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Predictor Factors of Delay Tuberculosis Diagnosis Based on Antibiotic Treatment History, Thoracic Radiography and Microbiological Examination

Inayati[1*)]; Ana Majdawati[2]

[1*)] Department of Microbiology, Faculty of Medicine and Health Sciences, University of Muhammadiyah Yogyakarta
[2] Departement of Radiology, Faculty of Medicine and Health Sciences, University of Muhammadiyah Yogyakarta

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A B S T R A C T

Health care system delay is Tuberculosis (TB) diagnosis delay which the first coming to health services until receiving Tuberculosis Drugs. It is caused by a history of previous antibiotic treatment, chest radiographic lesion, microscopic Acid-Fast Bacilli (AFB) and Gen x-pert examination. The aim is to determine predictor factors of suspected TB patients based on antibiotics treatment history, chest radiography, AFB examination and Gene-x-pert that affect healthcare services delay. Medical records of 449 suspected TB patients are presented 2x2 table, to determine the relationship between several variables with TB delay. Characteristics of suspected TB patients are 35.6% adult, 59.9% male, 55.5% senior high school and 49.9% trader. They suffered comorbid diseases Congestive Heart Failure (CHF) 56.8%. Comorbid hypertension (p-value 0.02) and CHF (p-value 0.01) are significantly associated with TB delay. Suspected TB patients had using tuberculosis drugs history 82.4% and quinolone 5.8% were not associated with delayed TB. Time of radiological examination (p-value 0.049) and time of examination of AFB (p-value 0.000) were associated with TB delay. The predictor factors that influence Health Care System Delay TB are the time of radiological and microscopic AFB examination and TB suspected patients who have comorbid Congestive Heart Failure (CHF) and Hypertension.

Kata kunci:

Keterlambatan pelayanan kesehatan
Faktor prediktor
Keterlambatan pasien
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**) corresponding author*

dr. Inayati, M,Kes., Sp.MK
Department of Microbiology, Faculty of Medicine and Health Sciences, University of Muhammadiyah Yogyakarta
Jl. Brawijaya, Geblagan, Tamantirto, Kec. Kasihan, Kabupaten Bantul, Daerah Istimewa Yogyakarta – Indonesia 55183

Email: inayati@umy.ac.id

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A B S T R A K

Health care system delay adalah keterlambatan diagnosis Tuberkulosis (TB) yang pertama kali datang ke pelayanan kesehatan sampai dengan menerima Obat Anti Tuberkulosis. Hal ini disebabkan oleh riwayat pengobatan antibiotik sebelumnya, lesi radiografi dada, mikroskopis Bakteri Tahan Asam (BTA) dan pemeriksaan Gen x-pert. Tujuan penelitian mengetahui faktor prediktor pasien suspek TB berdasarkan riwayat pengobatan antibiotik, foto toraks, pemeriksaan BTA dan Gene-x-pert yang mempengaruhi keterlambatan pelayanan kesehatan. Rekam medis dari 449 pasien suspek TB disajikan tabel 2x2, untuk mengetahui hubungan beberapa variabel dengan delay TB. Karakteristik pasien suspek TB adalah dewasa 35,6%, laki-laki 59,9%, SLTA 55,5% dan pedagang 49,9%. Mereka menderita komorbid Congestive Heart Failure (CHF) 56,8%. Komorbid hipertensi (nilai p 0,02) dan CHF (nilai p 0,01) secara signifikan berhubungan dengan delay TB. Pasien suspek TB memiliki riwayat penggunaan obat TB 82,4% dan kuinolon 5,8% tidak berhubungan dengan delay TB. Waktu pemeriksaan radiologi (nilai p 0,049) dan waktu pemeriksaan BTA (nilai p 0,000) berhubungan dengan delay TB. Faktor prediktor yang mempengaruhi Health Care System Delay TB adalah waktu pemeriksaan radiologis dan mikroskopis BTA, pasien suspek TB dengan komorbiditas Congestive Heart Failure (CHF) dan Hipertensi.

INTRODUCTION

The incidence of TB in Indonesia in 2020 was 71.440 - 196.725 with a mortality rate of 13.947. It was third ranking after India and China. It is estimated that there are 845.00 TB cases, 42.27% of cases have been recorded and 83% have been declared to have been treated until they have recovered. The remaining 57.73% of cases have not been recorded, either unreached, undetected or unreported (Ministry of Health, 2020). TB patients coming to Health Services are decrease until June 2021. TB deaths increase becaused reduced access to TB diagnosis and treatment and caused the decline in TB incidence slowed, almost stopped and it will get worse in 2021 and 2022. The immediate priority is to restore access and provision of essential TB services so that rates of detection and treatment of TB cases can recover, especially in severely affected countries (WHO, 2021).

The delay in diagnosing Tuberculosis (TB) called the total delay, is the time interval since the patient with clinical symptoms of TB, then comes to the health service followed by diagnosis (diagnosis delay) until the administration of Tuberculosis Drugs. The total delay consists of diagnostic delay and treatment delay. Diagnostic delay is from the onset of symptoms in the patient until the diagnosis of TB is established. The most common factor causing diagnostic delay TB is patient delay, which is low knowledge about TB around 63-70% with a delay of about 30 days and the healthcare system delay is 7 days (Segagni Lusignani et al., 2013) and 5 days (Gedeyon et al., 2019) . Health care system delay is the time it takes from first coming to the health care facility until the first time receive oral tuberculosis drugs (Gedeyon et al., 2019). Healthcare system delays caused by several factors, such as a of previous antibiotic treatment history and clinical symptoms, chest radiographic lesion characteristics (type of lesion, lesion location and extent of lesion), microscopic results of sputum AFB (Acid Fast Bacilli) and/or Gen x-pert examination (Rossato Silva et al., 2012) (Rossato Silva et al., 2012) (Sasaki et al., 2015). Health care system delay affects the delay in diagnosis and administration of OAT in TB cases. Delays in TB management are often inconsistent, due to differences in culture, environment and infrastructure (Gedeyon et al., 2019).

The factors that affect the health care system delay are the system in health services related to TB services which is broadly divided into 2 which consists of TB diagnostic time and TB treatment time. The ideal time for these two services is 5 days, and if more than 5 days is defined as health care system delay. The factors that affect the health care system delay are the system in health services related to TB services which is broadly divided into 2 which consists of TB diagnostic time and TB treatment time. Factors that cause delays in health care system delays that are important related to the following: health service management related to information on TB problems, service flow from the initial examination, diagnostic support examinations, administration of OAT. This factor is strongly influenced by patient compliance in following the flow of health services, health service resource services consisting of medical and non-medical personnel as supporting TB diagnostics and treatment (Gedeyon et al., 2019) Lack of awareness, access to informal or illegal drug dealers, inadequate service provision, fear of finding out HIV positive, poverty and delays in service provision due to longer waiting times lead to delayed delayed TB (Tedla et al., 2020).(Tedla et al., 2020)

Active TB patients who went to health facilities 6 months before being diagnosed with TB showed a significant delay in diagnosis in patients using antibiotics. Delay increased in exposure to combination antibiotics Fluoroquinolones and non-Fluoroquinolones, but not in the use of FQs or non-FQs alone. Due to delay in diagnosis, treatment costs become wasteful, therapy is delayed so that the disease becomes more severe, the risk of becoming MDR TB increases (Grossman et al., 2014) (Grossman et al., 2014) (Takiff & Guerrero, 2011) (Takiff & Guerrero, 2011).

Research on predictors of the occurrence of healthcare system delay is still lacking, especially regarding diagnostic delay so the aims of this study to determine TB diagnosis delay time (health care services delay) and predictor factors of suspected TB patien based on non-Tuberculosis drugs antibiotics treatment history, chest radiography examination and AFB sputum examination and/or Gen x-pert, so that the data obtained can help to improve the TB service system from various factors so that it can reduce the incidence of total TB delay

METHOD

Suspect TB patient medical record 449 samples were presented in a 2x2 table, to determine the significant relationship of history of drug administration of Quinolones and other antibiotics, thorax radiographic lesion characteristics (type, location and extent of lesion) and examination of AFB or Gene X-pert in patients with Delayed TB diagnosis (Suspect TB patients with a minimum time required for establishing a TB diagnosis is one week). Analyzing the relationship delay TB factors (delay diagnosis, Healthcare system delay) such as antibiotic treatment history, chest radiography (type of lesion, location of lesion and extent of lesion); sputum AFB examination or Gene X-pert. Unpaired categorical comparative statistical analysis, 2x2 table, namely the chi square test and if the Chi square conditions are not met then use the Mann-Whitney test, with a p value <0.05 which means it has a significant relationship and gets an Odds Ratio (OR) value between both of them.

This study has received approval from the ethics committee from 3 research sites according to the Ethycal clearance letter from 1). The Ethics Committee of the Yogyakarta City Hospital Health Service: No. 24/KEP/RSUD/IX/2021; 2) Medical and Health Research Ethics Committee (MHREC) Faculty of Medicine, Public Health and Nursing Universitas Gadjah Mada- Dr. Sardjito General Hospital No : KE/FK/0981/EC/20

RESULTS AND DISCUSSION

The results 449 suspected tuberculosis patients at the Yogyakarta City Regional General Hospital, PKU Muhammadiyah Hospital Gamping Sleman and Panembahan Senopati Hospital Bantul. Suspected TB Patients with delayed TB characteristics are described in table 1.

Characteristics of suspected TB patients include age group, gender, education level and occupation, are especially in the adult age group as much as 35.6%, male 59.9% with senior high school as much as 55.5%, type of work trader/private sector as much as 49.9%. It is similar with previous study that several factors affect patient delay TB , namely age, gender, employment status, economic status, education level, level of knowledge about TB, smoking status, distance from residence to health services and TB cadre

support (Islamiyah, 2015) (Islamiyah, 2015) . Rossato et al's study showed TB patients aged <60 years. Current smoking habits 41.5% smear-negative cases were more prevalent in the group of patients diagnosed a week or more after admission to hospital 84.2%. Cough and night sweats were more common in patients with a diagnosis in less than 6 days 53.6% (Rossato Silva et al., 2012).

Table 1
Characteristics of patients with suspected tuberculosis who have delayed TB

No	Variabel	Group	Delay TB	Non-Delay TB	Total	Persentase
1	Age	Teenage Age	52	18	70	15,6
		Adult	121	39	160	35,6
		Elderly	175	44	219	48,8
2	Gender	Male	208	61	269	59,9
		Female	140	40	180	40,1
3	Education	Un school	51	15	66	11,4
		Elementary School	28	6	34	7,6
		Junior High School	42	12	54	12,0
		Senior High School	194	55	249	55,5
		College	32	14	66	14,7
4	Occupation	Unemployment	67	18	85	18,9
		Student	47	14	61	13,6
		Laborer	9	25	64	14,3
		Civil Servant	10	3	13	2,9
		Trader/private sector	181	43	224	49,9
		Teacher/Lecturer	1	1	2	0,4

Table 2
Comorbid diseases and history of taking medication for suspected TB patients

No	Comorbid	Group	Amount	Percentage	*p-value*
1	Diabetes Mellitus (DM)	DM	54	13,7	0.74
		Non-DM	395	86,3	
2	Hypertension	Hypertension	112	22,4	0.02*
		Non-Hypertension	387	77,6	
3	HIV-AIDS	HIV AIDS	104	23,2	0.72
		Non-HIV AIDS	395	76,8	
4	Chronic Obstructive Pulmonary Disease (COPD)	COPD	57	12,7	0.38
		Non-COPD	392	87,3	
5	Congestive Heart Faiure (CHF)	CHF	255	56,8	0.01*
		Non-CHF	194	43.2	
6	Drugs Consumption	Quinolon group	26	5.8	0.36
		Other Antibiotics	53	11.8	
		Oral Tuberculosis drugs	370	82.4	

The study by G. D. Gosoniu et al. has identified gender- and illness-related features of TB that explain the problem of delay in diagnosis. The median interval from symptom onset to diagnosis was longest in India and shortest in Malawi. With adjustment for confounding, female sex (Bangladesh), and status of married woman (India) and housewife (Malawi) were associated with problem delay (Gosoniu et al., 2008) . In Ethiopia, patients aged > 55 years are 2.2 times at risk of delay compared to those aged 15-34 years (Yimer et al., 2014). Research in Yemen, found that men are 2.03 times at risk of delay than women (WHO, 2006). The same thing was found in Uganda that men risk 1.61 times delay compared to women (Buregyeya et al., 2014). However, in India men reduce the risk 0.42 times compared to women (Konda et al., 2014). Both men and women who do not work are 2.2 times at risk of being patient delay compared to those who work. Low income, gender, rural life, unemployment, aging and misunderstanding the microbial cause of tuberculosis are associated with delayed diagnoses. Systemic factors including low health care coverage, patient expenditures and entry into the health system by consulting a traditional healer or a non-skilled professional delay the beginning of tuberculosis treatment(Ndeikoundam Ngangro et al., 2012). Patients with suspected TB have different comorbidities. Table 2 shows suspected TB patients based on their comorbidities.

Comorbid diseases suffered by suspected TB patients, especially CHF as much as 56.8% and drug consumption history, especially anti-tuberculosis drugs as much as 82.4%. Statistical analysis results of the relationship between comorbid TB suspected patients and the incidence of delayed TB showed significant results in hypertension with a p value of 0.02 and CHF with a p value of 0.01. The majority of suspected TB patients had tuberculosis drugs consumption history by 82.4%. while the history of consumption of quinolone antibiotics was only 5.8%. There is no significant relationship between history of drug consumption and the incidence of delayed TB as shown in table 2. Several references state that comorbid diseases have a relationship with health care system delays, including Chronic

Obstructive Pulmonary Disease (COPD), Diabetes Mellitus (DM), HIV-AIDS, Covid-19. The sequelae or lesions in the lungs of these diseases can sometimes obscure the diagnosis, so that sometimes the diagnosis and administration of tuberculosis drugs is delayed (Segagni Lusignani et al., 2013)

Cardiovascular diseases such as hypertension, Congestive Heart Failure in this study are comorbidities that have a significant relationship with the incidence of Diagnostic delay because the symptoms of this disease are sometimes the same as TB such as shortness of breath, chest pain, sometimes accompanied by coughing so that the main disease is often treated first. The CXR picture of these patients also sometimes does not show the typical picture of TB and sometimes the results of AFB sputum are also not supportive. This causes the administration of OAT to be delayed.(Asres et al., 2018)(Lestari et al., 2020)

Several references state that comorbid factors that often cause delays in the health care system are several diseases as mentioned in table 2, especially DM. This is because the clinical symptoms of TB patients with DM are often asymptomatic so that the diagnosis takes longer and therapy is delayed (Xiao et al., 2021). In this study, DM did not have a significant relationship with the incidence of delay/delay in diagnosis of the health system, possibly because the number of TB patients in this study was not large (22.4%) and the CXR results showed typical TB lesions, which were quite large (83.5%).).). The administration of non-TB drugs in the form of antibiotics including quinolones did not have a significant relationship with the incidence of delays in the health care system. This remains a problem that cannot be ignored considering that administering these drugs will exacerbate TB disease and can cause Multidrug-Resistant TB (MDR-TB) and the risk of transmission to people around them, thereby increasing the incidence of MDR-TB (Lee et al., 2020).

Several variables were predicted to be related to the occurrence of TB delay, namely the time of CXR examination, CXR diagnosis, AFB examination time, AFB diagnosis, Gen Xpert examination time and Gen Xpert diagnosis. The predictor factors for TB delay based on the time of examination and diagnosis are as shown in table 3.

Table 3
Predictor Factors of TB Delay based on Time of Examination and Diagnosis

No	Variabel	Group	Amount	Percentage	*p-value*
1	CXR examination time	Non-Delay	414	92.2	0.049*
		Delay	35	7.8	
2	CXR Diagnosis	Normal	9	2.0	1.00
		TB	375	83.5	
		Suspect TB	62	13.8	
		Non-TB	3	0.7	
3	AFB examination time	Non-Delay	147	32.7	0.00*
		Delay	19	4.2	
4	AFB Diagnosis	Non-TB	35	7.8	0.84
		TB	130	28.9	
5	Gen Xpert examination time	Non-Delay	220	49	0.37
		Delay	34	7.6	
6	Gen-Xpert Diagnosis	Non-TB	36	8.0	0.76
		TB	218	48.5	
7	Number of suspected TB patients	Non-Delay	101	29.0	
		Delay	348	77.5	

Statistical analysis results regarding the relationship of several variables with the incidence of TB delay showed a significant radiological examination time with p value of 0.049 and a smear examination time with p value of 0.000. The length of time for AFB examination was significantly related to TB delay, while TB diagnosis was based on AFB. Time duration and TB diagnosis based on TCM/Gene X Pert were not significantly related to the incidence of TB delay. AFB positive patients had less delay in comparison to AFB negative patients ($p < 0.05$, OR 0.389, RR 0.64). It can be explained by the logics that early diagnosis and prompt treatment can be executed timely with AFB positive TB patients, which facilitates avoiding the delay in treatment initiation (Islam et al., 2020) . Several factors affect TB diagnostic services in radiology installations, including the availability of radiology equipment, the availability of Human Resources (HR, radiographers), the availability of readers or radiology doctors or clinicians (Datiko et al., 2020). Several references state that the delay in the health care system delay is influenced by the diagnostic delay (1-3 days) and treatment delay (1-2 days) so that the number of delays in the health care system delay is about 5-7 days (Segagni Lusignani et al., 2013) (Gedeyon et al., 2019).

The average time required for CXR examinbation, Laboratory AFB microscopic and TCM Gene Xpert examinations, as well as health care system delays showed less than the maximum time called delay or late. This means that the health care system service delay was good because there were no delays, the time used for services to TB patients was good as shown in the table 4.

Table 4.
Average Time required for Health Care System Delay.

No	Information	Time (days)
1	CXR examination	1,94
2	AFB-Sputum Examination- TCM/Gene X-pert	1,15
3	*Health care sistem delay*	3,67

LIMITATION OF THE STUDY

During the pandemic , the study experienced problems in retrieving medical record data, where the amount of data could not be maximized (10 medical record per day) because there was a limitation on the length of time in the hospital. In addition, some of the data is incomplete, so it has to be redone. This research involves several hospitals, while Ethycal Clereance and licensing arrangements cannot be carried out simultaneously in all hospitals, must take turns a maximum of 2 hospitals. This causes data retrieval can not be done immediately and so delayed

CONCLUSIONS AND SUGGESTION

The predictor factors that influence the occurrence of Health Care System Delay TB are the time of radiological examination, the time of microscopic examination of AFB and suspected TB patients who have comorbid Congestive Heart Failure (CHF) and Hypertension.

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ETHICAL CONSIDERATIONS

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Conflict of Interest Statement

The research was conducted without any conflict of interest to anyone. The study began with the problem of delay in diagnosis of tuberculosis in the hospital. This study aims to find the factors that influence the delay in the diagnosis of tuberculosis, so that it can be used as a useful predictor factor in the treatment of tuberculosis in general.

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