



The Impact of Blood Glucose Levels on Acid-Fast Bacteria Conversion in Tuberculosis Patients with Diabetes Mellitus

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Article Info	Abstract
<p>Article history: Received 24 January 2022 Revised 29 April 2022 Accepted 15 May 2022 Available online 01 August 2022</p> <p>Keywords: Blood Glucose Levels; Tuberculosis; AFB; Diabetes Mellitus</p> <p>Correspondence: shahrulrahman@umsu.ac.id</p> <p>How to cite this article: Shahrul Rahman, Andhyka Libawardana Pulungan, Kebba S. Bojang. The Impact of Blood Glucose Levels on Acid-Fast Bacteria Conversion in Tuberculosis Patients with Diabetes Mellitus. MAGNA MEDIKA Berk Ilm Kedokt dan Kesehat. 2022; 9(2): 120–127</p>	<p>Background: Tuberculosis (TB) is an infectious disease caused by Mycobacterium tuberculosis. Pulmonary tuberculosis in DM sufferers will aggravate hyperglycemia and spur ketoacidosis.</p> <p>Objective: To determine the effect of blood glucose levels on the conversion of acid-fast bacteria (AFB) in TB patients with DM</p> <p>Methods: This research is descriptive-analytical with a retrospective cohort approach. The data was taken from the data of TB patients with DM at the Pulmonary Hospital of North Sumatera Province from July 2018-September 2019. The sample is pulmonary tuberculosis-positive AFB patients with high blood glucose levels, which was carried out with total sampling. Forty-nine patients who met the inclusion criteria were included in the study.</p> <p>Results: Of those participants with increased blood glucose levels, 4 (7.3%) had AFB conversion, while 6 (2.7%) had no conversion. In those with decreased blood sugar, 32 (28.7%) had AFB conversion, while 7 (10.3%) did not, with a p-value of 0.014.</p> <p>Conclusion: There is a significant relationship between the effect of blood glucose levels on acid-fast bacteria conversion.</p>
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INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by the bacterium *Mycobacterium tuberculosis*. These bacteria usually affect the lungs (pulmonary TB) and other organs (extra pulmonary TB). These bacteria can be spread when people with TB lung disease expel the bacteria into the air, for example, through coughing.¹

Pulmonary tuberculosis is a potential opportunistic infection for people with diabetes mellitus (DM) because the condition of impaired immune defense due to hyperglycemia and acidosis, one of which is to inhibit the movement of phagocyte cells towards the area of infection and suppresses the activity of these cells that occur in people with diabetes and facilitate the spread primary infection. On the other hand, pulmonary TB in DM sufferers will aggravate hyperglycemia and ketoacidosis.²

Diabetes mellitus (DM) is a collection of symptoms found in a person due to an increase in glucose (glucose) levels in the blood continuously (chronically) as a result of insulin deficiency, both quantitatively and qualitatively. It is currently estimated that there are more than 350 million cases of DM in the world, and this number continues to increase, and it is estimated that this figure will increase by 50% by 2030.³ The number of DM sufferers in Indonesia continues to increase until now it is estimated that more than 5 million Indonesians or it means that 1 in 40 Indonesians have diabetes. Based on the 2013 Riskesdas data, the prevalence of DM in Indonesia reaches 2.5%.⁴

Diabetes can cause a worsening of symptoms and increase the severity of TB infection. Diabetes can be a risk factor for finding AFB in sputum, with a more extended conversion than AFB patients without diabetes, thereby increasing the risk of transmission and the risk of germ resistance. This is because people with diabetes have an impaired immune response in the body so that they can facilitate *M. tuberculosis* infection and cause pulmonary TB disease.^{5,6}

TB patients with DM have a higher number of blemishes in the sputum. Cultures are often positive two months after TB therapy, and a high rate of multi-drug resistance mycobacterium and radiographic images are atypical.⁷

TB patients whom DM accompanies are at risk of experiencing sputum conversion failure after undergoing TB treatment, 1.69 times higher risk of experiencing treatment failure, 1.24 times higher risk of experiencing anti-TB drug resistance, 3.89 times higher risk for relapse, and a 4.95 times higher risk of dying during treatment compared to TB patients.⁸

Based on the description above, the objective is the impact of blood glucose levels and acid-fast bacteria conversion on TB patients at the Pulmonary Hospital of North Sumatra Province.

METHODS

This type of research is descriptive-analytical with a retrospective cohort approach, where the data are taken as data from TB patients with DM at Pulmonary Hospital of North Sumatra Province from July 2018-September 2019. The sample is pulmonary tuberculosis-

positive AFB patients with high blood glucose levels with comorbid diabetes mellitus in the Pulmonary Hospital of North Sumatera Province, which was carried out by total sampling. The sample used in the study was 49 patients who met the inclusion criteria.

RESULTS

On table 1 the 49 respondents studied, the highest category was 18 (36.7%) respondents aged 40-49 years, 14 (28.6%) respondents aged 30-39, 11 (22.4%) respondents aged 20-29 years, 5 (10.2%) respondents aged 50-59% and 1 (2.0%) respondent aged 60-69 years. Of the

49 respondents studied, the highest category was male, with 34 respondents (69.3%), while there were 15 respondents (30.6%) with the female gender.

Based on Table 2, of the 49 respondents studied, the highest category was 36 respondents (73.5%) of those who experienced acid-fast bacteria conversion, while 13 respondents (26.5%) did not experience acid-fast bacteria conversion.

Based on table 3, it is known that of the 49 respondents, the highest category was 39 respondents (79.6%) who experienced a decrease in blood glucose level.

Table 1 Demographic Characteristics

Variable		N	%
Age (years)	20-29	11	22.4
	30-39	14	28.6
	40-49	18	36.7
	50-59	5	10.2
	60-69	1	2.0
	Total	49	100.0
Gender	Female	15	30.6
	Male	34	69.3
	Total	49	100.0

Table 2 Distribution of Acid-fast Bacteria Conversion

Conversion	F	%
Converted	36	73.5
Not-Converted	13	26.5
Total	49	100.0

Table 3 Distribution of Frequency and Percentage of Blood Glucose Level

Blood Glucose Level	F	%
Increased	10	20.4
Decreased	39	79.6
Total	49	100.0

Table 4 Correlation between Blood Glucose Levels and Acid-Fast Bacteria Conversion

Blood Glucose Levels	Conversion	Acid-Fast Bacteria	p-value
	Converted N (%)	Non-Converted N (%)	
Increased	4 (8.2%)	6 (12.2%)	0.014
Decreased	32 (65.3%)	7 (14.3%)	
Total	36 (73.5%)	13 (26.5%)	

On Table 4, it is found that in the category, blood glucose levels increased with acid-fast bacteria converted by 4 (8.2%) respondents, while those who were not converted were 6 (12.2%) respondents in the category of decreased blood glucose levels with acid-fast bacteria converted by 32 (65.3) respondents, while there were 7 (14.3%) respondents who were not converted. The p-value shows 0.014, which means p-value <0.05, that is, the effect <0.05, that is, the effect of blood glucose on the conversion of acid-fast bacteria has a significant relationship.

DISCUSSIONS

The characteristic demographics analysis shows the age of 40-49 years as many as 18 people (36.7%), followed by 30-39 years as many as 14 people (28.6%). There are 11 people in the 20-29 age group (22.4%), and in the 50-59 age group, as many as five people (10.2%). There are as many as one people in the 60-69 age group (2.0%). This result is in line with a study that examined the prevalence of diabetes mellitus in tuberculosis and therapeutic problems, showing that TB patients with DM were the most at 40-49 years old (58.0%).⁹In another study also explained that TB patients with DM at the age of 40 -49 are the largest age category at 62.0%.¹⁰ This is because epidemiologically, the spread of TB is more prevalent in adults attacking those adults

who have been infected with primary TB in their environment at a young age, but prevention is not well done so that it appears in adults. The second possibility is the existence of activities and works environment in groups of adults who interact with TB sufferers or environments that facilitate contracting TB.¹¹

From the analysis of the demographic characteristics of the study respondents, it was found that the majority of respondents were male; namely, 34 respondents (60.4%) and 15 respondents were women (30.6%). This study is in line with a previous study that explains that the largest category is male, which is 65% in 2019.¹² The same thing was also explained in another study that stated that most TB patients with DM were male.¹³ One of the reasons men are more at risk than women is because of smoking behavior of men. Smoking can increase the risk of getting TB to 2 times.¹⁴

From the frequency distribution table and the percentage of acid-fast bacteria conversion, of the 49 respondents studied, the highest category was 36 respondents (73.5%) experiencing acid-fast bacteria conversion, while 13 respondents (26.5%) did not experience acid-fast bacteria conversion. This is in line with the study than explained the conversion of acid-fast bacteria in tuberculosis patients was 72.0% converted and 28.0% not converted.¹⁵ Conversion status depended on the regularity of tak-

ing medication in the initial phase and monitoring of medication and the dosage of drugs taken. A high cure rate will follow a high conversion rate.¹⁶

In the table of the relationship between blood glucose levels and acid-fast bacteria conversion, it was found that in the category blood glucose levels increased, with decreased blood glucose with converted acid-fast bacteria by 32 respondents (65.3%), while those who were not converted were seven respondents (14.3%). The p-value is 0.014, while the significant p-value is $p < 0.05$, that is, the effect of blood glucose on acid-fast bacteria conversion has a significant relationship. This was similarly conveyed by the study before, which showed a p-value of 0.047, which means that it has a significant relationship between blood glucose levels and the conversion of acid-fast bacteria. This is also in line with what was conveyed by Fachri in 2018, who showed a p-value of 0.000 which means that it has a significant relationship between blood glucose levels and the conversion of acid-fast bacteria.^{17,18}

This finding is because achieving blood glucose control will give a good result by administering oral and diabetic drugs or insulin.¹⁹

The increased risk of failure, death during TB treatment, and recurrence among patients with high blood glucose levels is consistent with data from mouse and human studies showing that high blood glucose levels impair cell-mediated immunity. Furthermore, a study says poor control of blood glucose levels can exacerbate TB conditions, worsening the patient's prognosis. This is because high blood glucose levels can interfere with the body's defense

mechanism, disrupting wound healing, granulocyte function, cellular immunity, complement function, and decreased lymphokine response.²⁰

However, explanations regarding glucose control during anti-TB treatment may influence TB treatment outcomes. Previous researchers have argued that reasonable glucose control during TB treatment can improve treatment outcomes because animal studies have shown that glucose control can restore compromised immune systems. However, in general, the hyperglycemic effect is essential to make it easier for DM patients to experience an infection. This is because hyperglycemia will interfere with the function of neutrophils and monocytes (macrophages) in chemotaxis, adhesion, and phagocytosis of these cells. Therefore, TB patients with poor blood glucose control will fail acid-fast bacteria conversion in the intensive phase. However, this study assessed glucose control status only by medical records recorded by nurses or physicians before TB treatment. One prospective study suggested that the combined management of TB and DM improved clinical outcomes.^{21,22}

Handling of DM in TB must be monitored optimally to give better results in patients, so strenuous efforts must be made to achieve this control by start therapy earlier.

The high prevalence of DM and TB being in epidemic proportions has rightly earned them the names 'the converging epidemics' and 'double burden'.^{23,24} As per the WHO approximation, 15% of TB cases in the world are associated with DM.²⁵ People with DM have been reported to have a three-fold increased risk of active TB compared to the general population.^{26,27} On the other hand, TB in a patient

with diabetes is associated with poorer glycaemic control.^{28,29,30} This synergism between DM and TB in terms of epidemiology and outcome necessitates. Bi-directional screening for the presence of either TB or DM in the presence of the other disorder.³¹ The higher risk of TB in the diabetic population compels intensive screening for detection of TB at the earliest time to reduce transmission, morbidity, and mortality. WHO recommends TB surveillance among patients with DM in settings with medium to high TB burdens.³¹

In regions with a high prevalence of diabetes, screening for hyperglycemia in TB affected individuals is highly recommended.³² Screening for DM more than once during illness is sensible so that transient and new-onset DM can be identified. Detection and monitoring of hyperglycemia is an essential part of infection management in any patient with an infectious disease. Chronic infectious diseases like TB thrive in hyperglycemic individuals, and the outcome is unfavorable in a hyperglycemic milieu.³¹

CONCLUSION

The highest gender category was male, with the highest conversion category being 36 respondents (73.5%) experiencing acid-fast bacteria conversion, while 13 respondents (26.5%) did not experience acid-fast bacteria conversion. The highest blood glucose level category is 20.4% experiencing an increased level of blood glucose, while 79.6% experiencing a decreased level of blood glucose.

There is that in the category of increased blood glucose levels with AFB converted by 7.3%, while those who were not converted were 2.7%. In the category of decreased blood glucose levels, acid-fast bacteria converted by 28.7%, while 10.3% were not converted. The p-value shows 0.014, and the effect of blood

glucose on acid-fast bacteria conversion has a significant relationship.

REFERENCES

1. Smith I. Mycobacterium tuberculosis Pathogenesis and Molecular Determinants of Virulence. *Clinical Microbiology Reviews*. 2013. 16 (3). 463-496
2. Casqueiro J, Casqueiro J, and Alves C. Infections in patients with diabetes mellitus: A review of pathogenesis. *Indian Journal of Endocrinology and Metabolism*. 2012. 16 (Suppl 1), S27-S36.
3. American Diabetes Association. Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care*. 2009. 32 (S1), 562-567.
4. Mihardja L, Soetrisno U, and Soegondo S. Prevalence and clinical profile of diabetes mellitus in productive aged urban Indonesians. *J Diabetes Invest*. 2014. 5 (5), 507-512
5. Dooley KE, and Chaisson RE. Tuberculosis and diabetes mellitus: convergence of two epidemics. *Lancet Infect Dis*. 2009, 9(12): 737-746.
6. Restrepo BI. Diabetes and tuberculosis. *Microbiol Spectr*. 2016; 4(6): 1-19.
7. Siddiqui AN, Khayyam KU, and Sharma M. Effect of Diabetes Mellitus on Tuberculosis Treatment Outcome and Adverse Reactions in Patients Receiving Directly Observed Treatment Strategy in India: A Prospective Study. *BioMed Research International*. 2016, 1-11
8. Dooley KE, Tang T, Golub JE, Dorman SE, and Cronin W. Impact of Diabetes Mellitus on Treatment Outcomes of Patients with Active Tuberculosis. *Am J Trop Med Hyg*. 2009; 80(4): 634-639.

9. Baghaei P, Marjani M, Javanmard P, Tabarsi P, and Masjedi MR. Diabetes mellitus and tuberculosis facts and controversies. *Journal of Diabetes & Metabolic Disorders* 2013, 12(58), 1-8
10. Lengkong JVM. Characteristics Of Patients With Pulmonary Tuberculosis, Side Effects Of Antituberculosis Drugs, And Accuracy Of Diagnosis Of Patients With Pulmonary Tuberculosis. *European Journal of Molecular & Clinical Medicine* 2020, 07 (03), 4752-4770
11. Narasimhan P, Wood J, MacIntyre CR, and Mathai D. Risk Factors for Tuberculosis. *Pulmonary Medicine* 2013, 1-11
12. Raghuraman S, Vasudevan KP, Govindarajan S, Chinnakali P, Panigrahi KC. Prevalence of Diabetes Mellitus among Tuberculosis Patients in Urban Puducherry. *North American Journal of Medical Sciences* 2014, 6(1), 30-34.
13. Tenaye L, Mengiste B, Baraki N, Mulu E. Diabetes Mellitus among Adult Tuberculosis Patients Attending Tuberculosis Clinics in Eastern Ethiopia. *BioMed Research International* 2019, 1-7
14. Sajith, M., et al. 2015. Socio-Demographic characteristics of tuberculosis patients in a tertiary care hospital. *International Journal of Medical and Health Research*, 1(3): 25-28
15. Putra ON, Damayanti A, Nurrahman NWD, Devi T, Aluf W. Evaluation of Category I of Anti-tuberculosis Therapy in Intensive Phase Pulmonary TB by Conversion of Acid-Fast Bacilli Sputum. *Pharmaceutical Sciences and Research* 2019, 6(3), 183 - 188
16. Trebucq A, Schwoebel V, Kashongwe Z, et al. Treatment outcome with a short multidrug-resistant tuberculosis regimen in nine African countries. *Int J Tuberc Lung Dis* 2018, 22(1):17–25
17. Fachri M, Hatta M, Abadia S, et al. 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. *Respiratory Medicine Case Reports* 2018, 23: 158–162
18. Yorke E, Atiase Y, Akpalu J, Kantanka OS, Boima V, Dey ID. The Bidirectional Relationship between Tuberculosis and Diabetes. *Tuberculosis Research and Treatment* 2017, 1-6
19. Kelwade J, Parekh H, and Sethi BP. How many oral antidiabetic drugs before insulin? *Indian Journal of Endocrinology and Metabolism* 2017, 21 (1): 249-250
20. Geerlings SE, Hoepelman AIM. Immune dysfunction in patients with diabetes mellitus (DM). *Immunology and Medical Microbiology* 1999, 26 259-265
21. Yoon YS, Jung JW, Jeon EJ, Seo H, Ryu YJ, Yim JJ, et al. The effect of diabetes control status on treatment response in pulmonary tuberculosis: A prospective study. *Thorax*. 2017;72(3):263–70.
22. Rahman, S & Rejeki, AS, 2021. The Relationship Between The Level Of Knowledge And Attitude Of Type 2 Diabetes Mellitus Participants On Adherence With The Covid-19 Health Protocol. *Turkish Journal of Physiotherapy and Rehabilitation*. 32(3),20086-91
23. Dooley KE, Chaisson RE. Tuberculosis and diabetes mellitus: convergence of two epidemics. *Lancet Infect Dis*. 2009 Dec;9(12):737–46. Doi PMCID:

- PMC2945809. [PMC free article] [PubMed] [CrossRef] [Reference list]
24. Viswanathan V., Bajaj S., Kalra S., et al. RSSDI clinical practice recommendations for diagnosis, prevention, and control of the diabetes mellitus-tuberculosis double burden. *Int J Diabetes Dev Ctries.* 2017; 37:379–399.
 25. Lönnroth K, Roglic G, Harries AD. Improving tuberculosis prevention and care through addressing the global diabetes epidemic: from evidence to policy and practice. *Lancet Diabetes Endocrinol.* 2014;2(9):730–739.
 26. Siddiqui A. Role of Diabetes in prevalence of tuberculosis. *J Diabetes Metab.* 2012;02. <https://doi.org/10.4172/2155-6156.1000170>
 27. Ahmed M, Omer I, Osman SA, Ahmed-Abakur E. Association between pulmonary tuberculosis and Type 2 diabetes in Sudanese patients. *Int J Mycobacteriology.* 2017;6: 97. pmid:28317813
 28. Riza AL, Pearson F, Ugarte-gil C, Alisjahbana B, De S Van, Panduru NM, et al. and the Implications for Patient Services. 2016; 2: 740–753. [https://doi.org/10.1016/S2213-8587\(14\)70110-X.Clinical](https://doi.org/10.1016/S2213-8587(14)70110-X.Clinical)
 29. Cheng J, Zhang H, Zhao Yan L, Wang Li X, Chen Ming T. Mutual impact of diabetes mellitus and tuberculosis in China. *Biomed Environ Sci.* 2017;30: 384–389. pmid:28549496
 30. Shayo FK, Shayo SC (2021) Readiness of healthcare facilities with tuberculosis services to manage diabetes mellitus in Tanzania: A nationwide analysis for evidence-informed policy-making in high burden settings. *PLoS ONE* 16(7): e0254349. <https://doi.org/10.1371/journal.pone.0254349>Krishna S, Jacob JJ. Diabetes Mellitus and Tuberculosis. [Updated 2021 Apr 18]. In: Feingold KR, Anawalt B, Boyce A, et al., editors. *Endotext* [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK570126/>
 31. World Health Organization/International Union Against Tuberculosis and Lung Disease. Provisional collaborative framework for care and control of tuberculosis and diabetes. WHO/HTM/TB/ 2011.15. Geneva, Switzerland: WHO, 2011