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THE DIABETES-TUBERCULOSIS CO-EPIDEMIC: THE INTERACTION BETWEEN INDIVIDUAL AND SOCIO-ECONOMIC RISK FACTORS

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Abstract

Worldwide, tuberculosis (TB) is a major cause of morbi-mortality, about 30% of the population having a Mycobacterium tuberculosis infection. Patients with diabetes mellitus (DM) have a threefold increased risk of developing the disease. The prevalence of DM is rapidly increasing, especially in countries with low and middle income, where TB incidence is also increased, thus baffling the efforts for TB control. The DM-TB co-epidemic is more frequent in married, older men, with reduced level of education, low income, without a steady job, with lifestyle habits such as alcohol consumption, smoking, sedentarism, living in an urban environment, in crowded areas, in insanitary conditions. These patients have a higher body mass index (BMI) compared with those without DM and frequently present family history of TB, family history of DM, longer duration of DM and reduced glycemic control. TB associated with DM is usually asymptomatic, more contagious, multidrug resistant and is significantly associated with an increased risk of therapy failure, relapse and even death. Thus, the DM-TB comorbidity represents a threat to public health and requires the implementation of urgent measures in order to both prevent and manage the two diseases.

key words: *diabetes mellitus, tuberculosis, risk factors*

Introduction

Diabetes mellitus (DM) and tuberculosis (TB) are two chronic diseases which have a major impact on the mortality of the population, 5 million deaths caused by DM [1], respectively 1.4 million deaths caused by TB [2], being registered each year. Worldwide, there are 415 million people with DM, the equivalent of a prevalence of 8.8%, and this number will increase to 642 million by the year 2040 [1]. On the other hand, there have been an estimated 10.4 million incident cases of TB (142/100,000 people). Approximately 2 billion people have Mycobacterium tuberculosis infection, 5 to 15% of whom develop active TB [2,3]. Because DM increases threefold the risk of progression of latent TB infection (LTBI) in active tuberculosis [4-6], the association of the two diseases threatens the health of the entire population and requires routine bidirectional screening [7]. A total of 1 million (15%) of the TB cases are

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attributed to DM [8], this number being higher still than that of the people with HIV-TB co-infection [6,9]. The DM-TB comorbidity causes a higher risk of anti TB therapy failure, relapse after finishing treatment and death [10]. Furthermore, it increases the risk of persisting positive sputum exam after 2-3 months of treatment, developing pulmonary cavities and hemoptysis [10]. 95% of the people with TB, respectively 70% of those suffering from DM live in countries with low and middle income, their numbers amplifying each other [11,12]. Urbanization and lifestyle alteration have determined an increase in DM prevalence, thus enhancing the DM-TB co-epidemic, which can jeopardize the measures implemented to control TB, especially in low income countries.

The diabetes mellitus-tuberculosis comorbidity – individual risk factors

Age. Although DM-TB comorbidity has a higher incidence regardless of age, the majority of patients who associate DM and TB are aged over 40 years old and are significantly ($p<0.001$) older compared to patients with normoglycemia [3,4,9,12-22]. The explanation may be that the prevalence of type 2 DM is higher in elderly patients [6,23]. Age over 40 represents a risk factor for developing DM-TB co-epidemic in both TB and DM patients, the risk increasing proportionally with age [24-29].

Gender. Many studies have shown, over time, the preponderance of the male gender in the group of patients with DM-TB [3,9,12,13,21,26,27,30-35]. This aspect can be justified by smoking and alcohol consumption, as risk factors, through their cumulative effect [20]. However, there are studies which cannot identify statistically significant differences between the two genders [23] or which have detected an increased risk of DM-TB association in the case of women [14,17,24,28]. This difference can be caused by ethnic differences of tribal communities, with matriarchal families, in which women have activities similar to those conducted by man, having a preponderant role in social and economical life. Besides these aspects, another reason for increased prevalence of DM-TB in women from these tribal communities can be smoking and excessive alcohol consumption [36].

Anthropometric measurements (body mass index, waist circumference). The majority of the studies compared a group of TB-DM patients with a group of TB patients without DM, reporting a significantly higher medium BMI in those who have both diseases [6,13,16,20,29,30,33,34]. Most of TB-DM patients have the BMI between 18.50 and 22.99 kg/m^2, TB being statistically significant associated with DM in this group [17,21]. Accordingly, the risk of TB-DM association increases with the elevation of BMI, this being one of the main risk factors of the co-epidemic [9,16,20,22,26,27,29,34,37]. Also, BMI > 23 kg/m^2 is associated with an increased cardiometabolic risk [27]. On the other hand, patients with DM and TB have lower BMI compared with those without TB [12,21,32,38,39,41], fact that could be explained by the weight loss determined both by poorly controlled DM and by active TB [7,18]. Moreover, malnutrition can cause increased glycemia by stimulating the stress hormone production [40]. Thus, people with low BMI have a reduced risk of DM development, but are more prone to Mycobacterium tuberculosis infection. On the other hand, although high BMI increases the risk of DM development, it decreases the risk of developing TB [16,41,42]. Other studies, however, did not show a significant difference between BMI in TB-DM patients and those with TB and normoglycemia [12,15,18,24]. A waist circumference > 90 cm both in women and in men has been associated with DM in patients with TB, having a

statistically significant higher medium value compared to patients with TB and normoglycemia [13,18,20,24,27]. A waist circumference value over 87 cm in men, respectively 82 cm in women is related to a high cardiometabolic risk [27]. Contrary to these studies, some researchers have not been able to show a significant association between waist circumference and DM development in patients with TB [12].

Behavioral factors (smoking, alcohol consumption, drug consumption). The majority of patients are current smokers or have smoked, smoking being a risk factor significantly associated with DM-TB co-epidemic [16,24,32]. TB is associated with a longer period in which patients smoke daily [21]. On the other hand, there are studies that show a larger number of smokers in the DM-TB group, but a statistically significant difference compared with patients with DM without TB cannot be reported [15,20,26,27,43]. Alcohol consumption is also a risk factor significantly associated with DM-TB comorbidity [12,25,26,32,33]. However, other studies did not show a significant association between alcohol consumption and TB development [15,27,30,43], although there are studies that showed a higher number of alcohol consumers within the TB-normoglycemia group [14,22,28]. Drug consumption is a risk factor associated with TB, researchers reporting more drug consuming patients in the TB-normoglycemia group [22,28], but other studies did not confirm a significant difference between the two group of patients [15]. An important limitation in the conducted studies is represented by the frequent under-appreciation of drug and alcohol consumption in the case of self-reporting [28,44].

Alimentation. Urbanization determined changes in alimentation, not following the diet being considered a risk factor for developing obesity and DM [27,45]. The TB-DM co-epidemic is associated with hypercaloric diet, rich in fat and salt and poor in fiber [43-46]. It has replaced traditional food, lacking in fat and salt and rich in fiber [46] and is correlated with the increase of morbidity and mortality determined by diseases caused by an unhealthy diet [45]. Malnutrition is frequent in patients that associate TB and DM. The risk of developing this comorbidity is associated with vitamin A and vitamin D deficit, these having an essential role in immunity [47].

Physical activity. Changes in lifestyle, like sedentarism, increase the risk of DM development among TB patients [20,24,27,34, 43,45,48]. Along with a hypercaloric diet, physical inactivity increments the risk of developing obesity, thus increasing insulin resistance, one of the determinant factors of DM [43].

Family history of diabetes mellitus. Family history of DM is one of the most frequent and significantly associated risk factors with the development of DM in the group of patients with TB [12,16,18,20,21,24,29,33,34,37,48]. The TB patients have a three times higher risk of TB-DM association if they also have DM family history [20,24].

Family history of tuberculosis. The presence of TB family history among DM patients gives them a statistically significant higher risk of developing active TB [26,32,41,43]. On the other hand, other researchers did not find major differences between the groups of patients with DM, associating TB or not [30].

Family history of obesity. Family history of obesity is statistically significant associated with DM in patients with TB, thus increasing the risk of the co-epidemic [48].

Family history of arterial hypertension. A higher percentage of TB-DM patients have family history of arterial hypertension, compared

to those with TB without DM. However, the differences weren't of great significance [48].

The type of diabetes mellitus. Both type 1 and 2 DM increase the risk of developing TB, but the majority of people with DM-TB co-epidemic have type 2 DM [24,33,43,48], fact which can be explained by the higher prevalence of type 2, compared to type 1 DM. However, type 1 DM patients are more prone to Mycobacterium tuberculosis infection [6], the explanation for this correlation could be a longer duration of DM or a difficult control of hyperglycemia in patients with type 1 DM [6,34]. Furthermore, the risk of TB development increases in the patients treated with insulin [18,26,34,49] and with the duration of the disease longer than 5 years [12,14,25,26, 29,33,43,48]. Patients with the duration of DM over 10 years have a risk nine times higher of active TB development compared to patients with duration of the disease under 5 years [43]. Glycated hemoglobin (HbA1c) is increased in patients with DM-TB co-epidemic [26], poor glycemic control being statistically significant associated with TB [18,20,25,26,43].

The type of tuberculosis. The majority of patients with DM-TB comorbidity have pulmonary TB, this being significantly associated with DM [3,14,16,19,24,28,43,48]. On the other hand, extra-pulmonary TB is more frequently diagnosed in people with normoglycemia [5,6,15,20,24,30,48]. History of TB is a factor significantly associated with TB. Thus, patients with DM and history of TB have a risk 13 times higher of developing pulmonary TB compared to those without TB history [43]. Moreover, patients with DM-TB co-epidemic have positive sputum exam at the time of diagnosis, which persists positively 2-3 months from the beginning of the anti-TB therapy, and are more prone to hemoptysis, pulmonary cavities, fever and cough [10,28]. The radiological characteristics of these patients are atypical, a large part of them presenting lesions with basal localization, unlike patients without DM, which present lesions with apical localization [33]. This fact can represent an important diagnostic issue, since the basal localization can be misinterpreted as cancer or community-acquired pneumonia [5,33]. The DM-TB comorbidity is more frequently associated with multidrug resistant cases and an increased risk of death, therapy failure and relapse post-treatment compared to patients with normoglycemia [5,10,14,20,33].

History of arterial hypertension. Patients with TB and DM have the systolic arterial pressure higher than those with normoglycemia, arterial hypertension being a risk factor associated with DM [18,20,37]. On the other hand, there were no important differences regarding diastolic arterial pressure between the two groups [20]. Other studies, however, although reporting a higher number of patients with arterial hypertension in the TB-DM versus TB-normoglycemia group, did not find statistically significant differences between the two [24,48].

The diabetes mellitus-tuberculosis comorbidity – socio-economic determinants

Educational status. A significant percentage of patients with DM-TB co-epidemic have a low educational level, TB being negatively associated with schooling [11,14,16,21,26,30]. More than half of these did not finish primary school [14,16]. However, other studies did not show statistically significant differences regarding educational level [22,43].

Occupation. While DM is one of the most frequent risk factors associated with sedentarism in TB patients, most people with DM-TB comorbidity are unemployed or retired [14,16,22,26]. In comparison, patients with TB

and normoglycemia are more likely employed, students or inmates [14,28]. On the other hand, an association of TB with the occupational status of people with DM has not been reported [43].

Income. The low economic status is associated with active TB in patients with DM [11,17,21,26,39,45]. These are poorer compared with the people with DM without TB and also a large part of them have limited access to social security or quality medical services [17,50]. Moreover, it is estimated that the number of patients with DM will increase in the next decades in low and middle income countries, where TB incidence is already high [45], the DM-TB co-epidemic being a major health problem in these regions where poverty prevails. On the other hand, DM is positively correlated with high income in patients with TB [20,21,24].

Living conditions. As a consequence of low economical status, an important percentage of people with DM live or work in overcrowded or inadequately ventilated spaces, thus increasing the risk of developing TB [11,17,21,50]. TB is negatively associated with adequate conditions, like good floors and walls and good toilet facilities [21]. Moreover, patients with DM-TB comorbidity, unlike those with DM without TB, show social risk factors, like homelessness [28].

Marital status. The majority of patients with DM and TB are married [16,27,30,43], factor significantly linked to the risk of DM-TB co-epidemic development [16,30]. People with TB who are married are twice as prone to the risk of developing DM compared to those unmarried [16].

Environment. The sedentary lifestyle, unhealthy diet, overcrowding, but also easier access to medical services regarding screening, are factors commonly found in people which live in an urban environment. Thus, the DM-TB co-epidemic has a significantly higher prevalence in urban inhabitants, compared to the rural environment [11,17,26,35,43,46]. Patients with DM from an urban environment have a risk approximately six times higher of developing TB compared to those from a rural environment [43]. On the other hand, some researchers have shown a higher number of DM-TB patients in the rural environment [16]. People who migrate from countries with low and middle income to those with high income present a greater risk of developing DM compared to the native population, urbanization being associated with a high risk of obesity and DM [45]. Moreover, rapid urbanization represents an important problem regarding TB control [11].

Ethnicity. Hispanics with DM show a high risk of TB development compared to other ethnic groups [4,28,34]. Thus, ethnicity is considered to be a risk factor associated DM-TB, significantly contributing to the increase of the co-epidemic prevalence.

Conclusions

The DM prevalence is continuously escalating, especially in developing countries, where also TB incidence is high, needing the implementation of bidirectional screening, focused on prevention, diagnostic and adequate treatment, in order to limit the burden brought by the two diseases. The DM-TB co-epidemic represents one of the most important challenges of TB control and eradication programs, with a significant impact on public health, being associated with numerous individual and socio-economic risk factors.

Moreover, DM determines a high risk of anti-TB therapy failure and after treatment relapse, but, by far the most alarming risk is that of death during TB treatment. Some aspects are not yet completely solved, additional research being necessary regarding the pathophysiological mechanisms involved in the DM-TB association, but also in the management of the two diseases.

REFERENCES

1. International Diabetes Federation. IDF Diabetes Atlas – 7th Edition. Brussels, Belgium: International Diabetes Federation, 2015. Accesed on 24th January 2017 at: http://www.diabetesatlas.org/resources/2015-atlas.html.

2. World Health Organization. Global tuberculosis report 2016. Geneva, Switzerland: World Health Organization, 2016. Accessed on 24th January 2017 at http://www.who.int/tb/publications/global_report/en/.

3. Pal R, Ansari MA, Hameed S, Fatima Z. Diabetes mellitus as hub for tuberculosis infection: a snapshot. *Int J Chronic Dis* 2016: 5981574, doi: 10.1155/2016/5981574, 2016.

4. Jeon CY, Murray MB. Diabetes mellitus increases the risk of active tuberculosis: a systematic review of 13 observational studies. *PLoS Med* 5: e152, 2008.

5. Dooley KE, Chaisson RE. Tuberculosis and diabetes mellitus: convergence of two epidemics. *Lancet Infect Dis* 9: 737-746, 2009.

6. Ruslami R, Aarnoutse RE, Alisjahbana B, van der Ven AJ, van Crevel R. Implications of the global increase of diabetes for tuberculosis control and patient care. *Trop Med Int Health* 15: 1289-1299, 2010.

7. Kapur A, Harries AD. The double burden of diabetes and tuberculosis - public health implications. *Diabetes Res Clin Pract* 101: 10-19, 2013.

8. Lönnroth K, Roglic G, Harries AD. Improving tuberculosis prevention and care through addressing the global diabetic epidemic: from evidence to policy and practice. *Lancet Diabetes Endocrinol* 2: 730-739, 2014.

9. Zheng C, Hu M, Gao F. Diabetes and pulmonary tuberculosis: a global overview with special focus on the situation in Asian countries with high TB-DM burden. *Glob Health Action* 10: 1-11, 2017.

10. Baker MA, Harries AD, Jeon CY et al. The impact of diabetes on tuberculosis treatment outcomes: a systematic review. *BMC Med* 9: 81, 2011.

11. Stevenson CR, Forouhi NG, Roglic G et al. Diabetes and tuberculosis: the impact of the diabetes epidemic on tuberculosis incidence. *BMC Public Health* 7: 234, 2007.

12. Raghuraman S, Vasudevan KP, Govindarajan S, Chinnakali P, Panigrahi KC. Prevalence of diabetes mellitus among tuberculosis patients in urban Puducherry. *N Am J Med Sci* 6: 30-34, 2014.

13. Aftab H, Ambreen A, Jamil M et al. High prevalence of diabetes and anthropometric heterogeneity among tuberculosis patients in Pakistan. *Trop Med Int Health*, 2017. doi:10.1111/tmi.12842. [Epub ahead of print]

14. Abdelbary BE, Garcia-Viveros M, Ramirez-Oropesa H, Rahbar MH, Restrepo BI. Tuberculosis-diabetes epidemiology in the border and non-border regions of Tamaulipas, Mexico. *Tuberculosis* 101: S124-S134, 2016.

15. Gil-Santana L, Almeida-Junior JL, Oliveira CA et al. Diabetes is associated with worse clinical presentation in tuberculosis patients from Brazil: A retrospective cohort study. *PLoS One* 11: e0146876, 2016.

16. Sarker M, Barua M, Guerra F et al. Double trouble: prevalence and factors associated with tuberculosis and diabetes comorbidity in Bangladesh. *PLoS One* 11: e0165396, 2016.

17. Delgado-Sánchez G, García-García L, Castellanos-Joya M et al. Association of pulmonary tuberculosis and diabetes in Mexico: Analysis of the national tuberculosis registry 2000–2012. *PLoS One* 10: e0129312, 2015.

18. Ogbera AO, Kapur A, Abdur-Razzaq H et al. Clinical profile of diabetes mellitus in tuberculosis. *BMJ Open Diabetes Res Care* 3: e000112, 2015.

19. Wang Q, Ma A, Han X et al. Prevalence of type 2 diabetes among newly detected pulmonary tuberculosis patients in China: A community based cohort study. *PLoS One* 8: e82660, 2013.

20. Viswanathan V, Kumpatla S, Aravindalochanan V et al. Prevalence of diabetes and pre-diabetes and associated risk factors among tuberculosis patients in India. *PLoS One* 7: e41367, 2012.

21. Goldhaber-Fiebert JD, Jeon CY, Cohen T, Murray MB. Diabetes mellitus and tuberculosis in countries with high tuberculosis burdens: individual risks and social determinants. *Int J Epidemiol* 40: 417-428, 2011.

22. Restrepo BI, Camerlin AJ, Rahbar MH et al. Cross-sectional assessment reveals high diabetes prevalence among newly-diagnosed tuberculosis cases. *Bull World Health Organ* 89: 352-359, 2011.

23. Manjareeka M, Palo SK, Swain S, Pati S, Pati S. Diabetes mellitus among newly diagnosed tuberculosis patients in tribal Odisha: An exploratory study. *J Clin Diagn Res* 10: LC06-LC08, 2016.

24. Agarwal AK, Ginisha G, Preeti G, Dwivedi S, Swamai P. The association between diabetes and tuberculosis may be the next challenge for global tuberculosis control worldwide. *Indian J Endocrinol Metab* 20: 732-733, 2016.

25. Harries AD, Kumar AM, Satyanarayana S et al. Diabetes mellitus and tuberculosis: programmatic management issues. *Int J Tuberc Lung Dis* 19: 879-886, 2015.

26. Kumpatla S, Sekar A, Achanta S et al. Characteristics of patients with diabetes screened for tuberculosis in a tertiary care hospital in South India. *Public Health Action* 3 [Suppl 1]: S23-S28, 2013.

27. Faurholt-Jepsen D, Range N, PrayGod G et al. The role of anthropometric and other predictors for diabetes among urban Tanzanians with tuberculosis. *Int J Tuberc Lung Dis* 16: 1680-1685, 2012.

28. Restrepo BI, Fisher-Hoch SP, Crespo JG et al. Type 2 diabetes and tuberculosis in a dynamic bi-national border population. *Epidemiol Infect* 135: 483-491, 2007.

29. Alisjahbana B, Sahiratmadja E, Nelwan EJ et al. The effect of type 2 diabetes mellitus on the presentation and treatment response of pulmonary tuberculosis. *Clin Infect Dis* 45: 428-435, 2007.

30. Siddiqui AN, Khayyam KU, 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 Res Int* 2016: 7273935, 2016.

31. Caraffa E, Schepisi MS, Gualano G et al. The diabetes-tuberculosis co-epidemic: the role of international migration. *Int J Tuberc Lung Dis* 20: 771–777, 2016.

32. Lin YH, Chen CP, Chen PY et al. Screening for pulmonary tuberculosis in type 2 diabetes elderly: a cross-sectional study in a community hospital. *BMC Public Health* 15: 3, 2015.

33. Kouismi H, Hammi S, Bouti K et al. Pulmonary tuberculosis and diabetes mellitus profile. *Int J Med Surg* 2: 11-15, 2015.

34. Baghaei P, Marjani M, Javanmard P, Tabarsi P, Masjedi MR. Diabetes mellitus and tuberculosis facts and controversies. *J Diabetes Metab Disord* 12: 58, 2013.

35. Balakrishnan S, Vijayan S, Nair S et al. High diabetes prevalence among tuberculosis cases in Kerala, India. *PLoS One* 7: e46502, 2012.

36. Achanta S, Tekumalla RR, Jaju J et al. Screening tuberculosis patients for diabetes in a tribal area in South India. *Public Health Action* 3: S43-S47, 2013.

37. Pizzol D, Di Gennaro F, Chhaganlal KD et al. Tuberculosis and diabetes: current state and future perspectives. *Trop Med Int Health* 21: 694-702, 2016.

38. Fekadu S, Yigzaw M, Alemu S et al. Insulin-requiring diabetes in Ethiopia: associations with poverty, early undernutrition and anthropometric disproportion. *Eur J Clin Nutr* 64: 1192-1198, 2010.

39. Ponce-De-Leon A, Garcia-Garcia Md Mde L, Garcia-Sancho MC et al. Tuberculosis and diabetes in southern Mexico. *Diabetes Care* 27: 1584-1590, 2004.

40. Carreira S, Costeira J, Gomes C, André JM, Diogo N. Impact of diabetes on the presenting features of tuberculosis in hospitalized patients. *Rev Port Pneumol* 18: 239-243, 2012.

41. Lönnroth K, Williams BG, Cegielski P, Dye C. A consistent log-linear relationship between tuberculosis incidence and body mass index. *Int J Epidemiol* 39: 149-155, 2010.

42. Skowroński M, Zozulińska-Ziółkiewicz D, Barinow-Wojewódzki A. Tuberculosis and diabetes mellitus – an underappreciated association. *Arch Med Sci* 10: 1019-1027, 2014.

43. Amare H, Gelaw A, Anagaw B, Gelaw B. Smear positive pulmonary tuberculosis among diabetic patients at the Dessie referral hospital, Northeast Ethiopia. *Infect Dis Poverty* 2: 6, 2013.

44. Rajavashisth TB, Shaheen M, Norris KC et al. Decreased prevalence of diabetes in marijuana users: cross-sectional data from the National Health and Nutrition Examination Survey (NHANES) III. *BMJ Open* 2: e000494, 2012.

45. Girardi E, Schepisi MS, Goletti D et al. The global dynamics of diabetes and tuberculosis: the impact of migration and policy implications. *Int J Infect Dis,*

2017. doi: 10.1016/j.ijid.2017.01.018. [Epub ahead of print]

46. Renzaho AM. The post-2015 development agenda for diabetes in sub-Saharan Africa: challenges and future directions. *Glob Health Action* 8: 27600, 2015.

47. Wang Q, Ma A, Bygbjerg IC et al. Rationale and design of a randomized controlled trial of the effect of retinol and vitamin D supplementation on treatment in active pulmonary tuberculosis patients with diabetes. *BMC Infect Dis* 13: 104, 2013.

48. Baldé NM, Camara A, Camara LM, Diallo MM, Kaké A, Bah-Sow OY. Associated tuberculosis and diabetes in Conakry, Guinea: prevalence and clinical characteristics. *Int J Tuberc Lung Dis* 10: 1036-1040, 2006.

49. Dobler CC, Flack JR, Marks GB. Risk of tuberculosis among people with diabetes mellitus: an Australian nationwide cohort study. *BMJ Open* 2: e000666, 2012.

50. Lönnroth K, Jaramillo E, Williams BG, Dye C, Raviglione M. Drivers of tuberculosis epidemics: the role of risk factors and social determinants. *Soc Sci Med* 68: 2240-2246, 2009.