



## Case report

## Comparison of acid fast bacilli (AFB) smear for *Mycobacterium tuberculosis* on adult pulmonary tuberculosis (TB) patients with type 2 diabetes mellitus (DM) and without type 2 DM

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## ABSTRACT

**Background:** According to the Global Tuberculosis Report 2015, Indonesia ranked as second country in the world with the highest number of pulmonary tuberculosis cases. By 2015, the number of pulmonary TB new cases in Indonesia has increased to 330.910 cases of 2014 where 324.539 cases. DM is one of the most important factors that influence the occurrence worsening TB. Now is known that DM patients have body's immune response disorder thereby facilitating *M. tuberculosis* infection and causing TB.

**Method:** This research is cross sectional design. The sample in this research are adult pulmonary TB patients at General Hospital Grade C period October 1, 2013–March 31, 2016 as much as 225 patients.

**Result:** AFB smear results in patients with type 2 DM with smear 3 + was 14 (17.28%), 2 + was 15 (18.52%), 1 + was 15 (18.52%) and negative (–) was 37 (45.68%). AFB smear results in patients without type 2 DM with smear 3 + was 3 (2.08%), 2 + was 6 (4.17%), 1 + was 19 (13.19%), negative (–) was 112 (77.78%) and have no sputum was 4 (2.78%). Number of adult pulmonary TB patients were 225 patients. Of the 225 patients, found 81 patients with type 2 DM and 144 patients without type 2 DM.

**Conclusion:** AFB smear positive found more in adult pulmonary TB patients with type 2 DM compared to TB patient without type 2 DM. It also found statistically significant between type 2 DM with the AFB smear results on adult pulmonary TB patients.

## 1. Introduction

*Mycobacterium tuberculosis* infection particularly attacks the lungs (pulmonary TB) is a disease that is still a public health problem the world today. In 1993, the World Health Organization (WHO) has declared tuberculosis (TB) as a Global Health Emergency [1]. According to the Global Tuberculosis Report 2015, found 9.6 million new cases of pulmonary tuberculosis in 2014 with the number of cases occurs in Southeast Asia (58%), the Western Pacific (58%) and Africa (28%) [2]. Also reported that the prevalence and incidence of pulmonary tuberculosis in 2014 increased to 647/100.000 and 399/100.000 population from the previous year of 272/100.000 and 183/100.000

population, as well as the mortality rate from tuberculosis in 2014 that had increased to 41/100,000 population from the previous year, namely 25/100.000 from population [3].

Based on data from the Global Tuberculosis Report 2014, Indonesia entered the top six countries in the world with the number of cases of pulmonary tuberculosis highs along with India, China, Nigeria, Pakistan and South Africa, 4 whereas according to data from the Global Tuberculosis Report 2015, Indonesia has increased keperingkat at riding position with both countries in the world with the highest number of cases of pulmonary TB after India, with the number of cases of pulmonary tuberculosis by 10% of the total number of cases of pulmonary tuberculosis in the world [4].

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By 2015, the number of new cases of pulmonary TB in Indonesia increased to 330 910 cases of pulmonary TB in new cases in 2014, namely 324 539 cases. The highest number of cases of pulmonary TB were reported in the province of West Java, East Java and Central Java (three provinces, has a number of cases by 38% of the total number of new cases of pulmonary TB in Indonesia). By age group, new cases of pulmonary tuberculosis in 2015 found most frequently in the age group of 25–34 years with a percentage of 18.65%, followed by the age group 45–54 years (17.33%), 35–44 years (17.18%), 15–24 years (15.89%), 55–64 years (13.82%), 0–14 years (8.59%) and  $\geq 65$  years (8.54%) [5].

In 2014 discovered new cases of pulmonary tuberculosis with AFB is positive in Indonesia as many as 176 677 cases, decreased when compared with the new cases with smear-positive pulmonary TB were discovered in 2013, namely 196 310 cases. The highest number of cases reported in the province of West Java, East Java and Central Java. New cases with smear positive pulmonary TB in these three provinces for 40% of the total number of new cases with smear-positive pulmonary TB in Indonesia [6].

Diabetes mellitus (DM) is one of the most important risk factor in the deterioration of TB. Since the beginning of the 20th century, clinicians have observed an association between diabetes and TB, although it is still difficult to determine whether the DM that precede TB or TB that cause the clinical manifestations DM. People with diabetes mellitus have a disorder of the body's immune response so as to facilitate the infection of *M. tuberculosis* and cause TB disease so that people with diabetes have a risk of 2–3 times higher for pulmonary tuberculosis disease than patients without DM [7].

The frequency of diabetes in TB patients reported to be around 10–15% and the prevalence of TB 2–5 times higher in patients with diabetes compared with non-Diabetes [8]. DM patients who were diagnosed with TB have a higher risk of death during TB treatment and risk of relapse after completion of treatment [9]. Research Dobler et al. in Australia found people with diabetes who use insulin as a treatment have a higher risk of suffering from pulmonary tuberculosis [10], while research in Indonesia in the year 2001–2005 found 60 cases of DM among 454 patients TB [11–13]. The research also stated that 40% of patients with pulmonary tuberculosis discount risk history of diabetes and diabetic patient to undergo pulmonary tuberculosis by 4.7 times. Aim of this study is to compare the results of smear examination of *Mycobacterium tuberculosis* in patients with pulmonary TB disease adults with type 2 diabetes with the results of smear examination of *Mycobacterium tuberculosis* in adult pulmonary TB patients who are not accompanied by disease type 2 diabetes. Interest is learning the description of the basic characteristics (gender, age, patient type, category ATA, the results of treatment), conversion rate and clinical symptoms in adult pulmonary TB patients with type 2 diabetes who accompanied and not accompanied by type 2 diabetes. The hypothesis of this study is AFB smear positive found more in adult pulmonary TB patients with type 2 DM compared to TB patient without type 2 DM.

## 2. Materials and method

This research is a comparative cross-sectional study design. This research was conducted at the General Hospital of class C Jakarta in November 2016. On 56 Permenkes RI 2014 describes Hospital grade C is composed of medical personnel (at least 9 general practitioners, two general dentist, 2 basic medical specialists, 1 specialist support, and 1 dentist specialist), power pharmacy (at least one pharmacist head of pharmacy, two pharmacists who served in inpatient assisted by 4 technical personnel pharmacy, four pharmacists in inpatient assisted eight people power pharmaceutical technical, 1 pharmacist as coordinator reception, distribution and production), nursing staff (at least 2 nurses for every three beds), as well as having space Emergency room (ER) which is open 24 hours, outpatient, inpatient, ambulatory intensive, ambulatory surgery, childbirth, radiology, clinical laboratory, blood services, medical rehabilitation, pharmacy, nutrition and room

installations of body [14].

Diagnosis of pulmonary TB in adults in this study was established first with bacteriological examination. Bacteriological examination is a direct microscopic examination of acid fast bacilli (AFB) smear with interpretation of results according to International Union Against Tuberculosis and Lung Disease (IUALTD). If bacteriologic examination results are negative, then the diagnosis of pulmonary TB may be clinically performed using clinical examination and investigation (at least appropriate chest radiographic examination and established by trained physicians interpreting TB lesions) [15,16]. The criteria for the diagnosis of type 2 DM in this study were fasting blood glucose (FBG) level  $\geq 126$  mg/dl, blood glucose (BG) level  $\geq 200$  mg/dl with classic DM complaints, plasma glucose level  $\geq 200$  mg/dl 2 hours after Oral glucose tolerance test (OGTT), or HbA1c  $\geq 6.5\%$  examination using standardized methods by the National Glycohemoglobin Standardization Program (NGSP) [17–19].

The sample in this research was taken with total sampling technique totaling 225 patients that have met the criteria for inclusion and exclusion criteria. The inclusion criteria were adult patients with pulmonary TB age  $> 18$  years, pulmonary TB patients with type 2 DM, and pulmonary TB who are not accompanied by disease type 2 diabetes. These patients have complete data in medical record. The exclusion criteria were patients with extrapulmonary TB, TB patients are accompanied with type 1 DM disease and pulmonary TB patients who do not have the results of the BG level content, FBG and HbA1c.

This study uses secondary data about the event or the diagnosis of adult pulmonary TB are taken from the book form of TB registers and the medical records of adult pulmonary TB patients pulmonary clinic General Hospital C Class the period October 1, 2013–Mar 31, 2016. Data collected included: patient characteristics adult pulmonary TB (age, gender, type of patient, category ATA, treatment results, the conversion of smear, clinical symptoms); BG levels, FBG and HbA1c adult pulmonary TB patients; *M. tuberculosis* sputum smear examination results in adult pulmonary TB patients accompanied by type 2 DM disease and the results of smear examination *M. tuberculosis* in adult pulmonary TB patients who are not accompanied by disease type 2 DM.

This research used Chi Square test to determine the relationship between BG levels, FBG, HbA1c and type 2 DM disease with the results of smear examination in adult pulmonary TB patients. IBM SPSS Statistics version 23 statistical tools were used in this study.

## 3. Results

Table 1 are data indicate that patients with male sex has a higher number ie 138 patients (61.33%) compared with patients who are female, amounting to 87 patients (38.67%). The above data also show that the age group 45–54 years had the highest number with 76 patients (33.78%) followed by the age group of 55–64 years with the number 41 (18.22%), aged  $\geq 65$  years with the number of 34 patients (15.11%), aged 25–34 years with 29 patients (12.89%), aged 35–44 years with 26 patients (11.56%) and aged 15–24 years with a number of 19 patients (8.44%). For the category of patient type, the majority of patients based on the above data is the number of new patients with 208 patients (92.44%), then the patient relapsed with a number of 6 patients (2.67%), patients default with 4 patients (1.78%), patients failed by the number 1 patient (0.44%), and the type of patient, etc. with the number 6 (2.67%). For the category of ATA, the majority of patients using ATA Category I with the number of 208 patients (92.44%), while category II ATA is used by 17 patients (7.56%). For the category of results of treatment, patients with complete treatment has the highest number with 145 patients (64.45%), then the patient recovered with a number of 57 patients (25.33%), default by the number of patients 12 patients (5.33%), patients died with a total of 7 patients (3.11%) and patients moved by the number of 4 patients (1.78%).

The results of patients who had a BG levels  $\geq 200$  mg/dl was 50 patients (10.92%), while patients with low BG levels 100–199 mg/dl

**Table 1**  
Basic characteristics of study sample.

Basic Characteristic		Type 2 DM		Non- Type 2 DM	
		Amount	Percentage	Amount	Percentage
Gender	Male	48	21,3%	92	40,9%
	Female	33	14,6%	52	23,1%
Age	15–24	0	0	19	8,4%
	25–34	0	0	29	12,9%
	35–44	0	0	26	11,5%
	45–54	46	20,4%	31	13,8%
	55–64	25	11,1%	15	6,7%
	≥65	10	4,4%	24	10,7%
Type of TB Patient	New	76	33,8%	132	58,7%
	Relapse	3	1,3%	3	1,3%
	Default	1	0,4%	3	1,3%
	Failed	0	0	1	0,4%
	Move	0	0	0	0
	others	1	0,4%	5	2,2%
ATA Category	Category of I	76	33,8%	132	58,7%
	Category of II	5	2,2%	12	5,3%
Treatment Results	Recovery	38	16,9%	20	8,9%
	Treatment Completed	35	15,5%	108	48%
	Default	4	1,8%	9	4%
	Failed	0	0	0	0
	Move	1	0,4%	3	1,3%
	Dead	3	1,3%	4	1,8%

and < 100 mg/dl respectively amounted to 77 patients (16.81%) and 63 patients (13.76%). The above data also showed that the number of patients who had a fasting blood glucose level ≥ 126 mg/dl amounted to 64 (13.94%), while patients who had fasting blood glucose level 100–125 mg/dl and < 100 mg/dl respectively account for 10 patients (2.18%) and 13 patients (2.84%). For blood glucose postprandial (BGPP) levels, patients with examination results ≥ 200 mg/dl totaling 59 patients (12.88%), 140–199 mg/dl are 5 patients (1.09%), and < 140 mg/dl are 15 patients (3.27%). For A1C, patients who had ≥ 6.5% examination results were 18 patients (3.93%), 5.7–6.4% amounting to 1 patient (0.22%), and < 5.7 were 3 patients (0.66%).

The adult pulmonary TB patients with type 2 diabetes disease amounts to 81 patients (17.69%), whereas adult pulmonary TB patients who are not accompanied by disease totaled 144 type 2 diabetes patients (31.44%).

The number and percentage of clinical symptoms of pulmonary tuberculosis in patients with type 2 diabetes disease symptoms are most widely perceived is coughing ≥ 2 weeks were found in 77 patients (95.06%), then shortness of breath totaling 67 patients (82.72%), malaise totaling 66 patients (81.48%), body weight loss totaling 65 patients (80.25%), anorexia totaling 64 patients (79.01%), night sweats totaling 61 patients (75.30%), chest pain of 60 patients (74.07%), as well as coughing up blood and fever were each found in 58 patients (71.60%).

Clinical symptoms of TB in patients who are not accompanied by type 2 diabetes disease ≥ 2 weeks Cough is a symptom that is most felt by the number of 134 patients (93.06%), followed by shortness of breath were found in 118 patients (81, 94%), fever were found in 110 patients (76.39%), and anorexia with decrease of body weigh, each of which was found in 106 patients (73.61%), chest pain were found in 97 patients (67.36%), night sweats were found in 96 patients (66.67%), malaise found in 91 patients (63.19%), as well as coughing up blood were found in 81 patients (56.25%).

The majority of patients with pulmonary TB AFB (+) were accompanied with type 2 diabetes have a high conversion rate after the end of the intensive phase that is numbered 38 patients (86.76%). The above data also showed no adult pulmonary TB patients AFB (+) with type 2 diabetes who have not the result of the conversion by the end of the intensive phase.

**Table 2**  
AFB Examination Results in Patients with pulmonary TB are accompanied with type 2 diabetes and with out type 2 diabetes.

Chi Square Test	AFB Examination Results				P value
	3+	2+	1+	-	
Pulmonary tuberculosis with diabetes mellitus type 2	14	15	15	37	p = 0.000
Pulmonary TB is not accompanied by type 2 diabetes mellitus	3	6	19	112	

The majority of adult patients with pulmonary TB AFB (+) were not accompanied with type 2 diabetes have a conversion result at the end of an intensive phase with a number of 20 patients (71.43%), while for the result of the conversion is not only found in 1 patient (3.57%).

Table 2 data shows the results of smear examination in patients with pulmonary TB disease adult type 2 diabetes with a value +++ (3+) amounted to 14 patients (17.28%), the value ++ (2+) total 15 patients (18, 52%), the value + (1+) amounted to 15 patients (18.52%) and a negative value (-) amounted to 37 patients (45.68%). The above data also shows the majority of adult pulmonary TB patients who are not accompanied by disease type 2 diabetes mellitus have a smear test results negative (-) by the number of 112 patients (77.78%), while the results of smear examination with a positive value (3+/2+/1+) only held by a minority of adult pulmonary TB patients were accompanied with type 2 diabetes (+++ (3+) was found in 3 patients (2.08%), the value ++ (2+) was found in 6 patients (4.17%), the value + (1+) was found in 19 patients (13.9%)).

Table 3 data indicate that patients with pulmonary tuberculosis grown with the results of smear-positive (1+/2+/3+) are more common in patients with pulmonary tuberculosis adults with higher levels of BG, FBG or BGPP increased (BG ≥ 200 mg/dl, FBG ≥ 126 mg/dl or BGPP ≥ 200 mg/dl). In addition, found an association statistically significant between levels of BG (p value = 0.000), FBG (p value = 0.009), BGPP (p value = 0.012) with the results of the AFB in patients with pulmonary tuberculosis adult because p value based on the results calculations using Chi Square test was < 0.05. The above data also showed that patients with high levels of BG ≥ 200 mg/dl (OR = 4.179), FBG ≥ 126 mg/dl (OR = 4.420), BGPP ≥ 200 mg/dl (OR = 4.696) had a risk four times higher to obtain the results of smear examination with positive scores than patients with BG levels < 200 mg/dl, FBG < 126 mg/dl, and BGPP < 200 mg/dl. HbA1c levels, which is one of the diagnostic criteria were included in the study variables can not be linked to the results of smear examination because very few adult pulmonary TB patients who have HbA1c test results, which can not be calculated using Chi Square test because the data are homogeneous.

The above data in Table 4 indicate that patients with pulmonary tuberculosis grown with the results of smear-positive (3+/2+/1+) are more common in patients with pulmonary TB adults with the disease of

**Table 3**  
Relationship of BG, FBG and BGPP with AFB examination results.

Chi Square Test	AFB Examination Results	P value	CI 95%	OR		
					(1+/2+/3+) -	
BG (mg/dl)	≥200	26	24	p = 0.000	2.089–8.358	4.179
	< 200	28	108			
FBG (mg/dl)	≥126	39	25	p = 0.009	1.535–12.726	4.420
	< 126	6	17			
BGPP (mg/dl)	≥200	36	23	p = 0.012	1.503–14.673	4.696
	< 200	5	15			

**Table 4**  
Relations of Type 2 diabetes with AFB Examination Results.

Chi Square Test	AFB Examination Results		P value	CI 95%	OR
	(3+/2+/1+) –				
Pulmonary tuberculosis with diabetes mellitus type 2	44	37	p = 0.000	0.115–0.384	0.210
Pulmonary TB is not accompanied by type 2 diabetes mellitus	28	112			

type 2 diabetes than in patients with pulmonary TB adults who are not accompanied by type 2 diabetes. The above data also showed statistically significant association between type 2 diabetes disease with the results of smear examination in patients with adult pulmonary TB because p value < 0.005.

#### 4. Discussion

In the present research found cases of pulmonary TB is more common in patients with male sex compared with patients who are female. The results are consistent with research conducted by Alisjahbana et al., Park et al., Wang et al., Fengling et al., Syed Sulaiman et al., Dobler et al., Dooley et al., And Ruth Haryanti et al. [7–12,20,21] who discovered pulmonary TB patients with male gender higher compared to patients whose sex of female. These results are also consistent with the data from the Indonesia Health Profile 2013, 2014, 2015 issued by the Ministry of Health of Indonesia which states that cases of pulmonary TB is more common in males that compared to female [3,5]. Not only for sex, the subject/sample also found that cases of pulmonary TB is more common in the group age 45–54 years. This happens because the adult pulmonary TB patients who become research subjects are included in the category of Type 2 DM (BG  $\geq$  200 mg/dl, FBG  $\geq$  126 mg/dl or HbA1c  $\geq$  6.5%) were aged > 45 years (according to one risk factors for type 2 diabetes are aged > 45 years).

Distribution by type of patients showed the majority of patients were found in this study is a new patient. These results are consistent with research Fengling et al. and Ruth Haryanti Sihotang et al. [8,12] who also found the majority of patients who obtained is new patient. For treatment outcomes, the study found that the majority of patients received full treatment at the end of the treatment phase. These results are consistent with studies of Wang et al. [11] who also found the majority of patients received full treatment at the end of the treatment phase in the department of Friendship which found that the highest rate of treatment results in patients with MDR-TB is default. High rate of default on MDR TB cases might be due to the onset of depression, anxiety, and stress the socio-economic in TB treatment phase MDR. For ATA category, in this study, the majority of patients using the first category compared with the ATA category II. This is because the majority of the types of patients who are found in this study were new patients so that many categories of ATA given is ATA category I.

In this research, the clinical symptoms most commonly experienced are coughing  $\geq$  2 weeks. These results are consistent with research conducted Park et al. and Wang et al. [10,11] who found cough  $\geq$  2 weeks as clinical symptoms are most often perceived pasien. These results are also consistent with studies that find Indra Wijaya most clinical symptoms felt by the patient is coughing  $\geq$  2 weeks. In the present research found patients with pulmonary TB adults with DM type 2 have the results of AFB with a positive value (3+/2+/1+) is higher than the results of the AFB with a positive value in patients with pulmonary TB adults who are not accompanied DM type 2. These results are consistent with research conducted Park et al., Wang et al.,

Fengling et al. and Dooley et al. [10–12,20] who find adult pulmonary TB patients accompanied with DM had a smear test results with a positive value higher than the results of smear examination with a positive value in patients with pulmonary TB who are not accompanied DM. These results are also in accordance with Sukara research Safri Agung et al. and Vitello et al. [22] which found that DM patients with pulmonary TB disease have the results of smear examination with a positive value higher than the results of smear examination with grades negatif. Value positivity were found to be higher in patients with pulmonary tuberculosis DM likely due to a decline in system the body's defenses or immunocompromised in diabetic patients due to decreased function of alveolar macrophages to phagocytosis be disturbed.

AFB conversion rate at the end of the intensive phase of the subject/sample showed a high rate compared to the no conversion. These results are consistent with studies Fengling Mi et al. [12] who found AFB conversion results at the end of the intensive phase is higher than the figure does not konversi. These results are also consistent with studies Iis Kurniati and Ruth Haryanti Sihotang et al. [8,23] who found AFB conversion results in patients with pulmonary TB AFB (+) is higher than the figures do not konversi. However, AFB conversion rate in this study was not able to meet the national target of a minimum reach 80%. In this research to found an association statistically significant between levels of BG and FBG which is one of the criteria diagnostic.

#### 5. Conclusion

From these results it can be concluded as follows:

1. Patients who have adult pulmonary TB smear positive test results are more common in adult pulmonary TB patients with BG levels, FBG or BGPP increased.
2. Adult pulmonary TB patients with smear-positive test results are more common in adult pulmonary TB patients were accompanied diseases type 2 diabetes compared to adult pulmonary TB patients who are not accompanied by disease type 2 diabetes.
3. There is a statistically significant relationship between the level of BG, FBG, BGPP and type 2 diabetes disease with the results of smear examination in adult pulmonary TB patients.

#### Appendix A. Supplementary data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.rmcr.2018.02.008>.

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