
Poor	329	53,1
House cleanliness		
Good	404	65,2
Poor	216	34,8
House floor		
Good	467	75,3
Poor	153	24,7
Treatment status		
Recovered	124	20
Sick	496	80
Distance from home to health facility		
Very close (170 m - 1400 m)	155	25
Close (1401 m - 2500 m)	155	25
Far (2501 m - 5100 m)	155	25
Very far (5101 m - 24000 m)	155	25

In this study, the condition of the house of the patient which includes the area, lighting conditions, ventilation, humidity, cleanliness, and the condition of the floor of the house was also studied to determine the extent of the contribution of home environmental conditions to the determinants of patient recovery. Table 1 shows that a total of 435 patients (70.2%) had houses with a good area and the remaining 185 patients (29.8%) had houses with a poor area. According to the lighting conditions at home, a total of 296 patients (47.7%) had homes with good lighting and 324 other patients (52.3%) had homes with poor lighting conditions. 305 patients (49.2%) had good ventilation and 315 patients (50.8%) had poor ventilation. In terms of house humidity, 291 patients (46.9%) had houses with good humidity,

while the remaining 329 patients (53.1%) had houses with poor humidity. The next variable, cleanliness and floor condition of pediatric tuberculosis patients' houses in Semarang City, was dominated by patients who had houses with clean conditions and good floors, which were 404 patients (65.2%) and 467 patients (75.3%), respectively. Table 1 also shows that 124 patients (20%) were cured and 496 patients (80%) were still sick.

Based on the results of bivariate analysis in Table 2, it is known that out of 13 variables, there are 4 variables that have an association with the recovery of pediatric tuberculosis patients in Semarang City (p-value <0.05). The four variables included drug swallowing supervisor (p-value <0.001), lighting condition (p-value=0.013), ventilation condition (p-value=0.021), and house humidity (p-value <0.001). The other 9 variables, including age, gender, type of diagnosis, comorbidities, economic status, house area, house cleanliness, and distance to health care facilities, did not have an association with the recovery of pediatric tuberculosis patients in Semarang City (p-value >0.05).

In the variable of drug swallowing supervisor (PMO) has RR = 6.061; CI 95% = 4.482-8.197. This shows that patients who have a PMO have a greater chance of recovery 6.061 times compared to patients who do not have a PMO. The presence of a drug swallowing supervisor is related to the adherence of patients taking medication. According to previous research, patients who are adherent to taking medication have a 5.926 times chance of recovering from tuberculosis than patients who are not adherent to taking medication (Chusna & Fauzi, 2021). In addition to affecting recovery, adherence according to other studies can reduce the risk of relapse. Patients with poor adherence had a relapse rate of 50.5%, while the relapse rate of patients with good adherence was only 1.1% (Yan et al., 2018). To prevent relapse and increase the chance of recovery, according to a study, drug swallowing supervisors play an active role in increasing the motivation of tuberculosis patients to recover and encourage and observe patients to take routine drugs during the treatment period (Zhang et al., 2016).

In the variable of house lighting, the value of RR = 1.516; 95% CI = 1.101-2.087. This means that pediatric tuberculosis patients who have good home lighting conditions have a 1.516 times greater chance of recovery than pediatric tuberculosis patients who have poor home lighting conditions. It is known that the variable of house ventilation condition has a value of RR = 1.478; IK 95% = 1.072-2.038, meaning that pediatric tuberculosis patients with good house ventilation conditions have a 1.478 times greater chance of recovery compared to pediatric tuberculosis patients with poor house ventilation conditions. In the variable of house humidity condition, the value of RR = 1.917; IK 95% = 1.380-2.662, meaning that pediatric tuberculosis patients with good house humidity have a 1.917 times greater chance of recovery compared to pediatric tuberculosis patients with poor house humidity. This is in accordance with previous research which states that tuberculosis is more susceptible to developing in places that have inadequate ventilation and sunlight because these conditions make Mycobacterium not easy to move or be killed (Saraswati et al., 2018). A study highlighted that it is necessary to assess

the status of indoor ventilation as one of the strategies in controlling tuberculosis (Du et al., 2020). According to previous research, it was found that an environment with low temperature, high relative wind speed, and low relative humidity is a very favorable environmental condition for the transmission of tuberculosis (Li et al., 2021). The same fact was also found in India that areas with high rainfall and humidity can affect the risk of increasing tuberculosis cases (Kuddus et al., 2019).

Based on the results of the bivariate analysis in Table 2, variables that were suitable for logistic regression testing included age, drug swallowing supervisor (PMO), area, lighting conditions, ventilation, humidity, and distance from home to health facilities. After logistic regression test, 2 variables were found to have the strongest influence on the recovery of pediatric tuberculosis patients, including drug swallowing supervisor (\neg p-value<0.001; AOR= 13.997; 95% CI= 8.728-22.446), house humidity (\neg p-value=0.002; AOR= 2.059; 95% CI= 1.290-3.287).

Tabel 2. Hasil Analisis Bivariat

Variable	Recovered		Sick		RR (CI 95%)	p-value
	N	%	N	%		
Age						
5-14 years old	52	24,5	160	75,5	1,390 (1,014-1,906)	0,054
0-4 years old	72	17,6	336	82,4		
Gender						
Male	69	20,6	266	79,4	1,067 (0,777-1,466)	0,763
Female	55	19,3	230	80,7		
Type of diagnosis						
Clinically diagnosed	119	19,9	480	80,1	0,834 (0,382-1,824)	0,588
Bacteriologically confirmed	5	23,8	16	76,2		
Comorbid						
None	121	20	483	80	1,068 (0,381-3)	1
Preesent	3	18,8	13	81,3		
Economic status						
Rich	9	23,1	30	76,9	1,352 (0,558-3,275)	0,695
Modest	108	20	432	80	1,171 (0,584-2,348)	0,802
Poor	7	17,1	34	82,9	Ref	
Drug swallowing supervisor						
None	75	60	50	40	6,061 (4,482-8,197)	<0,001**
Preesent	49	9,9	446	90,1		
House Area						
Good	79	18,2	356	81,8	0,747 (0,54-1,031)	0,100
Poor	45	24,3	140	75,7		
House lighting						
Good	72	24,3	224	75,7	1,516 (1,101-2,087)	0,013*
Poor	52	16	272	84		
House ventilation						
Good	73	23,9	232	76,1	1,478 (1,072-2,038)	0,021*
Poor	51	16,2	264	83,8		
House humidity						
Good	78	26,8	213	73,2	1,917 (1,38-2,662)	<0,001**
Poor	46	14	283	86		
House cleanliness						
Good	77	19,1	327	80,9	0,876 (0,634-1,21)	0,487
Poor	47	21,8	169	78,2		
House floor						
Good	95	20,3	372	79,7	1,073 (0,739-1,559)	0,798
Poor	29	19	124	81		
Distance from home to health facility						
Very close (170 m - 1400 m)	19	12,3	136	87,7	0,679 (0,396-1,163)	0,205
Close (1401 m - 2500 m)	38	24,5	117	75,5	1,357 (0,879-2,096)	0,212
Far (2501 m - 5100 m)	39	25,2	116	74,8	1,233 (0,805-1,89)	0,168
Very far (5101 m - 24000 m)	28	18,1	127	81,9	Ref	

* = *p-value* <0,05** = *p-value* <0,001

Based on the results of multivariate analysis in Table 3, it is known that the variable of drug swallowing supervisor (PMO) increases the chance of recovery of pediatric tuberculosis patients by 13.997 times. This is in accordance with previous studies that suggest healthcare providers to provide supervisors to swallow drugs for each patient to increase the knowledge of patients (Fekadu et al., 2020). Swallowing supervisors do not have to be health workers but can be family members. In a study, it was stated that patients who had a supervisor

to swallow medicine from their family were more likely to have a high level of medication adherence. This is because tuberculosis patients generally carry a psychological burden and lack confidence in the healing process (Chen et al., 2020). In addition, the active interaction between the supervisor and the patient can improve the quality of health services that can determine the self-management behavior and treatment outcomes of the patient. Patients usually want to discuss directly related problems experienced during visits and participate more

in decision-making during treatment (Sri et al., 2021).

In addition, based on the results of multivariate analysis in Table 3, it is known that the humidity variable can also affect the chance of recovery of pediatric tuberculosis patients by 2.059 times. This is in accordance with previous research which shows that high humidity conditions increase the risk of tuberculosis in children by 1.2 times because these conditions will encourage pathogen replication and increase pathogen survival (Nie et al., 2022).

The coefficient of determination (Pseudo R²) was used to show the effect of supervision of drug swallowing and house humidity together on the recovery of pediatric tuberculosis patients in Semarang City. Based on Table 3, it is known that the value of the coefficient of determination (Pseudo R²) is 0.344 times, which means that 34.4% of the recovery of pediatric tuberculosis patients in Semarang City is influenced by these two variables and the rest is influenced by other variables outside the variables in this study.

Based on the results of the logistic regression analysis in Table 3, the logistic regression equation can be formulated as follows:

$$y = -2,603 + 2,639(\text{PMO}) + 0,722(\text{House humidity})$$

Recovery of pediatric tuberculosis patients in Semarang City with the characteristics of suffering from tuberculosis, having a drug swallowing supervisor, and good house humidity conditions. The following is the process of calculating the probability of recovery of pediatric tuberculosis patients based on these criteria:

$$y = -2,603 + 2,639(1) + 0,722(1) = 0,758$$

$$p = 1 / (1 + \exp[-(0,758)]) = 0,6809$$

$$p = 68,09\%$$

Thus, the probability of recovery of pediatric tuberculosis patients in Semarang City with the characteristics of suffering from tuberculosis, having a supervisor to swallow medicine, and good house humidity is 68.09%.

Through the logistic regression equation, it can also be used to predict the probability of recovery of pediatric tuberculosis patients

in Semarang City with the characteristics of having tuberculosis, not having a supervisor to swallow medicine, and poor house humidity. The following is the process of calculating the probability of recovery of pediatric tuberculosis patients based on these criteria:

$$y = -2,603 + 2,639(0) + 0,722(0) = -2,603$$

$$p = 1 / (1 + \exp[-(-2,603)]) = 0,0689$$

$$p = 6,89\%$$

Thus, the probability of recovery of pediatric tuberculosis patients in Semarang City with the characteristics of suffering from tuberculosis, not having a drug swallowing supervisor, and poor home humidity conditions is 6.89%.

The strengths of this study are the addition of new variables such as the distance of the patient's house to the health service facility and the calculation to predict the probability of recovery of a pediatric tuberculosis patient with certain criteria. Meanwhile, there are also some shortcomings in this study such as the absence of BCG immunization history and nutritional status variables that could better describe the condition of childhood tuberculosis patients. Future research related to childhood tuberculosis in Semarang City is expected to be able to add these variables.

CONCLUSION

Based on the results of this study, it can be concluded that after logistic regression analysis on the variables of age, PMO, area, lighting condition, ventilation, house humidity, and distance to health facility, the determinants that affect the recovery of pediatric tuberculosis patients in Semarang City are PMO and house humidity. Of the two variables, the results of this study showed that the most dominant factor in influencing the recovery of pediatric tuberculosis patients in Semarang City was the ownership of a drug swallowing supervisor (PMO). Based on these two variables, policy makers at the Semarang City Health Office are expected to monitor and ensure the ownership of a PMO for every TB patient, especially pediatric patients. Drug swallowing supervisors can come from health workers or from the family. The role of the family, especially parents, is very important in the adherence of children

to take medicine, so as to increase the chances of recovery and prevent relapse. To increase the awareness and knowledge of parents/guardians on the importance of tuberculosis treatment, the Semarang City Health Office needs to provide regular education to parents/guardians and assistance by health workers. It is also necessary to provide regular education to the parents/guardians of patients to maintain the condition of the house so that it is not humid and maintained cleanliness, especially in the bedroom area and places that are frequently used by tuberculosis patients.

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