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#### **Conference Paper**

# The Correlation of Chest Radiographic Image of Pulmonary Tuberculosis in Type 2 Diabetes Mellitus Patients with HbA1C Level

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#### Abstract

Globally, tuberculosis (TB) and diabetes mellitus (DM) are two significant factors of morbidity. Several studies show a bidirectional relation between these two diseases. Diabetes mellitus increases the risk of active TB infection. As a standard procedure, Glycated Hemoglobin (HbA1C) level is used for monitoring patients with DM. This study aimed to identify the correlation of chest radiographic image of pulmonary tuberculosis with the HbA1C level in type 2 DM patients. A descriptive analytical survey with the cross-sectional study was performed in 32 subjects with type 2 DM and pulmonary TB. Statistical analysis was done by using gamma test, and we found a significant (p=0.042) and robust (r= 1) correlation between HbA1C level and pulmonary TB lesion area. It is concluded that chest radiographic images of pulmonary TB are significantly correlated with the HbA1C level in patients with Type 2 DM.

Keywords: Chest radiography, pulmonary TB, HbA1C levels, DM

## **1. Introduction**

Tuberculosis (TB) and diabetes mellitus (DM) are two critical health issues. Many studies have shown a bidirectional relation between these two diseases [1, 2]. The relation between TB and DM is more prominent in developing countries where TB is endemic, and the burden of DM is increasing. This becomes the next challenge for global TB control worldwide [1-4].

TB is known as the leading killer among bacterial infections in the world. The disease is caused by *Mycobacterium tuberculosis* (MTB), which is rod-shaped, aerobic and acidresistant. In Indonesia, TB is a significant public health problem. Indonesia is a country with the fifth most sufferers in the world after India, China, South Africa, and Nigeria. Pulmonary TB attacks 9.4 million people and has killed 1.7 million people worldwide each year [5].

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Diabetes mellitus increases the risk of active TB infection by 3.11 times [2]. With an increase in DM pandemic that is 80% in a TB endemic area, then TB will be a significant problem in the future. Although the incidence rate of TB has decreased, it has not reached the expected rate which is 1 new case per 1 million population [6, 7]. Southeast Asia is a group of countries with a high burden of TB and the rapid growth of DM prevalence, but many researchers report on TB in relation to DM [2, 3].

One of the laboratory tests used to determine early complications and control the compliance of DM treatment is Glycated Hemoglobin (HbA1C). Evaluation of HbA1C level has become the gold standard for monitoring glycemic control in patients with DM. HbA1C is one of the fractions of hemoglobin in the human body which binds to glucose enzymatically. Excessive glucose will always bind to hemoglobin. HbA1C reflects glucose levels over the past three months (according to the viability of human red blood cells are approximately 100-120 days). Thus it can provide information on how high the glucose level in the previous three months. This HBA1C evaluation can see how much the patient's compliance with the treatment [8].

Chest radiographic examination is one of the diagnostic modalities performed when physical examination supported clinical symptoms in the presence of abnormalities in the lung or if there is a history of old pulmonary tuberculosis [9]. The chest radiological features of TB patients are determined by several factors including duration of illness and the immunological status of the patient. Most TB-DM patients have a typical radiological pattern consisting of confluent, cavity, and wedge-shaped lesions spreading from the hilum to the edges, especially in the lower zone of the lung, whereas in non-DM TB patients lesions are usually infiltrates in the upper lobe. In pulmonary TB with DM, TB lesions are found in the lower lung fields more than those in the upper lung field. Some other studies reported that the radiological pattern of pulmonary tuberculosis patients with DM tends to be atypical therefore the finding of the lesions in the lower lung field in DM patients should be considered as the possibility of TB infection so that proper diagnosis and treatment can be performed [10, 11]. This study aimed to determine the correlation between HbA1C levels with chest radiograph images of pulmonary TB in patients with type-2 DM.

### 2. Method

This was a cross-sectional study conducted in RSUD Cilegon, Banten Province, from January to March 2016. The subjects were patients aged 30 years old and above, diagnosed with type-2 diabetes, and having sputum smear results of positive and negative

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results. HbA1C levels were measured and grouped into normal (<5.7%), pre-diabetes (5.7 -6.4%) and diabetes ( $\geq$ 6.5%). In the diabetes group, HbA1C (glycemic control) was divided into: <7%, 7-9%, and> 9%. Pulmonary TB radiography is a typical pattern on chest radiological examination representing to pulmonary tuberculosis. The results of radiological examination were clear X-ray photos of postero-anterior (PA) position interpreted by a radiologist. The measurements of the lesions in the lungs were determined using criteria from the Indonesian Pulmonary and Respirology Doctor Association. Based on the extent of the process seen on chest X-ray (CXR), there are minimal and large lesions [12]. A minimal lesion is defined as the process affecting part of one or two of lungs in which the area does not exceed the second anterior intercostal space (lung volume that is located above the chondrosternal junction of the second rib of the front and the spinous process of the thoracic 4 or 5 vertebrae), and no cavity is found whereas a large lesion is a wider process than the minimal one. Ethical clearence was obtained from the Bioethics Commission of Medical/Health Research, Faculty of Medicine, Universitas Sultan Agung, Semarang. The correlation analysis was done by using the gamma test with SPSS version 17.

### **3. Results**

There were 32 subjects who met our inclusion criteria (Table 1 and Table 2). They were dominated by male patients (75%). Most of them had an elementary school education (37.5%). They were mostly laborers (34.4%). The mean age of the subjects was 53.7 years old, ranging from 33 to 69 year old. The duration of being DM varied between 0 years (newly diagnosed) and 10 years. The lowest HbA1C level was 6.7, and the highest was 14.6%. The random blood glucose level ranged from 112 to 652 mg/dl. Hemoglobin (Hb) level obtained a minimum of 10.2 and a maximum of 17.1%.

The clinical description of the respondent's condition (Table 3) showed that the new cases of pulmonary TB were found in 28 patients (87.5%). Pulmonary TB lesions with a broad category reached 90.6% of all respondents. Types of lung lesions in the form of consolidation/infiltrates were found in 32 respondents; cavities were obtained in 15 respondents and lesions of pleural effusion were obtained in 5 respondents. Half of the total respondents had HbA1C values in the range of 7-9%. There were 24 (75%) active smokers. All smokers were male with the duration of smoking ranged from 10 to 30 years, and they generally smoked 1 to 2 packs of cigarettes daily. The correlation analysis was done by using gamma test (Table 4) and we obtained a significant relation between HbA1C and pulmonary TB lesion (p = 0.042) with a positive and robust correlation (r= 1).

Variables		
Variables	n	Percentage (%)
Gender		
• Male	24	75.0
• Female	8	25.0
Education		
<ul> <li>Elementary school</li> </ul>	12	37.5
<ul> <li>Junior high school</li> </ul>	18	25.0
<ul> <li>Senior high school</li> </ul>	9	28.1
• Diploma	1	3.1
• Graduates	1	3.1
<ul> <li>Post Graduates</li> </ul>	1	3.1
Job		
<ul> <li>Unemployed</li> </ul>	4	12.5
• Laborers	11	34.4
Entrepreneur	8	25.0
Civil Workers	3	9.4
Retiree	1	3.1
Housewife	5	15.6

TABLE 1: Demographic characteristics of the study subjects.

TABLE 2: Numerica	l data	description.
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Variables (n=32)	Minimum	Maximum	Mean (SD)
Age (years)	33	69	53.7 (9.44)
Duration diagnosed as DM	0	10	2.31 (2.47)
HbA1C level (%)	6.7	14.6	9.2 (11.28)
Glucose levels (mg/dl)	112	652	314 (135.5)
Hb levels (gr/dl)	10.2	17.1	12.7 (1.56)

### 4. Discussion

The variables used for demographic data in our study were gender, age, education, and occupation. The chest radiographic features in our study were based on the extent of the lesions found which was categorized into minimal and extensive lesions. The severity of DM was based on HbA1C levels which were categorized into three levels:<7%, 7-9%, and > 9%.

The correlation between chest radiographic images of TB patients and HbA1C levels were analyzed with gamma test. It showed a positive correlation with very strong correlation coefficient. The results of our study support the previous research conducted by Chen Yuang Chiang which reported that glycemic control significantly affected the manifestation of radiographic images of pulmonary TB in DM patients [13].

Type of TB cases         Image: Construct of the sputum         28         87.5           • Old cases         4         12.5           BTA test of the sputum         22         65.6           • Negative         10         34.4           • Negative         10         34.4           The area of TB lung lesions         -         -           • Minimal         3         9.4           • Extensive         29         90.6           The type of lung lesion         -         -           • Consolidates/infiltrates         32         100           • Upper right         18         56.3           • Middle right         14         43.8           • Lower right         12         37.5           • Upper left         16         50           • Addele left         17         53.1           • Lower left         16         50.0	Variables	Frequency	Percentage (%)
Old cases         4         12.5           BTA test of the sputum         22         65.6           • Negative         10         34.4           The area of TB lung lesions         9.4         10           • Minimal         3         9.4           • Extensive         29         90.6           The type of lung lesion         10         34.4           • Consolidates/infiltrates         32         100           • Upper right         18         56.3           • Middle right         14         43.8           • Lower left         16 </td <td>Type of TB cases</td> <td></td> <td></td>	Type of TB cases		
BTA test of the sputum       22       65.6         • Negative       10       34.4         The area of TB lung lesions	• New cases	28	87.5
• Positive       22       65.6         • Negative       10       34.4         The area of TB lung lesions	• Old cases	4	12.5
Negative         10         34.4           The area of TB lung lesions         3         9.4           • Minimal         3         9.4           • Extensive         29         90.6           The type of lung lesion         -         -           • Consolidates/infiltrates         32         100           • Cavity         15         46.9           • Pleural effusion         5         15.6           The site of the lung lesion         -         -           • Upper right         18         56.3           • Middle right         14         43.8           • Lower right         12         37.5           • Upper left         12         37.5           • Middle left         17         53.1           • Lower left         16         50           HbA1C levels         -         -           • < 7%	BTA test of the sputum		
The area of TB lung lesions	Positive	22	65.6
Minimal3 $9.4$ • Extensive29 $90.6$ The type of lung lesion22 $100$ • Consolidates/infiltrates $32$ $100$ • Cavity15 $46.9$ • Pleural effusion5 $15.6$ The site of the lung lesion $-$ • Upper right18 $56.3$ • Middle right14 $43.8$ • Lower right12 $37.5$ • Upper left12 $37.5$ • Middle left17 $53.1$ • Lower left16 $50$ HbA1C levels $ -$ • < 7%	Negative	10	34.4
• Extensive2990.6The type of lung lesion $$	The area of TB lung lesions		
The type of lung lesion       Image: mathematical stress in the stress is stress in the	• Minimal	3	9.4
$\cdot$ Consolidates/infiltrates32100 $\cdot$ Cavity1546.9 $\cdot$ Pleural effusion515.6The site of the lung lesion- $\cdot$ Upper right18 $\cdot$ Upper right14 $\cdot$ 43.8 $\cdot$ Lower right12 $\cdot$ 1237.5 $\cdot$ Upper left12 $\cdot$ 37.5 $\cdot$ Middle left17 $\cdot$ 53.1 $\cdot$ Lower left16 $\cdot$ 50 $\cdot$ 7%3 $\cdot$ 7%3 $\cdot$ 7% $\cdot$ 9%14 $\cdot$ 78 $\cdot$ 788 $\cdot$ 78 $\cdot$ 79	Extensive	29	90.6
• Cavity1546.9• Pleural effusion515.6The site of the lung lesion $ -$ • Upper right1856.3• Middle right1443.8• Lower right1237.5• Upper left1237.5• Middle left1753.1• Lower left1650• HbA1C levels $ -$ • < 7%	The type of lung lesion		
• Pleural effusion515.6The site of the lung lesion• Upper right1856.3• Middle right1443.8• Lower right1237.5• Upper left1237.5• Middle left1753.1• Lower left1650HbA1C levels• < 7%	Consolidates/infiltrates	32	100
The site of the lung lesion       Image: Mark Stress	• Cavity	15	46.9
• Upper right       18       56.3         • Middle right       14       43.8         • Lower right       12       37.5         • Upper left       12       37.5         • Upper left       12       37.5         • Middle left       17       53.1         • Lower left       16       50         HbA1C levels       -       -         • < 7%	<ul> <li>Pleural effusion</li> </ul>	5	15.6
• Middle right1443.8• Lower right12 $37.5$ • Upper left12 $37.5$ • Middle left17 $53.1$ • Lower left1650HbA1C levels• < 7%	The site of the lung lesion		
• Lower right       12       37.5         • Upper left       12       37.5         • Middle left       12       37.5         • Middle left       17       53.1         • Lower left       16       50         HbA1C levels       -       -         • < 7%	<ul> <li>Upper right</li> </ul>	18	56.3
Upper left         12         37.5           Middle left         17         53.1           Lower left         16         50           HbA1C levels         -         -           < 7%	Middle right	14	43.8
• Middle left       17       53.1         • Lower left       16       50         HbA1C levels       -       -         • < 7%	<ul> <li>Lower right</li> </ul>	12	37.5
<ul> <li>Lower left</li> <li>HbA1C levels</li> <li>&lt; 7%</li> <li>3</li> <li>6.3</li> <li>7 - 9 %</li> <li>15</li> <li>50.0</li> <li>&gt; 9%</li> <li>14</li> <li>43.7</li> <li>Smoker</li> <li>Yes</li> <li>8</li> <li>25</li> </ul>	Upper left	12	37.5
HbA1C levels       Image: Constraint of the system of the sy	Middle left	17	53.1
• < 7%	Lower left	16	50
• 7 - 9 %       15       50.0         • > 9%       14       43.7         Smoker           • Yes       8       25	HbA1C levels		
<ul> <li>&gt; 9%</li> <li>14</li> <li>43.7</li> <li>Smoker</li> <li>Yes</li> <li>8</li> <li>25</li> </ul>	• < 7%	3	6.3
Smoker • Yes 8 25	• 7 – 9 %	15	50.0
• Yes 8 25	• > 9%	14	43.7
	Smoker		
• No 24 75	• Yes	8	25
	• No	24	75

TABLE 3: The study subject distribution based on the condition of the disease.

TABLE 4: Correlation of HbA1C levels with the extent of lung TB lesions.

		TB lung lesion extent		а	р
		Minimal	Extensive		
HbA1C levels	< 7%	3	0	1	0.042*
	7-9%	0	14		
	>9%	0	15		
	Total	3	29		
*n-value $< 0.05$ considered as significant					

\*p-value < 0,05 considered as significant

Cavity lesion type was observed in 46.9% of the total subjects in our study. This finding is in accordance with an earlier study which described that the frequency of cavitation remained high in diabetics of all ages. An increased frequency of cavitation



in DM patients is not due to longer disease duration. The mechanisms altering the frequency of cavitation in DM patients are unclear and require further study [13, 14].

The site of pulmonary TB lesions is generally present in the upper lobes. However, in our study, it was mostly found to be evenly distributed in all lung fields. This is consistent with previous study which reported that in diabetics, lung lesions might occur at lower sites. It was mentioned that diabetes and aging were the same predisposing factors for the pulmonary radiographic feature of TB patients [13].

We obtained a positive correlation with very strong correlation coefficient in our study. This finding is in line with previous studies assessing the effect of type 2 DM on clinical severity and treatment outcomes in patients with pulmonary TB. In the study, it was reported that in patients with pulmonary tuberculosis with type-2 diabetes had more severe clinical appearance than those ones without type-2 DM. Cavitation was found in 75% of pulmonary TB patients with type-2 diabetes. Type-2 DM may potentially cause multi-drug resistance in pulmonary TB patients. Diabetes mellitus and the severity of pulmonary radiographic features are a major contributing factor to TB treatment failure [15]. Several limitations were present in our study. There were many confounding factors such as gender age, and smoking habits were not included in the analysis.

### **5.** Conclusion

Chest radiograph image of pulmonary TB is strongly and positively correlated with the HbA1C level in type-2 DM patients. In this study, it was reported that patients with pulmonary TB and type-2 DM had a more severe clinical picture than pulmonary TB patients without type-2 DM. The results of this study support previous research which states that glycemic control significantly affects the manifestation of radiographic pulmonary TB in DM patients.

#### References

- [1] Baghaei P. 2013. Diabetes mellitus and tuberculosis facts and controversies. J Diabetes Metab Disord 12(1) p 58
- [2] Alisjahbana B. 2006. Diabetes mellitus is strongly associated with tuberculosis in Indonesia. International Journal of Tuberculosis and Lung Disease 10(6) pp 696– 700
- [3] Dobler CC, Flack JR and Marks GB. 2012. Risk of tuberculosis among people with diabetes mellitus: an Australian nationwide cohort study. *BMJ Open* 2(1) pe000666



- [4] Guptan A and Ashok S. 2000. Tuberculosis and diabetes: an appraisal. *Ind. J. Tub.* 47(3) pp3–8
- [5] Wijaya I. 2015. Tuberculosis paru pada penderita diabetes melitus. Cermin Dunia Kedokteran 42(6) pp 412–7
- [6] Wulandari DR and Sugiri YJ. 2013. Diabetes mellitus dan permasalahannya pada infeksi tuberculosis. Jurnal respiratory Indonesia 33(2) pp126–34
- [7] Chiang CY. 2015. The influence of diabetes, glycemic control, and diabetes-related comorbidities on pulmonary tuberculosis. *PLoS ONE* 10(3) p e0121698
- [8] Higgins T. 2013. HbA1c for screening and diagnosis of diabetes mellitus. *Endocrine*. 43(2) pp 266–73
- [9] Ralph AP. 2010. A simple, valid, numerical score for grading chest x-ray severity in adult smear-positive pulmonary tuberculosis. *Thorax* 65(10) pp 863–9
- [10] Patel AK, Rami KC and Ghanchi FD. 2011. Radiological presentation of patients of pulmonary tuberculosis with diabetes mellitus. *Lung India*? 28(1) p 70
- [11] Rami H Fiona P Critchley JAand Laith J. 2017. Association between diabetes mellitus and active tuberculosis: A systematic review and meta-analysis. PLoS ONE 12(11): p e0187967
- [12] Perhimpunan Dokter Paru Indonesia 2011 Pedoman penatalaksanaan TB (consensus TB). Perhimpunan Dokter Paru Indonesia. pp 1–55
- [13] Chiang CY. 2014. Glycemic control and radiographic manifestations of tuberculosis in diabetic patients. *PLoS ONE* 9(4)
- [14] Li-Kuo H Hsueh-Han W Yi-Chun L and Shi-Chuan C. 2017. The impact of glycemic status on radiological manifestations of pulmonary tuberculosis in diabetic patients. *PLoS ONE* 12(6): p e0179750
- [15] Chang JT. 2011. Effect of type 2 diabetes mellitus on the clinical severity and treatment outcome in patients with pulmonary tuberculosis: a potential role in the emergence of multidrug resistance. J Formos Med Assoc;110(6) pp 372–81