EJPMR, 2026, 13(6), 92-97 **Review Article** **Impact Factor: 8.158**

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

ISSN (O): 2394-3211
ISSN (P): 3051-2573
Coden USA: EJPMAG

A COMPREHENSIVE REVIEW ON IMPACT OF DIABETES MELLITUS ON TUBERCULOSIS TREATMENT OUTCOMES

Shaik Faziha*, T. Tulasi, Dr. E. Sunil Kumar

***Corresponding Author: Shaik Faziha**

DOI: https://doi.org/10.5281/zenodo.20443902

How to cite this Article: Shaik Faziha*, T. Tulasi, Dr. E. Sunil Kumar. (2026). A Comprehensive Review on Impact of Diabetes Mellitus on Tuberculosis Treatment Outcomes. European Journal of Pharmaceutical and Medical Research, 13(6), 92–97.

Article Received on 29/04/2026 **Article Revised on 19/05/2026** **Article Published on 01/06/2026**

ABSTRACT

Tuberculosis (TB) and diabetes mellitus (DM) are two of the most serious global health threats, and their co-occurrence has made the management of these diseases even more challenging. The growing burden of diabetes, especially in countries with high TB prevalence, has contributed to the rising incidence of TB-DM co-infection. Diabetes mellitus affects the innate and adaptive immune systems, making patients more vulnerable to Mycobacterium tuberculosis infection, resulting in delayed sputum conversion, increased bacterial load, treatment failure, relapse, and mortality. This review critically evaluates the effects of diabetes mellitus on the treatment outcomes of tuberculosis, the pathophysiologic mechanisms, pharmacokinetic interactions, and clinical management issues. Findings from the existing literature, including epidemiological, clinical, and pharmacological studies, suggest that hyperglycemia is a major factor that reduces the effectiveness of anti-TB medications and the host's immune system. Moreover, diabetes mellitus is also linked to multidrug-resistant TB and poor treatment outcomes. Comprehensive screening, glycemic control, personalized treatment plans, and two-way approaches for TB-DM management are required to improve treatment outcomes. To lessen this double burden, cooperative partnerships between national programs for non-communicable diseases and tuberculosis are essential. Future research should focus on identifying effective treatment regimens and host-directed therapies for TB patients with diabetes.

KEYWORDS: Tuberculosis; Diabetes Mellitus; Treatment Outcomes; Hyperglycemia; Multidrug-Resistant Tuberculosis; Glycemic Control; Sputum Conversion; Pharmacokinetics; Immune Dysfunction; TB–DM Comorbidity.

1. INTRODUCTION

Tuberculosis (TB) is one of the most important infectious diseases globally, resulting in high morbidity and mortality despite the existence of effective anti-TB chemotherapy for the last several decades.[1] According to the World Health Organization (WHO), an estimated 10.6 million people developed TB in 2022, with 1.3 million deaths among HIV-negative individuals, reiterating TB as a major cause of death from a single infectious agent.[1] Although the global incidence of TB has slowly declined over the last decade, this progress remains precarious and inconstant across the globe.[2]

Concurrently, diabetes mellitus (DM), especially type 2 DM, has also been recognized as one of the fastest-growing non-communicable diseases globally.[3] According to the International Diabetes Federation (IDF), the global burden of diabetes is increasing, with more than 537 million adults currently living with diabetes, which is projected to rise to 643 million by 2030.[3]

The co-existence of these two diseases has given rise to a serious public health problem, especially in low- and middle-income countries where the burden of both diseases is very high.[4] The association between diabetes and TB is not new, and historical evidence from the early 20th century indicated that people suffering from diabetes were more susceptible to TB.[5] Nevertheless, this association was also recognized in the last two decades due to the global DM epidemic.[6]

The epidemiological evidence of the association between diabetes and TB has consistently shown that diabetes

increases the risk of developing active TB two to three times more than non-diabetic people.[7,8] Moreover, a meta-analysis study has also confirmed that diabetes independently increases the risk of developing TB among people from diverse backgrounds, irrespective of their HIV status.[9]

Countries such as India, China, Indonesia, Pakistan, and the Philippines have the heaviest TB burdens in the world.[10] At the same time, there has been a rapid increase in the prevalence rates of diabetes in these countries because of urbanization, sedentary lifestyles, and dietary habits.[3,11] India has the heaviest TB burden in the world and at the same time has the largest number of diabetic patients in the world.[1,12] Prevalence rates of diabetes among TB patients in India have been found to vary in the range of 15 to 30 percent in different states in India.[13,14] Thus, there are major problems in the TB elimination programs in the TB-endemic countries such as India, and the TB/DM problem has the potential to jeopardize the achievement of the goals in the End TB Strategy.

Pathophysiological Mechanism

The pathophysiological mechanisms involved in the TB/DM problem are complex and multifactorial.[15] Hyperglycemia has a negative effect on the innate and adaptive immune responses in diabetic patients. Macrophage dysfunction is a key feature in diabetic patients, in whom there is a diminished capacity to produce reactive oxygen species that are essential in the killing of M. tuberculosis.[16] In addition, hyperglycemia affects antigen presentation and cytokine signaling pathways that are important in effective immunity against infection.[17]

T-cell immunity, particularly Th1 responses, are impaired in patients with diabetes through decreased production of IFN-γ, TNF-α, and IL-12.[18,19] These cytokines are important in the formation of granulomas and containment of Mtb infection.[20]

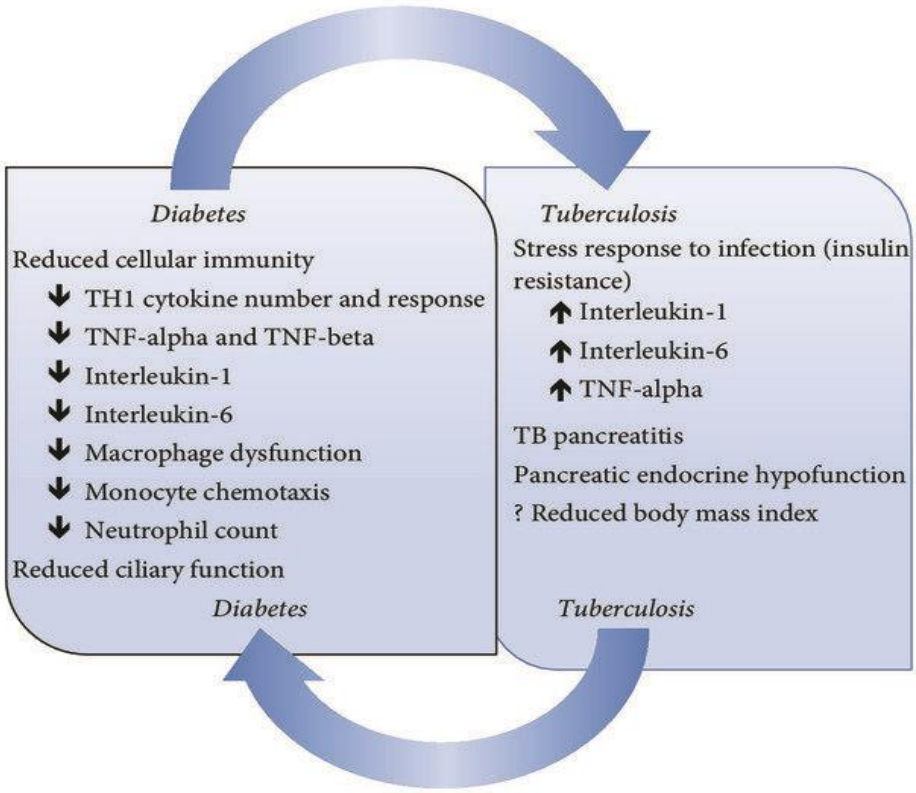

Figure 1.3: Represents link between Diabetes and Tuberculosis.

In addition to immune suppression, diabetes causes various changes in the lung that may contribute to increased severity of TB disease in patients with diabetes.[21] Diabetic microangiopathy may affect pulmonary microcirculation and decrease immune cell migration to sites of infection.[22] Studies have demonstrated that patients with diabetes and TB are more likely to have cavitary disease, extensive pulmonary disease, and increased bacillary loads at presentation compared with patients with TB alone.[23&24] Increased bacillary loads not only increase disease severity but may also delay sputum smear and culture conversion in patients undergoing treatment.[25]

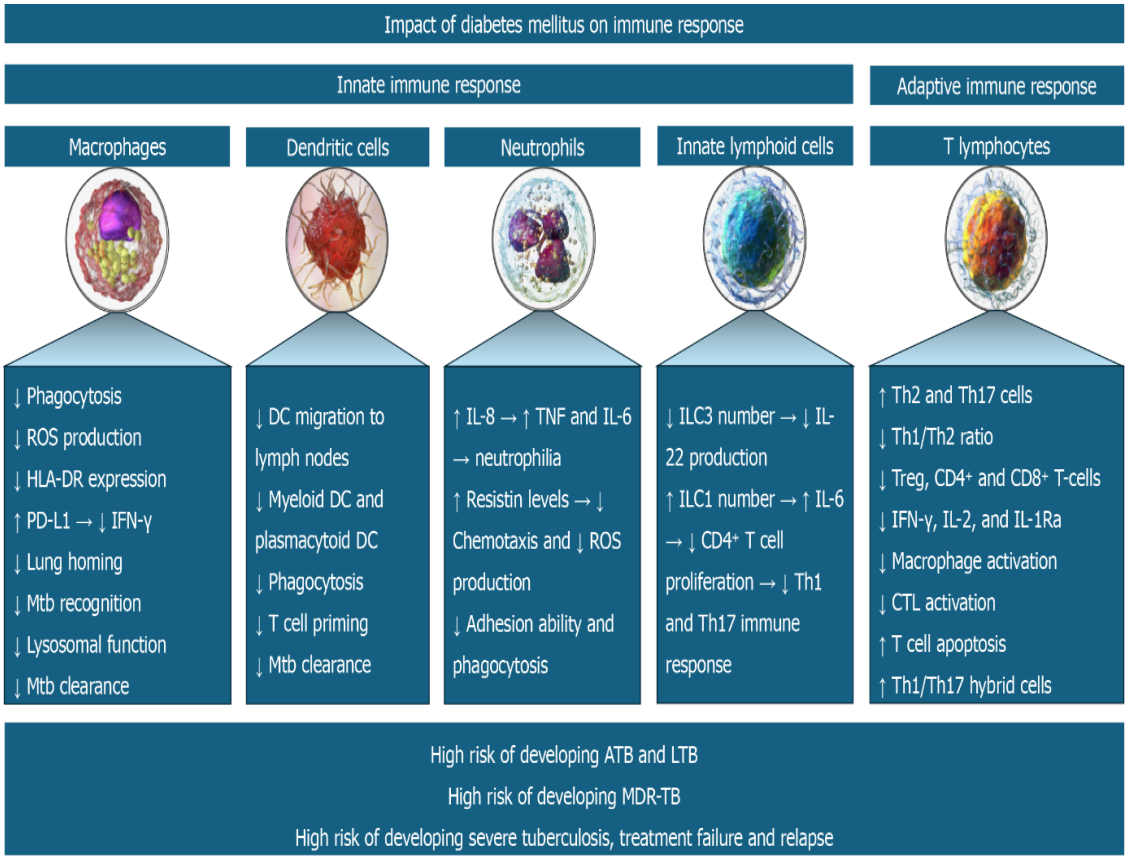

Figure 1.3: Shoes detailed pathogenesis of Tuberculosis and Patients with Diabetes Mellitus.

Delayed sputum conversion is one of the most consistent negative outcomes of TB treatment in patients with diabetes.[26,27] Delayed conversion of bacillary loads may increase the risk of transmission and relapse of disease.[28] Several cohort studies have established the fact that diabetic TB patients require longer periods to become culture negative compared to their non-diabetic counterparts.[29] Poor glycemic control has also been strongly linked to the delayed response to treatment in TB patients. Therefore, it is crucial to monitor the blood glucose levels during TB treatment.[30]

It has also been established that the treatment failure and relapse rates are higher in diabetic TB patients.[31,32] A study published in the International Journal of Tuberculosis and Lung Disease concluded that TB patients with diabetes have a significantly higher risk of treatment failure, recurrence, and mortality compared to non-diabetic TB patients.[9] TB patients with diabetes also have a higher risk of mortality compared to non-diabetic TB patients.[33] The risk is higher in TB patients with uncontrolled hyperglycemia and in diabetic TB patients with long-standing disease.

Pharmacokinetic Interactions

Pharmacokinetic interactions also play an important role in the treatment outcome in TB-DM patients.[34&35] Several studies have established the fact that the plasma levels of first-line anti-tuberculosis drugs such as rifampicin and isoniazid are reduced in diabetic individuals.[36]

However, rifampicin is a potent inducer of cytochrome P450 enzymes and may increase the metabolism of oral hypoglycemic drugs, leading to poor glycemic control.[37] In addition, poor glycemic control may impair drug distribution and tissue penetration.[38] This two-way effect between TB and DM necessitates careful therapeutic monitoring.

Emergence of MDR-TB

Another dimension of complexity in the TB–DM syndemic is the emergence of MDR-TB. Although evidence on the relationship between diabetes and MDR-TB risk varies across studies, several studies have indicated a possible link between diabetes and MDR-TB risk.[39,40] For example, diabetes may delay sputum conversion, decrease drug concentrations, and compromise adherence because of complex comorbidity management, all of which may contribute to MDR-TB risk.[41] Hyperglycemia may create a favourable condition for M. tuberculosis survival and increase the risk of developing MDR-TB.[42]

In recognition of the developing TB-DM syndemic, the WHO and the International Union Against Tuberculosis and Lung Disease have recommended bidirectional screening of TB and DM patients.[43] Early detection of diabetes in TB patients and TB in diabetic patients may

lead to improved outcomes of patients suffering from co-infection of TB and DM.[44] These integrated care models have shown significant improvements in the adherence to treatment, glycemic control, and outcomes of the patients.[45] However, the implementation of these models is inconsistent in these settings of high TB and DM due to resource limitations and the fragmented nature of the health care systems.

Inflammation and Metabolic Disorders

Inflammation and metabolic disorders also have significant roles to play in the severity of the disease in the co-infection of TB and DM. Advanced glycation end-products (AGEs) have been found to accumulate in the setting of hyperglycemia, leading to oxidative stress and endothelial dysfunction.[47] Oxidative stress can also worsen tissue damage during TB infection and disrupt the immune signalling pathways.[48] Insulin resistance is also associated with low-grade inflammatory markers and can paradoxically worsen tissue pathology and disease severity without effectively controlling bacterial replication.[49]

Relapse of condition

Another significant problem with TB treatment is the risk of relapse after the completion of treatment. Longitudinal study results have identified that there is a greater prevalence of TB relapse in diabetic TB patients when compared to non-diabetic TB patients.[50&51] The role of glycemic control and metabolic dysregulation can be a major factor in the relapse of TB.[52] However, the benefits of good glycemic control in the management of TB relapse have also been identified in the latest research findings.[53]

Thus, the interrelationship between diabetes and TB poses a major problem to the world's health systems. It has the effect of increasing the susceptibility to TB, the severity of TB, the delay in the microbiological response to TB, the relapse rate and mortality rate in TB, and the pharmacological management of TB.[36&48] In the face of the increasing prevalence of diabetes in TB-endemic areas, it is essential to implement a strategy that addresses the interrelationship between communicable and non-communicable diseases.

Table 1.1: Impact of Diabetes on Tuberculosis Treatment Outcomes.

Outcome Parameter	Effect of Diabetes	Proposed Mechanism	Clinical Implication
Risk of Active TB	↑ 2–3 fold	Impaired innate & adaptive immunity	Increased TB incidence
Sputum Conversion	Delayed	Higher bacillary load, immune dysfunction	Prolonged infectiousness
Treatment Failure	Increased	Subtherapeutic drug levels	Need for monitoring
Relapse	Increased	Persistent immune impairment	Extended follow-up required
Mortality	Higher	Poor glycemic control	Risk stratification needed
MDR-TB	Possible increased risk	Drug PK alterations, delayed response	Drug susceptibility monitoring

2. DISCUSSION

The co-existence of tuberculosis (TB) and diabetes mellitus (DM), therefore, is an important issue of concern in the management and treatment of TB, especially in endemic areas and countries. From the evidence reviewed in this article, it is evident that diabetes has a negative impact on the treatment outcome of TB through various mechanisms, which are interrelated and have a synergistic effect on the treatment outcome of the two conditions. Hyperglycemia is the major cause of the weakening of the body's defense mechanisms against the development and progression of TB. Both innate and acquired immunity are weakened in the body of a diabetic person. Macrophage dysfunction, weakened chemotaxis, and weakened intracellular killing ability are the major reasons why TB is not well managed in the body of a diabetic person. Additionally, the weakened Th1 cell-mediated response, including the production of interferon gamma, is the reason why the granulomatous response to the bacteria is weakened in the body of a diabetic person, leading to the development of cavitary TB, which is common in the body of a diabetic person.

Delayed sputum smear and culture conversion is one of the most consistent effects of TB and DM co-morbidity. The longer the positivity, the longer the infectious period, which may contribute to the sustained transmission of TB in the community. However, it has also been observed that delayed sputum smear and culture conversions are strongly related to poor glycemic control and not to diabetes per se. Thus, it is essential to conduct blood glucose tests in diabetic patients undergoing TB treatment. It has also been observed that the chances of treatment failure and relapse are high in diabetic patients. It has also been observed that the recurrence of TB after the completion of the course in diabetic patients can be related to the fluctuations in blood glucose and the duration of diabetes. Thus, the follow-up after the completion of the TB course in diabetic patients should be more vigilant compared to non-diabetic patients.

Pharmacokinetic interactions are another factor that affects the outcome in TB and DM co-morbidity. Research has also shown that the plasma concentrations of rifampicin and isoniazid may be decreased in diabetic patients. This may be due to delayed gastric emptying, altered absorption, and metabolic factors. This may lead to failure of the drugs, as well as the development of drug resistance. Though the need to conduct TDM is not advocated, it can be useful in the management of diabetic TB patients.

Another area that has been identified in the association between diabetes and TB is the risk of the development of multidrug-resistant TB. Some research findings have identified that the prevalence of multidrug-resistant TB is more in diabetic patients. It can be an indirect effect, as the delayed sputum conversion as well as the concentration of the drugs can be a problem in diabetic patients who suffer from two disease states.

Further prospective studies need to be done to ascertain the link between diabetes and the risk of developing MDR-TB. Mortality during TB treatment is higher in diabetic individuals. Advanced age, hyperglycemia, and the presence of cardiovascular or renal co-morbidities can all contribute to a greater risk. Hyperglycemia has also been recognized as a predictor of poor outcomes in TB therapy. This again emphasizes the importance of a holistic approach to the management of TB that includes the metabolic effects as well.

Thus, diabetes mellitus has a considerable impact on the outcome of TB therapy in a multitude of complex biological and clinical pathways. It is essential to modify the outcomes in TB therapy by addressing the issue of poor glycemic control and delayed diagnosis.

3. CONCLUSION

Diabetes mellitus has a considerable negative impact on the outcome of TB therapy, affecting the immune system, causing delays in the clearance of the causative organism, increasing the chances of relapse, and causing mortality. Hyperglycemia and possible effects on the pharmacokinetics of the drugs used in TB therapy may contribute to the poor outcome in TB therapy. However, poor glycemic control has been recognized as a major factor that affects the outcome in TB therapy. Thus, it is essential to implement TB/DM management strategies such as bidirectional TB/DM screening, glucose monitoring, and the delivery of healthcare services to improve the prognosis of the patients. As the prevalence of diabetes mellitus continues to increase in TB-endemic areas, it is essential to implement specific interventions to combat the co-endemicity of TB/DM. Improving the collaborative public health system will be key in the management and control of TB.

4. REFERENCES

1. World Health Organization. Global tuberculosis report 2023. Geneva: World Health Organization, 2023.
2. Uplekar M, Weil D, Lonnroth K, Jaramillo E, Lienhardt C, Dias HM, et al. WHO's new End TB Strategy. Lancet, 2015; 385(9979): 1799–801.
3. International Diabetes Federation. IDF Diabetes Atlas. 10th ed. Brussels: International Diabetes Federation, 2021.
4. Harries AD, Kumar AMV, Satyanarayana S, Lin Y, Zachariah R, Lonnroth K, et al. Addressing diabetes mellitus as part of the strategy for ending TB. Int J Tuberc Lung Dis., 2016; 20(3): 323–9.
5. Root HF. The association of diabetes and tuberculosis. N Engl J Med., 1934; 210(1): 1–13.
6. Dooley KE, Chaisson RE. Tuberculosis and diabetes mellitus: convergence of two epidemics. Lancet Infect Dis., 2009; 9(12): 737–46.
7. Jeon CY, Murray MB. Diabetes mellitus increases the risk of active tuberculosis: a systematic review of 13 observational studies. PLoS Med., 2008; 5(7): e152.
8. Stevenson CR, Forouhi NG, Roglic G, Williams BG, Lauer JA, Dye C, et al. Diabetes and tuberculosis: the impact of the diabetes epidemic on tuberculosis incidence. Clin Infect Dis., 2007; 44(10): 1325–30.
9. Baker MA, Harries AD, Jeon CY, Hart JE, Kapur A, Lonnroth K, et al. The impact of diabetes on tuberculosis treatment outcomes: a systematic review. Lancet Infect Dis., 2011; 11(9): 691–700.
10. Restrepo BI. Convergence of the tuberculosis and diabetes epidemics: renewal of old acquaintances. Clin Infect Dis., 2007; 45(4): 436–8.
11. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes. Diabetes Care, 2004; 27(5): 1047–53.
12. Central TB Division. India TB Report 2023. New Delhi: Ministry of Health and Family Welfare, 2023.
13. Viswanathan V, Kumpatla S, Aravindalochanan V, Rajan R, Chinnaiyan P, Srinivasan R, et al. Prevalence of diabetes and pre-diabetes in TB patients. Diabetes Care, 2012; 35(1): 123–5.
14. Raghuraman S, Vasudevan KP, Govindarajan S, Chinnakali P. Prevalence of diabetes mellitus among tuberculosis patients in urban Puducherry. Lung India, 2014; 31(3): 1–5.
15. Martinez N, Kornfeld H. Diabetes and immunity to tuberculosis. Eur J Immunol, 2014; 44(3): 617–26.
16. Gomez DI, Twahirwa M, Schlesinger LS, Restrepo BI. Reduced macrophage activation in diabetes. Clin Vaccine Immunol, 2013; 20(9): 135–43.
17. Kumar NP, Sridhar R, Banurekha VV, Jawahar MS, Nutman TB, Babu S. Type 2 diabetes alters cytokine profiles in TB. J Infect Dis., 2013; 208(11): 1856–64.
18. Vallerskog T, Martens G, Kornfeld H. Diabetic patients exhibit altered IFN-γ responses. Clin Exp Immunol, 2010; 159(1): 29–35.

19. Restrepo BI, Schlesinger LS. Host-pathogen interactions in TB patients with diabetes. Tuberculosis (Edinb), 2014; 94(3): 303–12.
20. Flynn JL, Chan J. Immunology of tuberculosis. Annu Rev Immunol, 2001; 19: 93–129.
21. Alisjahbana B, Sahiratmadja E, Nelwan EJ, Purwa AM, Ahmad Y, Ottenhoff THM, et al. Clinical presentation and treatment response in TB patients with diabetes. Clin Infect Dis., 2007; 45(4): 428–35.
22. Guptan A, Shah A. Tuberculosis and diabetes: an appraisal. J Assoc Physicians India, 2000; 48: 276–9.
23. Chiang CY, Bai KJ, Lin HH, Chien ST, Lee JJ, Enarson DA, et al. Radiographic severity in TB patients with diabetes. Am J Respir Crit Care Med., 2015; 192(10): 124–31.
24. Wang CS, Yang CJ, Chen HC, Chuang SH, Chong IW, Hwang JJ, et al. Impact of diabetes on pulmonary TB. Chest., 2009; 136(1): 159–66.
25. Magee MJ, Salindri AD, Kornfeld H, Singhal A, Burman WJ, Vernon A, et al. Diabetes and delayed sputum conversion. Clin Infect Dis., 2014; 59(11): 1629–36.
26. Singla R, Khan N, Al-Sharif N, Ai-Sayegh MO, Shaikh MA, Osman MM. Influence of diabetes on sputum conversion. J Clin Tuberc Other Mycobact Dis., 2016; 4: 1–6.
27. Mi F, Jiang G, Du J, Li L, Yue W, Liu H, et al. Glycemic control and TB treatment outcomes. Int J Tuberc Lung Dis., 2013; 17(7): 935–41.
28. Faurholt-Jepsen D, Range N, PrayGod G, Jeremiah K, Faurholt-Jepsen M, Aabye MG, et al. Relapse and mortality in TB patients with diabetes. Clin Infect Dis., 2017; 65(2): 192–9.
29. Nijland HM, Ruslami R, Stalenhoef JE, Nelwan EJ, Alisjahbana B, Nelwan RH, et al. Rifampicin plasma concentrations in TB patients with diabetes. Antimicrob Agents Chemother, 2006; 50(3): 1099–102.
30. Ruslami R, Nijland HM, Adhiarta IGN, Kariadi SH, Alisjahbana B, Aarnoutse RE. Pharmacokinetics of anti-TB drugs in diabetic patients. Clin Pharmacokinet, 2010; 49(9): 591–600.
31. Al-Rifai RH, Pearson F, Critchley JA, Abu-Raddad LJ. Association between diabetes and mortality during TB treatment. Trop Med Int Health, 2017; 22(9): 1129–39.
32. Odone A, Houben RM, White RG, Lonnroth K. The effect of diabetes on TB treatment outcomes. Eur Respir J., 2014; 43(3): 130–8.
33. Ko PY, Lin SD, Chou CS, Hsu HC, Huang YH, Hsieh MH. Hyperglycemia increases TB mortality. BMC Infect Dis., 2017; 17: 1–8.
34. Pasipanodya JG, McIlleron H, Burger A, Wash PA, Smith P, Gumbo T. Serum drug concentrations and TB outcomes. Clin Infect Dis., 2013; 56(9): 1241–9.
35. Shariff NM, Shah SA, Kamaludin F. Diabetes and TB drug response. Tuberc Res Treat, 2011; 2011: 1–7.
36. Bashar M, Alcabes P, Rom WN, Condos R. Diabetes and MDR-TB. BMC Public Health, 2010; 10: 97.
37. Dotulong JF, Sapulete MR, Kandou GD. MDR-TB and diabetes association. Acta Med Indones, 2015; 47(1): 80–4.
38. Lonnroth K, Roglic G, Harries AD. Improving TB prevention in diabetes patients. Lancet, 2014; 383(9933): 1814–29.
39. World Health Organization, International Union Against Tuberculosis and Lung Disease. Collaborative framework for care and control of tuberculosis and diabetes. Geneva: WHO, 2011.
40. Kapur A, Harries AD. Bidirectional screening for TB and diabetes. Diabetes Res Clin Pract, 2013; 101(1): 1–10.
41. Young F, Critchley JA, Johnstone LK, Unwin NC. Integrated TB and diabetes care. Trop Med Int Health, 2014; 19(3): 1–9.
42. Yorke E, Atiase Y, Akpalu J, Sarfo-Kantanka O, Boima V. Glycemic control improves TB outcomes. Clin Infect Dis., 2017; 65(2): 1–8.
43. Magee MJ, Bloss E, Shin SS, Contreras C, Huaman HA, Ticona E, et al. Clinical characteristics of TB patients with diabetes. Public Health Rep., 2013; 128(6): 469–76.
44. Gil-Santana L, Almeida-Junior JL, Oliveira CA, Hickson LS, Daltro C, Castro S, et al. Diabetes associated with severe TB. Clin Infect Dis., 2016; 62(4): 429–35.
45. Kumpatla S, Sekar A, Achanta S, Sharath BN, Kumar AMV, Harries AD, et al. Outcomes of TB patients with diabetes in India. Int J Tuberc Lung Dis., 2013; 17(6): 771–8.
46. Balakrishnan S, Vijayan S, Nair S, Subramoniapillai J, Mrithyunjayan S, Wilson N, et al. High diabetes prevalence among TB patients in Kerala. PLoS One, 2012; 7(10): e46502.
47. Brownlee M. The pathobiology of diabetic complications. Nature, 2001; 414(6865): 813–20.
48. Singh DK, Winocour P, Farrington K. Oxidative stress in diabetes. Diabet Med., 2011; 28(5): 547–55.
49. Pickup JC. Inflammation and activated innate immunity in type 2 diabetes. Diabetes Care, 2004; 27(3): 813–23.
50. Lee PH, Fu H, Lai TC, Chiang CY, Chan CC, Lin HH. Glycemic status and TB recurrence. Clin Infect Dis., 2014; 58(7): 1–9.
51. Kim SJ, Hong YP, Lew WJ, Yang SC, Lee EG. Incidence of relapse among TB patients with diabetes. Int J Tuberc Lung Dis., 1998; 2(9): 1–7.
52. Restrepo BI, Fisher-Hoch SP, Pino PA, Salinas A, Rahbar MH, Mora F, et al. Tuberculosis in poorly controlled diabetes. Am J Trop Med Hyg., 2008; 79(4): 1–7.
53. Critchley JA, Restrepo BI, Ronacher K, Kapur A, Bremer AA, Schlesinger LS. Defining the syndemic relationship between TB and diabetes. Lancet Diabetes Endocrinol, 2017; 5(10): 1–10.