

The Difference in Average Cholesterol in the BMI Group of TB-DM Sufferers at Dr Soetomo General Academic Hospital Surabaya

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KEYWORDS

Total
cholesterol

BMI (Body
Mass Index)

Diabetes
Mellitus
(DM)

Tuberculosis
(TB)

ABSTRACT:

Introduction: Diabetes Mellitus (DM) is a chronic metabolic disorder characterized by high blood glucose levels and impaired metabolism of carbohydrates, fats, and proteins due to inadequate insulin function. Individuals with DM are more susceptible to tuberculosis (TB) infection due to decreased metabolic function and compromised immune responses, including macrophage activity. Cholesterol plays a crucial role in macrophage phagocytosis of Mycobacterium tuberculosis. Patients with active TB generally have lower cholesterol levels compared to healthy individuals. This study investigates the relationship between cholesterol levels and Body Mass Index (BMI) in patients with Type 2 DM and TB.

Objectives: To analyze differences in total cholesterol levels among BMI groups of Type 2 DM patients with TB at Dr Soetomo General Academic Hospital Surabaya.

Methods: A cross-sectional study design was employed, involving 83 patients diagnosed with Type 2 DM and TB between 2021 and 2022. Data on cholesterol levels, BMI, and demographic characteristics were obtained from medical records. Statistical analysis was conducted using ANOVA to assess differences in cholesterol levels across BMI groups.

Results: Among the 83 patients, 54% were male, and 61% were aged between 46 and 65 years. Most patients had normal cholesterol levels (75.9%) and normal BMI (61%). The ANOVA test showed no statistically significant difference in total cholesterol levels among the BMI groups ($p = 0.90$, $p > 0.05$).

Conclusions: There was no significant difference in total cholesterol levels among BMI groups in Type 2 DM patients with TB at Dr. Soetomo General Academic Hospital Surabaya during 2021–2022. These findings suggest that BMI does not significantly influence cholesterol levels in this patient population.

1. Introduction

Diabetes mellitus (DM) is still a disease that is a challenge for every country in the world because it is the top 10 deadliest disease. Throughout the world in 2019, the number of people suffering from type 2 diabetes mellitus reached 463 million people (Saeedi, 2019). According to the National Center for Biotechnology Information, in 2019, the prevalence of diabetes in men was 9.6% and women 9.0% of the total population. In 2030, it is estimated that the number of patients suffering from DM will increase to 578 million people, and will continue to reach 700 million people in 2045, representing 10.9% of the world's total adult population. Additionally, in 2019, approximately 4.2 million adults aged 20 to 99 years died from DM and its complications. Health costs incurred for the management of DM are estimated at 760 billion USD worldwide. (Banday, 2020). The prevalence of recurrent pulmonary TB cases in Surabaya City increased from 139 cases in 2015 to 167 cases in both 2016 and 2017. Surabaya City ranked first in the prevalence of TB-positive cases combined with diabetes mellitus in East Java Province. Diabetes mellitus cases in East Java rose from 102,599 in 2017 to 115,460 in 2018. This high prevalence has led to an increasing number of TB patients who had already been diagnosed with diabetes mellitus.

In patients with DM, there was a decrease in TH1 cytokines, TNF alpha, TNF beta, IL-1, IL-6 as well as a decrease in macrophage function which resulted in impaired monocyte phagocytosis and chemotaxis function. (Arango, 2014) Hyperglycemia is also thought to damage the ability of human breathing to expel pathogens. This is what causes patients with DM to be more susceptible to TB infection. (Ernest Yorke, 2017). In 2019, the highest number of new cases of tuberculosis (TB) occurred in the Southeast Asia region, accounting for 44% of the total new cases in the world and Indonesia was ranked second after India in the number of TB cases. (Noviyani, 2021). The prevalence of relapsed pulmonary TB cases in the city of Surabaya increased from 139 cases in 2015 to 167 cases in 2016 and in 2017 the city of Surabaya was in first place with positive TB. According to the Ministry of Health, cases of diabetes mellitus in East Java increased by 329.8%. The city of Surabaya recorded the highest number of diabetes mellitus sufferers in this province, with the number increasing from 102,599 in 2017 to 115,460 in 2018. This prevalence has led to an increase in Many DM sufferers also experience TB.

When β cells are unable to work or fail, glucose in the blood will increase. Defects in the synthesis of insulin precursors, or insulin itself, as well as impaired secretion mechanisms, can lead to failure of the insulin secretory function, the main driver of β -cell failure is the pathophysiology of type 2 DM (Galicia-Garcia U, 2021). Many patients with T2DM have high levels of fat or obesity and the distribution is dominant in the abdominal area. It is this adipose tissue that creates insulin resistance through various mechanisms including increasing free fatty acids and stopping the regulation of adipokines. (Goyal R, 2023) In contrast to DM cases, patients who fail TB treatment are usually found to have low cholesterol. Cholesterol is an essential ingredient for macrophages to phagocytose *Mycobacterium tuberculosis*. High levels of total cholesterol result from increased oxidized cholesterol and increased phagocytosis. Patients with active TB generally have lower cholesterol levels than healthy people due to the low phagocytosis process of *Mycobacterium tuberculosis* by macrophages. (Ngo, 2021).

2. Methods

This type of research uses a cross-sectional research design. The variables studied were age, gender, total cholesterol levels, and Body Mass Index. The population in this study were all type 2 DM sufferers who had TB recorded in the medical records of Dr Soetomo General Academic Hospital, Surabaya. This study involved a total of 266 medical records with 83 medical records as inclusion criteria. Statistical analyses were conducted using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, N.Y., USA). Continuous variables were analyzed with one-way analysis of variance (One-way ANOVA). For cases where data were not homogeneous or normally distributed, the Kruskal-Wallis test was applied. Categorical variables were assessed using the Chi-Square test. All variables were evaluated for collinearity. Pearson correlation analysis was used to examine relationships between variables. Independent variables included age, gender, and BMI, categorized as underweight ($<18.5 \text{ kg/m}^2$), normal weight ($18.5\text{--}24.9 \text{ kg/m}^2$), and overweight ($>25 \text{ kg/m}^2$). A p-value of <0.05 was considered statistically significant.

3. Results

Table 1 Demographic profile of patients with tuberculosis and type 2 diabetes mellitus at Dr. Sutomo 2021 – 2022

Variable	Frequency	Percentage (%)
Age Group		
18 - 25 years old	1	1.2%
26 – 45 years	18	21%
46 – 65 years	51	61%
>65 years	13	15%
Gender		
Man	45	54%
Woman	38	46%

The demographic profile of patients suffering from tuberculosis and type 2 diabetes mellitus at Dr. Soetomo General Academic Hospital for the 2021 – 2022 period is grouped into several variables, including gender and age. The demographic profile found that men were more susceptible to tuberculosis with type 2 diabetes mellitus than women, although not much different. The highest age range is also found at the age of 46 – 65 (productive age).

Table 2. Frequency distribution of type 2 diabetes mellitus patients with tuberculosis according to Body Mass Index (BMI)

BMI	n	%
<i>Underweight</i>	16	19,2
<i>Normoweight</i>	51	61
<i>Overweight</i>	16	19,2
Total	83	100

In the Body Mass Index profile, it was found that the average population had a normal body weight.

Table 3. Frequency distribution of cholesterol levels in patients with type 2 diabetes mellitus and tuberculosis

Cholesterol	n	%
<i>Normocholesterol</i>	63	75,9
<i>Hypercholesterolemia</i>	20	24.1
Total	83	100

In the total cholesterol profile, it was found that the average population had normal cholesterol.

Table 4. Baseline characteristics of TB-DM sufferers according to BMI group

No	Variable	Underweight n=16	Normoweight n=51	Overweight n=16	p value
1	Age	49.93 (SD±11.55)	53.62 (SD±12.53)	54.06 (SD±10.09)	0,51 ^a
2	Gender				
	Man	10	29	6	0,30 ^b
	Woman	6	22	10	
3	body height	159.43(SD±7.25)	160.75 (SD±6,96)	164.25(SD±8.48)	0.30 ^Δ
4	Body weight	44.12(SD±4.63)	59.09 (SD±7.33)	73.81(SD±10.74)	0.00 ^Δ
5	Body mass index	17.32 (SD±0.95)	22.82 (SD±1.94)	27.74(SD±2.12)	0.00 ^Δ

α = one way anova

β = chi square

Δ = kruskal wallis

Based on this research, the variable values for age, gender, and height show that this difference is not statistically significant ($p > 0.05$).

Table 5. Differences in average cholesterol in the BMI group of TB-DM sufferers

Variable	Underweight N=16	Normoweight N=51	Overweight N=16	p Value
Average cholesterol levels	172.18 (SD±63.14)	171.81 (SD±43.23)	158.61 (SD±9.16)	0.90 ^a

A = one-way anova

This research found no significant differences between BMI groups in TB-DM sufferers at RSUD Dr. Soetomo General Academic Hospital Surabaya in 2021-2022.

4. Discussion

Diabetes mellitus (DM) is classified into several types, including type 1 DM, caused by absolute insulin deficiency; type 2 DM (T2DM), resulting from insulin resistance and inadequate receptor function that leads to increased insulin secretion; gestational diabetes, which occurs during pregnancy; and other less common types (Solis-Herrera C, 2018). T2DM is further characterized by hyperglycemia, hyperinsulinemia, and hyperlipidemia (dyslipidemia). The relationship between T2DM and dyslipidemia varies across different ethnic groups. For example, it is linked to high cholesterol levels in South Africa and elevated triglyceride levels in South Texas (Restrepo et al., 2021).

Body mass index (BMI) also plays a role in the risk of TB and DM. A study by Choi et al. (2021) revealed that underweight individuals, especially those with DM, had a higher risk of TB compared to those with normal weight without DM. However, individuals with severe obesity, regardless of DM status, demonstrated a reduced risk of TB when compared to the control group.

Cholesterol, a lipophilic molecule, is vital for human metabolism. It serves as a structural component of cell membranes, contributes to membrane fluidity, and acts as a precursor for synthesizing vitamin D, steroid hormones, and sex hormones. It also facilitates the absorption of fat-soluble vitamins, such as A, D, E, and K (Huff, 2023; Horrnaener, 2023). However, elevated levels of low-density lipoprotein (LDL) cholesterol, a condition known as hypercholesterolemia, can pose significant health risks. Genetic factors, such as mutations affecting LDL receptor regulation in the liver, are a common cause of hypercholesterolemia. LDL endocytosis is the body's primary mechanism for reducing cholesterol levels. Lifestyle modifications, including increased physical activity, weight management, and heart-healthy diets, are crucial in managing hypercholesterolemia. For high-risk individuals, statins can be prescribed to effectively lower the risk of atherosclerotic cardiovascular disease (ASCVD) (Huff et al., 2023).

The interplay between T2DM and TB adds complexity to cholesterol metabolism. T2DM increases the risk of active TB by 2-3 times compared to non-diabetic individuals, and poorly controlled T2DM is associated with higher TB treatment failure rates and increased mortality (Nyirenda, 2023). Even with good glycemic control, T2DM patients often exhibit dyslipidemia, characterized by elevated serum triglycerides, total cholesterol, very-low-density lipoprotein (VLDL), and intermediate-density lipoprotein (IDL) (Phalazy, 2017; Feingold, 2023). Based on the study in South Korea there is an inverse association between total cholesterol levels and tuberculosis (TB) risk. Individuals with lower total cholesterol levels were found to have a higher risk of developing TB. Specifically, subjects in the lowest quartile of total cholesterol had a 1.35-fold increased risk of TB compared to those in the highest quartile. (Jo, 2021) On the other hand, the study in *Frontiers in Cardiovascular Medicine* found that higher cholesterol levels are associated with reduced inflammation and lower mortality during tuberculosis (TB) treatment. This suggests that higher cholesterol may provide protection against more severe inflammatory effects during TB therapy. (Chidambaram, 2021)

This inverse relationship was particularly evident in individuals under 65 years of age, those without diabetes mellitus, and those without obesity. The study suggests that lower cholesterol levels may be associated with a compromised immune response, potentially increasing susceptibility to TB infection. However, it's important to note that while low cholesterol levels were associated with higher TB risk, the study does not establish a direct causal relationship. Further research is needed to fully understand the underlying mechanisms linking cholesterol levels and TB risk.

In TB patients, *Mycobacterium tuberculosis* profoundly affects cholesterol metabolism in macrophages. Mtb uses cholesterol as a primary carbon source for its growth. It increases macrophage cholesterol uptake through receptors like Lrp2, LOX1, and CD36, leading to intracellular cholesterol accumulation and the formation of foam cells, which facilitate Mtb proliferation (Agarwal, 2021). Additionally, TB induces the expression of genes involved in cholesterol synthesis, such as AACS, HMGCS1, HMGCR, MVD, and DHCR24 (Zhanpeng Chen, 2024).

Interestingly, patients with both DM and TB often exhibit normal blood cholesterol levels despite increased intracellular cholesterol accumulation in macrophages (Martinez, 2024). This phenomenon may explain why cholesterol levels show no significant differences across BMI groups in individuals with concurrent DM and TB. This interplay underscores the intricate relationship between cholesterol metabolism, DM, and TB, highlighting the need for tailored therapeutic approaches in managing these comorbidities.

5. Conclusion

There were no significant differences in total cholesterol between groups Body Mass Index (BMI) in Type 2 DM Patients with TB at Dr Soetomo Hospital Surabaya in 2021 – 2022.

References

1. Agarwal, P., Gordon, S., & Martinez, F. O. (2021). Foam Cell Macrophages in Tuberculosis. *Frontiers in immunology*, 12, 775326. <https://doi.org/10.3389/fimmu.2021.775326>
2. Arango Duque, G., & Descoteaux, A. (2014). Macrophage cytokines: involvement in immunity and infectious diseases. *Frontiers in immunology*, 5, 491. <https://doi.org/10.3389/fimmu.2014.00491>
3. Banday, e. a., 2020. Pathophysiology of diabetes: An overview.. [Online] Available at: https://doi.org/10.4103/ajm.ajm_53_20
4. Chen, Z., Kong, X., Ma, Q., Chen, J., Zeng, Y., Liu, H., Wang, X., & Lu, S. (2024). The impact of *Mycobacterium tuberculosis* on the macrophage cholesterol metabolism pathway. *Frontiers in immunology*, 15, 1402024. <https://doi.org/10.3389/fimmu.2024.1402024>
5. Choi, H., 2021. *Body Mass Index, Diabetes, and Risk of Tuberculosis: A Retrospective Cohort Study*. *Front. Nutr.* 8:739766.. [Online] Available at: doi: 10.3389/fnut.2021.739766
6. Feingold KR. Obesity and Dyslipidemia. [Updated 2023 Jun 19]. In: Feingold KR, Anawalt B, Blackman MR, et al., editors. *Endotext* [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK305895/>
7. Galicia-Garcia U, et al, 2021. Pathophysiology of Type 2 Diabetes Melitus.. [Online] Available at: <https://pubmed.ncbi.nlm.nih.gov/32872570/>
8. Goyal R, et al. 2023. Diabetes Melitus Type 2. [Online] Available at: <https://www.ncbi.nlm.nih.gov/books/NBK513253/> [Accessed 23 April 2023].
9. Hofmaenner, D. A., Kleyman, A., Press, A., Bauer, M., & Singer, M. (2022). The Many Roles of Cholesterol in Sepsis: A Review. *American journal of respiratory and critical care medicine*, 205(4), 388–396. <https://doi.org/10.1164/rccm.202105-1197TR>
10. Huff T, Boyd B, Jialal I. Physiology, Cholesterol. [Updated 2023 Mar 6]. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK470561/>
11. Jo, Y. S., Han, K., Kim, D., Yoo, J. E., Kim, Y., Yang, B., Choi, H., Sohn, J. W., Shin, D. W., & Lee, H. (2021). Relationship between total cholesterol level and tuberculosis risk in a nationwide longitudinal cohort. *Scientific reports*, 11(1), 16254. <https://doi.org/10.1038/s41598-021-95704-1>
12. Martinez, N., & Kornfeld, H. (2014). Diabetes and immunity to tuberculosis. *European journal of immunology*, 44(3), 617–626. <https://doi.org/10.1002/eji.201344301>
13. Ngo, M., 2021. Diabetes-Associated Susceptibility to Tuberculosis: Contribution of Hyperglycemia vs. Dyslipidemia. [Online] Available at: <https://doi.org/10.3390/microorganisms9112282>
14. Noviyani, A., Nopsopon, T., & Pongpirul, K. (2021). Variation of tuberculosis prevalence across diagnostic approaches and geographical areas of Indonesia. *PloS one*, 16(10), e0258809. <https://doi.org/10.1371/journal.pone.0258809>
15. Nyirenda, J. L. Z., Bockey, A., Wagner, D., & Lange, B. (2023). Effect of Tuberculosis (TB) and Diabetes mellitus (DM) integrated healthcare on bidirectional screening and treatment outcomes among TB patients and people living with DM in developing countries: a systematic review. *Pathogens and global health*, 117(1), 36–51. <https://doi.org/10.1080/20477724.2022.2046967>

16. Ouellet, H., Johnston, J. B., & de Montellano, P. R. (2011). Cholesterol catabolism as a therapeutic target in *Mycobacterium tuberculosis*. *Trends in microbiology*, 19(11), 530–539. <https://doi.org/10.1016/j.tim.2011.07.009>
17. Palazhy, S., & Viswanathan, V. (2017). Lipid Abnormalities in Type 2 Diabetes Mellitus Patients with Overt Nephropathy. *Diabetes & metabolism journal*, 41(2), 128–134. <https://doi.org/10.4093/dmj.2017.41.2.128>
18. Restrepo, B. I., Kleynhans, L., Salinas, A. B., Abdelbary, B., Tshivhula, H., Aguilón-Durán, G. P., Kunsevi-Kilola, C., Salinas, G., Stanley, K., Malherbe, S. T., Maasdorp, E., Garcia-Viveros, M., Louw, I., Garcia-Oropesa, E. M., Lopez-Alvarenga, J. C., Prins, J. B., Walzl, G., Schlesinger, L. S., & Ronacher, K. (2018). Diabetes screen during tuberculosis contact investigations highlights opportunity for new diabetes diagnosis and reveals metabolic differences between ethnic groups. *Tuberculosis (Edinburgh, Scotland)*, 113, 10–18. <https://doi.org/10.1016/j.tube.2018.08.007>
19. Saeedi, P., Petersohn, I., Salpea, P., Malanda, B., Karuranga, S., Unwin, N., Colagiuri, S., Guariguata, L., Motala, A. A., Ogurtsova, K., Shaw, J. E., Bright, D., Williams, R., & IDF Diabetes Atlas Committee (2019). Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. *Diabetes research and clinical practice*, 157, 107843. <https://doi.org/10.1016/j.diabres.2019.107843>
20. Solis-Herrera, C., Triplitt, C., Reasner, C., DeFronzo, R. A., & Cersosimo, E. (2018). Classification of Diabetes Mellitus. In K. R. Feingold (Eds.) et. al., *Endotext*. MDText.com, Inc. <https://pubmed.ncbi.nlm.nih.gov/25905343/>
21. Yorke, E., Atiase, Y., Akpalu, J., Sarfo-Kantanka, O., Boima, V., & Dey, I. D. (2017). The Bidirectional Relationship between Tuberculosis and Diabetes. *Tuberculosis research and treatment*, 2017, 1702578. <https://doi.org/10.1155/2017/1702578>
22. Chidambaram V, Zhou L, Ruelas Castillo J, Kumar A, Ayeh SK, Gupte A, Wang J-Y and Karakousis PC (2021) Higher Serum Cholesterol Levels Are Associated With Reduced Systemic Inflammation and Mortality During Tuberculosis Treatment Independent of Body Mass Index. *Front. Cardiovasc. Med.* 8:696517. doi: 10.3389/fcvm.2021.696517