

Prevalence of Type 2 Diabetes Mellitus Among Pulmonary Tuberculosis Patients in Pakistan

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ABSTRACT

Background: Individuals with diabetes are vulnerable to a weakened immune response, increasing the risk of pulmonary tuberculosis (TB), particularly in low- to middle-income countries like Pakistan with prevalent poverty and unsanitary conditions. This study aimed to determine the prevalence of T2DM in Pulmonary TB patients.

Methods: This cross-sectional study was conducted at the Primary Health Care (PHC) Center in Sikandar Abad and private clinics in Hyderabad, Pakistan. A total of 200 individuals, irrespective of age and gender, diagnosed with primary pulmonary tuberculosis and undergoing either first-line or second-line therapy, were recruited during a period of six months from 1st April 2022 to 30th September 2022 through simple random sampling. All TB patients were screened for Diabetes. The collection of relevant information, including demographic and clinical details, was executed using a standardized study proforma. Data analysis was performed using SPSS version 25, allowing for statistical exploration and interpretation of the findings.

Results: Prevalence of DM in TB patients was (38%) 19. The average age of the participants was 36.6 ± 14.8 years. The computed BMI of $17.14 \pm 2.9 \text{ kg/m}^2$ revealed that the majority of the patients were underweight. Weight loss was the symptom that co-occurred with TB and DM.

Conclusion: Study revealed a notable 38% prevalence of Type 2 Diabetes Mellitus (T2DM) among Pulmonary TB patients, indicating a risk of co-occurrence. This co-morbidity poses an important public health concern, emphasizing the importance of understanding the interplay between these two conditions.

Keywords: Pulmonary Tuberculosis (PTB), Diabetes Mellitus(T2DM), BMI.

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How to cite: Mustafa K, Jehangir F, Kamal F, Rafique T, Shah AG, Murtaza I Prevalence of Type 2 Diabetes Mellitus Among Pulmonary Tuberculosis Patients in Pakistan. Pak J Med Dent. 2024;13(4): 03-10. Doi: <https://doi.org/10.36283/ziun-pjmd13-4/002>

Received: Sun, Aug 20, 2023 **Accepted:** Tue, Aug 27, 2024 **Published:** Thu, Oct 24, 2024

INTRODUCTION

In-depth research has been done to comprehend the impacts of diabetes and tuberculosis and possible preventative methods. These conditions are frequently encountered worldwide¹. Diabetes and TB symptoms accentuate one another, making treatment for both conditions more difficult to manage. Both diseases carry an elevated chance of onset with age². The risk of coexistence between diabetes mellitus and tuberculosis becomes greater due to deficiencies in monocytes and macro-phages³. It is necessary to look into the connections between diseases like diabetes and tuberculosis in order to understand the reasons behind this challenge and the emergence of multi-drug resistance. Based on the studies in the past, diabetes mellitus has been established as a risk factor for Tuberculosis. Furthermore, individuals with tuberculosis and diabetes frequently respond poorly to anti-tuberculosis treatment, resulting in complicated mortality⁴.

In the context of an overview and meta-analysis, the prevalence of diabetes among TB patients exhibited significant variability even within countries. For instance, in India, the prevalence ranged widely from 5% to 66%, in Pakistan from 8% to 40%, in Nepal from 4% to 25%, and in Bangladesh from 8% to 13%. Notably, in Oman, out of 426 TB cases, the prevalence of Diabetes Mellitus (DM) was reported at 27%⁵.

Certain lipid profiles in TB patients increase their risk of developing diabetes, underscoring the significance of maintaining stable lipid levels as a preventive approach. In order to comprehend the variables influencing their co-occurrence, it is crucial to research the incidence of both illnesses⁶. HIV-seronegative patients should have routine testing since they are more likely to develop diabetes and tuberculosis as co-morbid conditions. When examining tuberculosis patients, it is imperative to take note of any family history of diabetes because these individuals are also more likely to develop the condition⁷. According to recent studies, one in ten people with tuberculosis also have diabetes as a co-morbid illness⁸. Compared to the group with tuberculosis alone, the prevalence of the tuberculosis-diabetes association is higher⁹. Research on an Indian community revealed a significant prevalence of undiagnosed diabetes, which raises the possibility of a co-morbid relationship between diabetes and tuberculosis¹⁰.

The addition of metformin to the regimen for treating co-existing diabetes and tuberculosis has a beneficial effect and aids in avoiding relapse¹¹. Due to the severity of these two illnesses, the community has a higher chance of acquiring diabetes among

tuberculosis patients. Though the specific mechanism of their interconnectivity is still not fully known, several studies imply that reduced alveolar macrophage migration in tuberculosis patients may be the main factor contributing to their vulnerability to diabetes¹². The presence of diabetes complicates tuberculosis treatment and increases drug resistance. Regular screening and adherence to proper medication regimens are necessary to prevent further complications¹³. Patients with a history of tuberculosis and diabetes as a co-morbid condition are at a higher risk of recurrent tuberculosis, which further compromises their immunity¹⁴. Cohesive management plans for pulmonary tuberculosis have been shown to improve outcomes and prevent the occurrence of other co-morbid conditions such as diabetes mellitus¹⁵.

Since the prevalence of DM has been rising in Pakistan over the recent years and so has PTB. Given the absence of recent local-level statistics on the co-occurrence of both pressing issues together, our study was undertaken to observe the prevalence of Type 2 Diabetes Mellitus among Pulmonary Tuberculosis patients.

METHODS

A cross-sectional study was conducted at PHC Sikandar Abad and private clinics in Hyderabad for a period of 6 months from 1st April 2022 to 30th September 2022, involving a total of 200 participants by calculating sample size calculator of WHO after receiving ethical approval from Ziauddin University Karachi's Ethical Review Committee (Reference Code: 190322KMFM). A simple random sampling technique was used. All consenting individuals regardless of age, who were diagnosed to have primary pulmonary Tuberculosis on first line or 2nd line therapy, were included in the study. Individuals who refuse to participate in the study, were excluded.

The participants' Hb1AC levels were seen and their BMI was calculated during outpatient visits. Other socio-demographic data was collected in written form for further analysis. The collected data was analyzed using SPSS version 25. Numerical variables were described using mean and standard deviation, while categorical variables were presented as percentages. Chi square test was computed to examine the associations between sociodemographic factors and the prevalence of tuberculosis-diabetes mellitus (TB-DM), with a 95% confidence interval. A p-value less than 0.05 was considered statistically significant.

RESULT

The study included a total of 200 participants, with 104 (52%) being male and 96 (48%) females. The prevalence of DM in TB patients was (38%) 19. The

mean age of the participants was calculated to be 36.6±14.8 years, indicating a significant variation in age among the study population. The average body mass index (BMI) of tuberculosis (TB) patients was found to be 17.14±2.99, indicating that most participants were underweight. Table 1 demon-

strates the demographics of the study population. Table 2 illustrates the traits of Diabetic TB patients vs non-diabetic TB patients. Figure 1 shows the medications and comorbidities of Diabetic TB patients. Figure 2 demonstrates the burden of DM in TB patients.

Table 1: Demographic and Anthropometric Details of TB Patients

Variables	Mean ±S. D , n(%)
Age	36.66±14.81
Weight kgs	43.99± 8.94
Height m	1.59±0.098
BMI kg/m ²	17.14±2.99
Males	104(52%)
Females	96(48%)
Illiterate	116(58%)
Literate	84(42%)
Poor	158(79%)
Lower Middle Class	20(10%)
Middle Class	18(9%)
Higher middle class	4(2%)
Homemaker	60(30%)
Labor	44(22)
Landlord	2(1%)
Retired	6(3%)
Student	42(21%)
unemployed	46(23%)
History of Hypertension	8 (4%)
History of Myocardial Infarction	2 (1%)
Past History of Anti-Psychotic Use	2 (1%)

Table 2: Characteristics of Diabetic Pulmonary TB Patient's vs Non-Diabetic Pulmonary TB patients.

Variables	Diabetic TB Patients N(%)	Non-Diabetic TB patients N(%)	Chi square	p-value
Gender male	20(19.2)	84(80.8)	0.02	0.123
female	18(18.8)	78(81.3)		
Education Literate	24(20.7)	92(79.3)	0.830	0.111
Illetrate	14(16.7)	70(83.3)		
Socioeconomic status poor	2(15.2)	134(84.8)	15.15	0.005
Lower middle class	6(30)	14(70)		
Middle class	6(33.3)	12(66.7)		
Higher middle class	2(50)	2(50)		

Occupation unemployed	10(21.7)	36(78.3)	31.54	<0.001
Student	0(0)	42(100)		
Home maker	18(31)	42(69)		
Laborer	6(13.6)	38(86.4)		
Landlord	2(100)	0(0)		
Retired	2(33.3)	4(66.7)		
BMI				
underweight	11(7.8)	130(92.2)	41.16	<0.001
Normal	25(45.5)	30(54.5)		
Overweight	0(0)	2(100)		
Obese	2(100)	0(0)		
Age				
young	4(4.8)	80(95.2)	24.2	0.001
middle	28(27.2)	75(72.8)		
elderly	6(46.2)	7(53.8)		

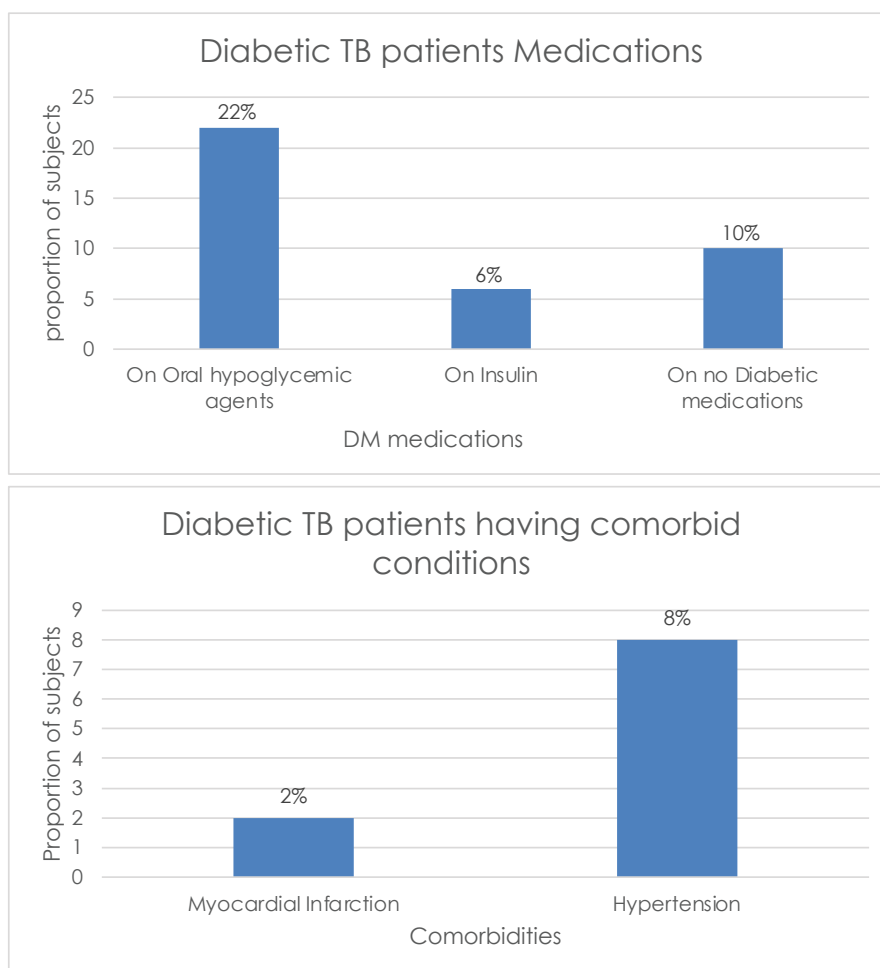


Figure 1: Diabetic TB Patients' Medications and Comorbid Conditions

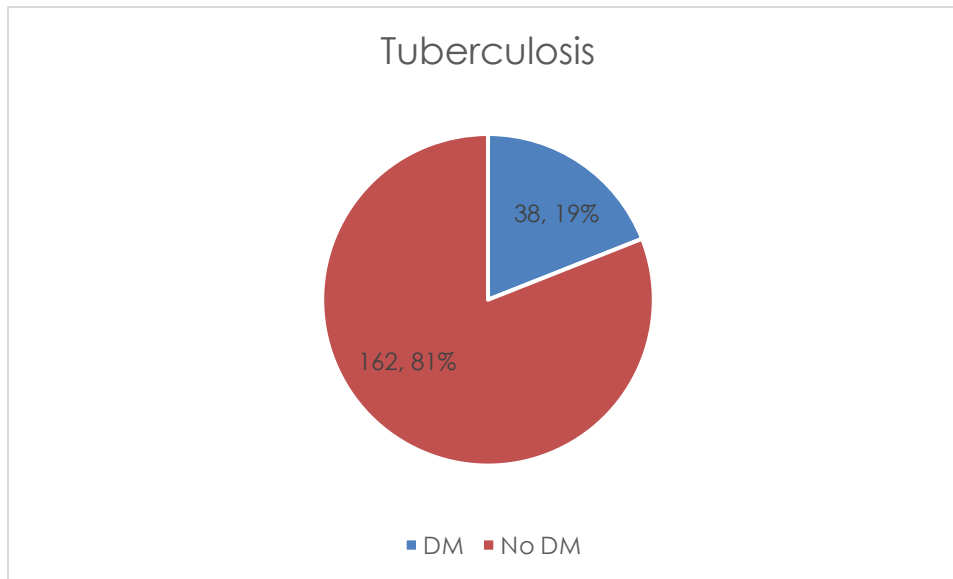


Figure 2: Prevalence of DM in Tuberculosis Patients

DISCUSSION

Tuberculosis (TB) combined with diabetes mellitus (DM) is a significant health challenge globally, particularly in economically unstable countries with a population of low-income and middle-class individuals¹⁶. The prevalence of DM among TB patients varies between 1.8% and 45%, with the majority falling within the range of 10% to 30%.¹⁷ The co-epidemics of DM and TB have become a growing concern, particularly in low- and middle-income countries, as the global burden of DM continues to rise¹⁸. In a study conducted in Vietnam, participants aged 15 years and older had a 29% prevalence of prediabetes and a 13.7% prevalence of diagnosed diabetes. The association between TB and DM was found to be more prevalent in the 40-64 age group. Regular screening of patients is crucial to effectively manage and control these complications. Having a family history of DM was found to increase the odds ratio for developing DM among TB patients, with a 95% confidence level¹⁹. Patients with a family history of DM should undergo regular checkups and take measures to control their blood sugar levels, as they have a higher likelihood of developing DM compared to those without a family history. It is a well-known fact that DM leads to micro and macrovascular complications. Therefore, it is important to be tested for diabetes and take preventive measures if identified as being at high risk. Participants who neglect regular screening and fail to monitor their blood sugar levels increase their chances of developing DM and TB. Regular screening of diabetic patients and maintaining stable glycemic levels can help reduce the risk of developing TB.

Gender does not appear to have an impact on the

association between TB and DM. Dietary modifications and avoiding foods that elevate blood sugar levels are beneficial in controlling glucose levels²⁰. TB combined with DM poses a significant health challenge worldwide. Nigeria has reported the highest prevalence rate at 15%. The prevalence of DM is higher among patients with HIV/TB co-infection. A meta-analysis of 16 studies revealed a pooled prevalence rate of DM among TB patients²¹.

Sub-Saharan Africa has considerably higher rates of DM among TB patients²². In a study with 499 participants, 21% were diagnosed with DM, and 59.5% of participants used metformin²³. The use of metformin did not significantly impact sputum culture conversion in TB patients²⁴. However, metformin showed effectiveness in patients with cavitary pulmonary TB and DM, as well as in preventing the association between TB and DM. Rifampicin demonstrates a 25% overall exposure in patients with both diabetes and those without diabetes who have tuberculosis. However, the impact of isoniazid usage is less pronounced in diabetic individuals with tuberculosis compared to those without diabetes, as evidenced by lower plasma concentrations of 5.4 mg/h/l versus 10.6 mg/h/l ($p = 0.015$) and 1.6 mg/h/l versus 2.8 mg/h/l ($p = 0.013$).

Considering the variations in plasma concentration observed in individual patient profiles, it is advisable to prescribe medications on an individual basis. To enhance our understanding of optimal dosages for anti-tuberculosis medications in patients with tuberculosis and diabetes, it is crucial to conduct clinical trials involving larger dosages of these drugs. Additionally, tailored dosing strategies for isoniazid and

rifampicin based on measurements of plasma concentrations should be investigated further.²⁵ Rifampicin resistance occurred due to mutations at a frequency of 10⁻⁷-10⁻⁸, but the current study showed higher mutation frequency²⁶. Drug resistance in tuberculosis (TB) can lead to reduced treatment options, worse treatment outcomes, and increased healthcare expenses. Understanding the drug resistance patterns can aid in assessing the efficacy of existing TB control strategies and devising more successful TB treatments. In regions with a substantial TB burden, approximately 15% of TB patients are estimated to have diabetes mellitus (DM)²⁷. Patients who receive a positive diabetes diagnosis may subsequently be prescribed a sensitive anti-tuberculosis treatment (ATT) regimen to ensure complete recovery from pulmonary tuberculosis, even in cases with resistance. Based on our findings, there appears to be a connection between diabetes and rifampin resistance. Therefore, we propose the integration of diabetes surveillance into TB programs, particularly in evolving epidemiological conditions. Additionally, quantifying the discrepancies in TB diagnostic outcomes is necessary to establish a global research framework for meaningful comparisons of study results²⁸.

This study did not throw any light on patterns of drug resistance in Diabetic patients. Also, the exact reason for the association between Tuberculosis and Diabetes requires bigger scale studies. This study also fails to tell whether Diabetes is linked to extrapulmonary Tuberculosis or not.

CONCLUSION

The findings revealed a significant correlation between diabetes and tuberculosis, with a higher prevalence of diabetes among TB patients. Most patients had been diagnosed with diabetes before being diagnosed with TB. Poor socioeconomic status influenced TB-DM co-morbidity. To prevent the co-occurrence of tuberculosis and diabetes mellitus, it is crucial to implement preventive measures such as maintaining glycemic control, regular screenings, and routine healthcare visits. In Pakistan, diabetes mellitus is a prevalent condition, and the presence of tuberculosis further complicates the treatment process, leading to drug resistance and additional challenges in managing patients.

ACKNOWLEDGMENT

We extend our sincere gratitude to our esteemed co-authors whose dedicated contributions were pivotal in shaping this manuscript. Their expertise, insightful inputs, and collaborative efforts significantly enriched the content and quality of the document. We would also like to express our heartfelt appreciation to the patients who generously participated in our study. Their willingness to contribute

time and valuable insights played an indispensable role in the success of our research.

CONFLICT OF INTEREST

There is no conflict of interest.

ETHICAL APPROVAL

The study was conducted following approval from the Ethical Review Committee of Ziauddin University Karachi. Reference Code: 190322KMFM.

PATIENT CONSENT

The consent was obtained from the patients included in the research study.

AUTHORS' CONTRIBUTION

KM and FJ conceived the idea and did the bench work. FK, TR, A, and GS did the manuscript writing. IS did the proofreading.

REFERENCES

1. Nyirenda JLZ, Bockey A, Wagner D, Lange B. 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. *Pathog Glob Health*. 2023 Feb;117(1):36-51. doi: 10.1080/20477724.2022.2046967. Epub 2022 Mar 17. PMID: 35296216; PMCID: PMC9848381.
2. Maharjan B, Chalise HN, Thapa M. Tuberculosis and Diabetes Mellitus Comorbidity among the Ageing Population: A Threat to the Public Health System of Nepal. *J Nepal Health Res Counc*. 2018 Jul 3;16(2):110-117. PMID: 29983421.
3. Blanca IR. Diabetes and tuberculosis. Understanding the host immune response against Mycobacterium tuberculosis infection. 2018;21. Available from: https://link.springer.com/chapter/10.1007/978-3-319-97367-8_1.
4. Ayelign B, Negash M, Genetu M, Wondmagegn T, Shibabaw T. Immunological impacts of diabetes on the susceptibility of Mycobacterium tuberculosis. *J Immunol Res*. 2019;2019. doi:10.1155/2019/6196536.
5. Al Amri S, Singh J, Al Balushi L, Al Ghafri T, Al Balushi MN, Al Marbouai H, Al Dhuhli KS, Al Nairi KK, Al Badi MS, Al Mujaini SM, Abd-Ellatif EE. Prevalence and Associated Factors of Diabetes Mellitus Type 2 Among Tuberculosis Patients in Muscat, Oman, 2017-2020. *Oman Med J*. 2023 Jul 31;38(4):e526. doi: 10.5001/omj.2023.82. PMID: 37670907; PMCID: PMC10475877.
6. Ugarte-Gil C, Alisjahbana B, Ronacher K, Riza AL, Koesoemadinata RC, Malherbe ST, Cioboata R, Llontop JC, Kleynhans L, Lopez S, Santos P, Marius C, Villaizan K, Ruslami R, Walzl G, Panduro NM, Dockrell HM, Hill PC, Mc Allister S, Pearson F, Moore DAJ, Critchley JA, van Crevel R. Diabetes Mellitus Among Pulmonary Tuberculosis Patients From 4 Tuberculo-

- sis-endemic Countries: The TANDEM Study. *Clin Infect Dis.* 2020 Feb 14;70(5):780-788. doi: 10.1093/cid/ciz284. PMID: 30958536.
7. Munseri PJ, Kimambo H, Pallangyo K. Diabetes mellitus among patients attending TB clinics in Dar es Salaam: A descriptive cross-sectional study. *BMC Infect Dis.* 2019 Oct 19(1):1-8. Available from: <https://link.springer.com/article/10.1186/s12879-019-4539-5>.
8. Mabula PL, Kazinyingia KI, Chavala EC, Mosha V, Msuya SE, Leyaro BJ. Prevalence and risk factors for diabetes mellitus among tuberculosis patients in Moshi Municipal Council, Kilimanjaro Tanzania. *East Afr Health Res J.* 2021;5(1):69-74. doi: 10.24248/eahrj.v5i1.653. Epub 2021 Jun 11. PMID: 34308247; PMCID: PMC8291211.
9. Kottarath MD, Mavila R, V. A, Nair S. Prevalence of diabetes mellitus in tuberculosis patients: a hospital based study. *Int J Res Med Sci [Internet].* 2017 Jan. 14 [cited 2024 Sep. 23];3(10):2810-4. Available from: <https://www.msjonline.org/index.php/ijrms/article/view/1821>.
10. Paradkar M, Padmapriyadarsini C, Jain D, Shivakumar SVBY, Thiruvengadam K, Gupte AN, Thomas B, Kinikar A, Sekar K, Bharadwaj R, Dolla CK, Gaikwad S, Ellilarasi S, Lokhande R, Reddy D, Murali L, Kulkarni V, Pradhan N, Hanna LE, Pattabiraman S, Kohli R, S R, Suryavanshi N, B M S, Cox SR, Selvaraju S, Gupte N, Mave V, Gupta A, Bollinger RC; TRIUMPH-REPORT India Study Team. Tuberculosis preventive treatment should be considered for all household contacts of pulmonary tuberculosis patients in India. *PLoS One.* 2020 Jul 29;15(7):e0236743. doi: 10.1371/journal.pone.0236743. Erratum in: *PLoS One.* 2020 Dec 31;15(12):e0244914. doi: 10.1371/journal.pone.0244914. PMID: 32726367; PMCID: PMC7390377.
11. Ma Y, Pang Y, Shu W, Liu YH, Ge QP, Du J, Li L, Gao WW. Metformin reduces the relapse rate of tuberculosis patients with diabetes mellitus: experiences from 3-year follow-up. *Eur J Clin Microbiol Infect Dis.* 2018 Jul;37(7):1259-1263. doi: 10.1007/s10096-018-3242-6. Epub 2018 Apr 20. PMID: 29679254.
12. Amin S, Khattak MI, Shabbier G, Wazir MN. Frequency of pulmonary tuberculosis in patients with diabetes mellitus. *Gomal J Med Sci.* 2011;9(2).
13. Van Crevel R, Koesoemadinata R, Hill PC, Harries AD. Clinical management of combined tuberculosis and diabetes. *Int J Tuberc Lung Dis.* 2018 Dec 1;22(12):1404-1410. doi: 10.5588/ijtld.18.0340. PMID: 30606312.
14. Kumar NP, Fukutani KF, Shruthi BS, Alves T, Silveira-Mattos PS, Rocha MS, West K, Natarajan M, Viswanathan V, Babu S, Andrade BB, Kornfeld H. Persistent inflammation during anti-tuberculosis treatment with diabetes comorbidity. *Elife.* 2019 Jul 4;8:e46477. doi: 10.7554/eLife.46477. PMID: 31271354; PMCID: PMC6660216.
15. Mukhtar F, Butt ZA. Risk of adverse treatment outcomes among new pulmonary TB patients co-infected with diabetes in Pakistan: A prospective cohort study. *PLoS One.* 2018 Nov 8;13(11). doi:10.1371/journal.pone.0207148.
16. Boadu AA, Yeboah-Manu M, Osei-Wusu S, Yeboah-Manu D. Tuberculosis and diabetes mellitus: The complexity of the comorbid interactions. *Int J Infect Dis.* 2024 Sept;146:107140. doi:10.1016/j.ijid.2024.107140.
17. McMurry HS, Mendenhall E, Rajendrakumar A, Nambiar L, Satyanarayana S, Shivashankar R. Coprevalence of type 2 diabetes mellitus and tuberculosis in low-income and middle-income countries: A systematic review. *Diabetes Metab Res Rev.* 2019 Jan;35(1):e3066. doi: 10.1002/dmrr.3066. Epub 2018 Sep 25. PMID: 30144270.
18. Hossain MJ, Al-Mamun M, Islam MR. Diabetes mellitus, the fastest growing global public health concern: Early detection should be focused. *Health Sci Rep.* 2024 Mar 22;7(3):e2004. doi: 10.1002/hsr2.2004. PMID: 38524769; PMCID: PMC10958528.
19. Hoa NB, Phuc PD, Hien NT, Hoa VQ, Thuong PH, Anh PT, Nhung NV. Prevalence and associated factors of diabetes mellitus among tuberculosis patients in Hanoi, Vietnam. *BMC Infect Dis.* 2018 Nov 29;18(1):603. doi: 10.1186/s12879-018-3519-5. PMID: 30497410; PMCID: PMC6267094.
20. Hayashi S, Chandramohan D. Risk of active tuberculosis among people with diabetes mellitus: systematic review and meta-analysis. *Trop Med Int Health.* 2018 Oct;23(10):1058-1070. doi: 10.1111/tmi.13133. Epub 2018 Aug 29. PMID: 30062731.
21. Gautam S, Shrestha N, Mahato S, Nguyen TPA, Mishra SR, Berg-Beckhoff G. Diabetes among tuberculosis patients and its impact on tuberculosis treatment in South Asia: a systematic review and meta-analysis. *Sci Rep.* 2021 Jan 22;11(1):2113. doi: 10.1038/s41598-021-81057-2. PMID: 33483542; PMCID: PMC7822911.
22. Alebel A, Wondemagegn AT, Tesema C, Kibret GD, Wagnaw F, Petruca P, et al. Prevalence of diabetes mellitus among tuberculosis patients in Sub-Saharan Africa: a systematic review and meta-analysis of observational studies. *BMC Infect Dis.* 2019 March 13;19(1):1-0. doi:10.1186/s12879-019-3892-8.
23. Lee YJ, Han SK, Park JH, Lee JK, Kim DK, Chung HS, Heo EY. The effect of metformin on culture conversion in tuberculosis patients with diabetes mellitus. *Korean J Intern Med.* 2018 Sep;33(5):933-940. doi: 10.3904/kjim.2017.249. Epub 2018 Mar 16. PMID: 29540054; PMCID: PMC6129638.
24. Yu X, Li L, Xia L, Feng X, Chen F, Cao S, et al. Impact of metformin on the risk and treatment outcomes of tuberculosis in diabetics: a systematic review. *BMC Infect Dis.* 2019 Oct 17;19(1):1-1.

doi:10.1186/s12879-019-4548-4.

25. Mtabho CM, Semvua HH, van den Boogaard J, Irongo CF, Boeree MJ, Colbers A, Burger DM, van Crevel R, van der Ven AJAM, Kibiki GS, Tostmann A, Aarnoutse RE. Effect of diabetes mellitus on TB drug concentrations in Tanzanian patients. *J Antimicrob Chemother.* 2019 Dec 1;74(12):3537-3545. doi: 10.1093/jac/dkz368. PMID: 31651031; PMCID: PMC7183353.

26. Habibi MR, Bakhtiar A, Indiasuti DN, Meliana RY. Diabetes Mellitus and history of tuberculosis treatment as risk factors of developing multidrug-resistant tuberculosis at TB Polyclinic Dr. Soetomo General

Hospital 2019-2020. *Jurnal Ilmiah Universitas Batanghari Jambi.* 2022 Nov 1;22(1):537-43. doi:10.33087/ji-ubj.v22i1.1908.

27. Pan Y, Yu Y, Yi Y, Dou X, Lu J, Zhou L. The differences in drug resistance between drug-resistant tuberculosis patients with and without diabetes mellitus in northeast China: a retrospective study. *BMC Infect Dis.* 2023 March 15;23(1):1-9. doi:10.1186/s12879-023-08130-1.

28. Kumar A. Occurrence of diabetes mellitus with rifampicin resistance in patients of pulmonary tuberculosis. *J Card Dis Res.* 2023 May 19;14(3). ISSN: 0975-3583, 0976-2833.

