Artikel Penelitian

Association of Multidrug-Resistant Tuberculosis (MDR-TB) Patients on Profile of Liver and Kidney Function

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Abstrak

Pendahuluan: terapi pasien yang mengalami tuberkulosis (TB) resistan obat (MDR-TB) masih belum tertangani dengan baik, lebih toksik, dan pengobatan lebih mahal. Organ hati merupakan metabolisme utama, dan ginjal merupakan organ utama dalam eksresi. Penelitian ini bertujuan untuk mengetahui hubungan TB resistan obat (MDR-TB) terhadap profil fungsi hati dan ginjal. **Metode:** penelitian ini merupakan penelitian potong lintang dengan teknik pengambilan sampel konsekutif. 24 responden yang mengalami TBC resistan obat tanpa HIV, yang telah melakukan tes biokimia. **Hasil:** jenis kelamin pasien MDR-TB pada fungsi hati; ALT (p=0,124), dan AST (p=0,077) dan fungsi ginjal; BUN (p=0,270), kreatinin (p=0,137). Usia pasien MDR-TB pada fungsi hati; ALT (p=0,5877) dan AST (p=0,093) dan fungsi ginjal; BUN (p=0,423), kreatinin (p=0,142). Komorbiditas pada pasien MDR-TB pada fungsi hati; ALT (p=0,756) dan AST (p=0,244) dan fungsi ginjal; BUN (p=0,816), kreatinin (p=0,612). **Simpulan:** Tidak ada hubungan jenis kelamin, usia, dan komorbiditas TBC resistan obat terhadap fungsi hati dan ginjal.
Kata kunci: Ginjal, Hati, Multidrug-Resisten Tuberkulosis

Abstract

Introduction: *Therapy of multidrug-resistant tuberculosis (MDR-TB) patients is still not handled properly, is more toxic, and is more high-priced. The liver is the primary metabolism, and the kidney is the main excretion organ. The study aims to know the association of multidrug-resistant tuberculosis (MDR-TB) patients on profile of liver and kidney function* ***Methods:*** *The research is a cross-sectional study with consecutive sampling. Twenty-four respondents were confirmed as MDR-TB patients without HIV who had done biochemical tests.* ***Results:*** *We found that sex of MDR-TB patients on liver function; ALT (p = 0.124) and AST (p = 0.077) and kidney function; BUN (p = 0.270), creatinine (p = 0.137). Age of MDR-TB patients on liver function; ALT (p = 0.587) and AST (p = 0.093) and kidney function; BUN (p = 0.423), creatinine (p = 0.142). Comorbid on MDR-TB patients on liver function; ALT (p = 0.756) and AST (p = 0.244) and kidney function; BUN (p = 0.816), creatinine (p = 0.612).* ***Conclusions:*** *There were no association in sex, age, and comorbid of MDR-TB on liver and kidney function.*
Keywords*: Kidney, Liver; Multidrug-Resistant Tuberculosis*

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INTRODUCTION

Mycobacterium tuberculosis, the aerobic acid-fast rod-shaped, causes tuberculosis (TB). TB usually attacks the lungs and other organs, including the brain, intestine, kidneys, or spine. TB is one of the oldest documented human diseases and the largest among infectious diseases, despite a diminished live vaccine and antibiotics worldwide.[1,2,3] High burden countries (HBC) for tuberculosis based on three indicators: TB, TB/HIV, and MDR-TB.[4] Bacteria of *M. tuberculosis* against the kinds of first-line drug treatments such as rifampicin and isoniazid called multidrug-resistant tuberculosis (MDR-TB).[5] New and previously treated TB cases have been tested for resistance to rifampicin and reported globally, approximately 30% (2.0 million) of the 6.7 million in 2017. There were 24% for new TB patients, and 160.684 cases of multidrug-resistant TB and rifampicin-resistant TB (MDR/RR-TB) were notified globally.[4] Indonesia ranked third among the top 30 high burden countries and ranked fifth the high MDR-TB. In 2018, only 46 percent of those cases to begin treatment among 9.038 patients were diagnosed.[6]

TB cases worldwide have increased due to the emergence of MDR-TB that encourages more toxic second-line drugs such as ethionamide, cycloserine,

kanamycin, and capreomycin. Moreover, treatment of MDR-TB is more delicate, more toxic, more expensive, and ineffective than the remedy of patients contaminated by susceptible strains.[5] Metabolism and excretion are the processes of removing an administered drug from the body. The main organ of metabolism is the liver (xenobiotic metabolism), and the organ primarily tasked with excretion is the kidney, although many metabolisms and excretion sites exist. The collection of the drug or its metabolism in toxic concentrations can be any severe pathology of either organ.[7,8,9] Within this research, we would like to know the association of multidrug-resistant tuberculosis (MDR-TB) patients on liver and kidney function.

METHODS

The research is a cross-sectional study with consecutive sampling. The data was collected from 2017-November 2019. Twenty-four respondents were confirmed with inclusion criteria including MDR-TB without HIV undergoing therapy, comorbid, biochemical examination records (AST, ALT, creatinine, and urea) and age groups (adolescents (10-19 years old), adults (19-59 years old), and elderly (≥ 60 years old).[10]

Patient characteristics were collected from the patient records, including diagnosis, sex, age, comorbid, the status of the liver and kidney biochemical test at General Hospital of Abdul Wahab Sjahranie Samarinda, East Kalimantan. Research permit No. 070/Diklit/3776/X/2019.

The data were determined and analyzed using One-Way Anova. The data was parametric and had normal distribution and homogeneous variants. If necessity was matched, the test would be replaced with alternative non-parametric.

RESULTS

The purpose of the study is to know the association of multidrug-resistant tuberculosis (MDR-TB) patients on the liver and kidney function at the General Hospital of Abdul Wahab Sjahranie Samarinda. We found twenty-four MDR-TB patients based on inclusion criteria. The data of characteristics are shown in table 1.

Data of biochemical tests on liver and kidney function were collected by medical records of patients. We proceeded with the data with statistical analysis to confirm whether there was a statistical difference or not. We first analyzed the data using the One-way Anova, and the results were not normally distributed ($p < 0.05$). Because the data were not normally distributed, we used a non-parametric test (Kruskal-Wallis Test).

The statistical analysis results it was not different significantly between sex of MDR-TB patients on liver function; ALT ($p = 0.124$) and AST ($p = 0.077$) and kidney function; BUN ($p = 0.270$), creatinine ($p = 0.137$), table 2.

Table 1. Characteristics of Multidrug-Resistant Tuberculosis at General Hospital of Abdul Wahab Sjaranie Samarinda

Characteristics	Number n = 24	Percentage
Sex		
Male	13	54
Female	11	46
Age (Year)		
Adolescent (10-19)		4.2
Male	1	
Female	0	
Adult (19-59)		87.5
Male	12	
Female	9	
Elderly (≥ 60)		8.3
Male	1	
Female	1	
Comorbid		
Diabetes mellitus	4	17
Noncomorbid	20	83

Table 2. Sex on Biochemical test for Liver and Kidney Function

Characteristics Sex	ALT, U/L (Mean ± SD)	*p value*	AST, U/L (Mean ± SD)	*p value*
	20.16 ± 12.98	0.124	26.66 ± 9.59	0.077
	BUN, U/L (Mean ± SD)	***p value***	**Creatinin, U/L (Mean ± SD)**	***p value***
	38.45 ± 48.42	0.270	1.09 ± 1.32	0.137

Age of MDR-TB patients on liver function; ALT (p = 0.587) and AST (p = 0.093) and kidney function; BUN (p = 0.423), creatinine (p = 0.142) was not different significantly, table 3.

Table 3. Age on Biochemical test for Liver and Kidney Function

Characteristics Age	ALT, U/L (Mean ± SD)	*p value*	AST, U/L (Mean ± SD)	*p value*
	20.16 ± 12.98	0.587	26.66 ± 9.59	0.093
	BUN, U/L (Mean ± SD)	***p value***	**Creatinin, U/L (Mean ± SD)**	***p value***
	38.45 ± 48.42	0.423	1.09 ± 1.32	0.142

Furthermore, it was not different significantly between comorbid on MDR-TB patients on liver function; ALT (p = 0.756) and AST (p = 0.244) and kidney function; BUN (p = 0.816), creatinine (p = 0.612), table 4.

Table 4. Comorbid on Biochemical test for Liver and Kidney Function

Characteristics Comorbid	ALT, U/L (Mean ± SD)	*p value*	AST, U/L (Mean ± SD)	*p value*
	20.16 ± 12.98	0.756	26.66 ± 9.59	0.244
	BUN, U/L (Mean ± SD)	***p value***	**Creatinin, U/L (Mean ± SD)**	***p value***
	38.45 ± 48.42	0.816	1.09 ± 1.32	0.612

DISCUSSION

The study results showed that most MDR-TB patients are 19-59 years old in males and females. The predominance of males, several socio-economic factors such as men being wage-earner, the smaller opportunity of awareness about the disease on TB prevalence in low-and middle-income countries is remarkably elevated among men than women. Moreover, males in the high-yielding age group have found it inopportune to attend or often retard to Directly Observed Treatment (DOTS) centers because of their work timings.[11,12] The female, either 40 years or older, has been a risk factor for MDR-TB because the more senior age can exacerbate the physical condition associated with the progressive loss of tissue and organ function and the occurrence of oxidative stress.[13,14] Furthermore, the women who suffer a lot of MDR-TB have the role of women as caregivers or live in the same place as MDR-TB patients so that susceptible to MDR-TB infection. However, it needs further studies because TB is multifactorial.[15,16]

The comorbid disease of the study is diabetes mellitus (DM). DM can amplify the side effects of OAT, especially renal disorders and peripheral neuropathy. However, if managed properly, the results of treatment are similar to non-DM cases.[17,18] Anti-Diabetic Drugs (OAD) are not contraindicated during MDR-TB treatment but usually require a higher dose of OAD so that it needs special handling.[17]

The ALT enzyme is directly related to hepatocellular damage. It is more specific to hepatocellular injury than AST, whereas an increase of AST can also be due to muscle, heart, or kidney injury. However, elevated ALT and AST enzymes can be a sign of drug-induced hepatotoxicity.[19,20] Creatinine is recommended for measuring glomerular filtration ability as well as monitoring the route of kidney disease. Urea can evaluate kidney function and help diagnose acute renal failure.[21] Serum creatinine is a more detailed assessment of renal function than urea. In contrast, urea can also be elevated in gastrointestinal (GI) bleeding, dehydration, catabolic states, and a high protein diet. However, an increase in urea still occurs early in kidney disease.[22]

The average of ALT and AST levels on the data is within normal ranges. Patients of MDR-TB may not have reached six months of treatment or have the time to implement drug-induced dysfunction. The incidence of hepatotoxicity in the treatment of MDR-TB patients only occurred at a median time of about six months after starting treatment.[20] Treatment of MDR-TB patients consists of first-line OAT and

second-line OAT. Second-line OATs are less toxic to the liver than the first-line OAT. Examination of ALT and AST levels before starting treatment and monitoring elevated liver enzymes during treatment are recommended.[17]

The data of our study indicates serum urea and creatinine levels in MDR-TB patients are within normal ranges. It can be patients who have not received initial treatment with injections of kanamycin or capreomycin having nephrotoxic side effects. A study states that most patients with MDR-TB is undergoing therapy with elevated creatinine will return to normal levels before injection or before MDR-TB treatment is complete.[23] In addition, nephrotoxic side effects of MDR-TB treatment are less common; however, comorbidity such as DM causes worsens kidney function[24].The incidence of renal disorders was found to be more common in men than women.[25]

The results indicate that there is no difference sex, age, and comorbid on liver and kidney function the level of liver and kidney of MDT-TB patients. The previous studies were obtained in the study of Gezahegn, et al. (2020) that sex and age were not significantly associated with liver dysfunction.[26] Research conducted by Shamaei, et al. (2017) also did not show significant differences in liver dysfunction with respect to sex, age, and comorbid on MDR-TB treatment.[27] However, in a study by Saito, et al. (2019) there was a significant difference in age with kidney dysfunction, while sex did not find a significant difference.[28]

The limitation of the study is the small sample size. It is suggested that further research be carried out cohort study to follow the direct effects during treatment of patients' multidrug-resistant tuberculosis with large sample size.

CONCLUSION

There were no association in sex, age, and comorbid on biochemical test for liver and kidney function. The data also not showed changes in liver function as indicated by ALT and AST levels and on kidney function as indicated by creatinine and urea levels. It is concluded, there are no hepatotoxicity and nephrotoxicity in treating multidrug-resistant tuberculosis patients at the General Hospital of Abdul Wahab Sjahranie Samarinda.

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