# The Prevalence of Type-2 Diabetes and its Related Factors in Pulmonary Tuberculosis (TB) Patients of North of Iran

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Received: 26 September 2018 / Received in revised form: 14 March 2019, Accepted: 23 March 2019, Published online: 25 April 2019 © Biochemical Technology Society 2014-2019 © Saves Educational Society 2008

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# Abstract

Introduction: The prevalence rate of type-2 diabetes is increasing considerably in developing countries. Diabetes increases the risk of pulmonary TB and exacerbates the clinical manifestations of TB in the light of impairment to the immune system. The study was conducted to determine the prevalence of type-2 diabetes in patients with pulmonary TB and its related factors in Mazandaran during a five-year period. Materials and methods: By a cross-sectional method the relevant data were extracted from the medical records of TB patients treated in health centers of Mazandaran from 2013 to 2017. The collected data was analyzed using SPSS 20, software. Demographic and diabetes-related information was extracted from the patient records and Chi-square, Pearson and logistic regression were used to determine the relationship between type-2 diabetes and pulmonary TB. Mantel-Haenszel Test and logistic regression were used to eliminate the effects of confounding variables. P-value equal or less than 0.05 was considered as significant. Results: In this study, 1316 patients over 25 years of age with pulmonary TB were examined, of whom 76.7% were males (p = 0.001) with the mean age of  $48.70 \pm 18.10$  years old. The prevalence of type-2 diabetes in these patients was 20.06%. The highest prevalence of type-2 diabetes was in the age group of 45-64 years (39.4%) (P=0.000) and the highest prevalence of type-2 diabetes was in the BMI group more than 30 (40%) (P=0.000). The ratio of women with type-2 diabetes in pulmonary TB patients was 1.5 times that of men (P = 0.001). Conclusion: According to the results, the prevalence of type-2 diabetes in pulmonary TB patients in Mazandaran was high. Increasing BMI and age may increase the likelihood of comorbidity of type-2 diabetes and pulmonary TB. For better treatment of pulmonary TB, the identification and treatment of patients with type-2 diabetes is of particular importance. A regular screening of type-2 diabetes among patients with pulmonary TB is suggested.

Key words: Type-2 diabetes, Pulmonary TB, Prevalence, Iran.

# Introduction

Type-2 diabetes is a metabolic disorder characterized by high levels of blood glucose that can cause many side effects in different organs (Hassanzade et al., 2017). Diabetes is among the relatively common chronic diseases in the world, and the emergence and prevalence of this disease is increasing in many societies, especially in developing countries (Larejani and Zahedi, 2001). Diabetes has always been as one of the most significant elements in the recurrence of pulmonary TB (Kermansaravi and Metanat, 2012). Uncontrolled diabetes by weakening the immune system, can lead to proliferation of tuberculosis and result in pulmonary TB (Rastegari et al., 2014). Diabetes is one of the known risk factors for active TB and a serious danger for the activation of latent TB. The simultaneity of diabetes and TB seems to cause negative outcomes in the treatment of diabetic patients with tuberculosis compared to non-diabetic TB patients. The incidence of diabetes in TB patients has been reported up to 49% (Baghaei et al., 2015).

TB is the greatest cause of mortality from single-factor infectious diseases (even more than AIDS, malaria, and measles) in the world (Rastegari et al., 2014; Beiranvand et al., 2014). Approximately, one third of the world's population is infected by Mycobacterium

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tuberculosis, and about 10% of them are at risk for active disease in their lives (Viswanathan et al., 2012). In 2015, 1.8 million people died from TB (Kermansaravi and Metanat, 2012). TB in 85% of the cases is in pulmonary form and in 15% manifests as extra pulmonary (Dye, 2006; Ruslami et al., 2010; Vega Torres, Conde and Diaz, 1996; Asefzadeh and Bijani, 2008). Any impairment of immunity including malnutrition, cancers, HIV infection, and various metabolic diseases can activate the latent TB infection and causes illness (Kermansaravi and Metanat, 2012; Vega Torres, Conde and Diaz, 1996; Asefzadeh and Bijani, 2008).

Type-2 diabetes is associated with increased risk of TB contributing to TB epidemic and can cause many problems (Ruslami et al., 2010). With 250 million increase in Diabetes Mellitus in the world, anticipations of its doubling in the next 20 years, and given the relationship between these two diseases, the World Health Organization (WHO) has encountered some worries in controlling TB (Dye, 2006).

The comorbidity of Pulmonary TB and type-2 diabetes is considered a global health threat, and the relationship between diabetes and TB and its synergistic role in the development of human disease has been widely recognized (Dooley and Chaisson ,2009). In Iran, the prevalence of type-2 diabetes in men has been estimated to be 9.84 compared to 10.68% among women (Haghdoost et al., 2009). The prevalence of TB in 2011 was 10.88 per 100,000 people in Iran (Organization, 2011). Drug-resistant TB is higher in diabetic patients than in non-diabetic patients (Alavi and Khoshkhoy, 2012). Increased susceptibility to TB among patients with type-2 diabetes depends to several factors: the direct effects of hyperglycemia and insulin resistance, and the indirect effects of macrophages and lymphocytes functioning (Kumar Nathella and Babu ,2017). The epidemic of diabetes poses important challenges for TB control (Demlow, Oh and Barry, 2015). The conducted studies have reported the prevalence of diabetes in TB patients. In a study by Bridson and colleagues in Australia in 2015, the prevalence of diabetes in TB patients was 23% (Bridson et al., 2015). Moreover, in a study by Dooley et al. in 2009, a strong relationship between TB and diabetes was confirmed (Dooley and Chaisson ,2009). The prevalence of diabetes in TB patients in Iran has been reported to be 17-23% (Vega Torres, Conde and Diaz, 1996; Bridson et al., 2015).

Therefore, conducting extensive studies on the prevalence of type-2 diabetes in pulmonary TB patients and the effective factors can help health policy makers to come up with effective strategies. The increased incidence of type-2 diabetes and its effect on the incidence of pulmonary TB followed by severe complications due to the simultaneity of these two diseases has been proved in many studies. Given the lack of research in Iran particularly in Mazandaran, this study was conducted to determine the prevalence of type-2 diabetes in patients with pulmonary TB and its related factors in Mazandaran in 2013-2017.

#### **Materials and Methods**

By a cross-sectional study all patients diagnosed with TB from 2013 to 2017, who were 2009 patients, of whom 1316 patients had pulmonary TB and other inclusion criteria were entered into the study. The inclusion criterion was having pulmonary TB diagnosis in the Department of Prevention and Care of Diseases of the directorate of Health of Mazandaran-Babol University of Medical Sciences 2013 to 2017. Non-Iranians and those under 25 years of age were excluded from the study. Data collection tool was a software for recording and analyzing TB patients (TB Register Application) with data transferability without manipulating databases using SPSS 20, by which demographic variables such as gender, age, occupation, place of life, history of imprisonment, weight, as well as epidemiological and clinical data including TB type (pulmonary, extra-pulmonary), date of onset of symptoms, date of diagnosis and type-2 diabetes and group treatment were recorded. The collected data was analyzed using SPSS 20 software. The ratio was used to describe the qualitative variables, logistic regression tests were utilized for variables like age, gender, occupation, education, place of residence, marital status, weight and BMI, and Chi-square, Pearson or logistic regression were used to determine the relationship between type-2 diabetes and pulmonary TB. Moreover, Mantel-Haenszel Test and logistic regression were used to eliminate the effects of confounding variables. P-value equal or less than 0.05 was considered as significant.

# Results

In this study, from 2013 to 2017, 1316 patients with pulmonary TB with an average age of  $48.70 \pm 18.10$  years were examined with their age range varying from 25 to 94 years. Among the patients under study, 1009 (76.7%) were males. 795 people (60.4%) lived in urban and 521 (39.6%) in rural areas. Of the patients under study, 1170 (88.9%) were covered by Mazandaran University of Medical Sciences and 145 (11.1%) were covered by Babol University of Medical Sciences. Other demographic data are demonstrated in table 1.

Variable		Frequency of pulmonary TB	Frequency of Type-2	Prevalence of	X <sup>2</sup>	Р
		(%)	Diabetes (%)	Type-2 Diabetes		
Gender	Female	307 (23.32)	82 (31.06)	26.71	11.03	0.001
	Male	1009 (76.68)	182 (68.94)	18.03		

Table 1: The relationship between type-2 diabetes and prevalence of pulmonary TB patients in Mazandaran from 2013 to 2017

	Married	839 (63.86)	194 (73.76)	23.12		
	Single	248 (18.87)	20 (7.62)	8.06	29.33	0.000
Marital status	Divorced	124 (9.44)	23 (8.74)	8.06		
	Widow/widower	103 (7.85)	26 (9.88)	25.24		
Place of residence	Rural	521 (39.58)	111 (42.05)	21.30	0.83	0.3
	Urban	795 (60.42)	153 (57.95)	20.15		
	≤18.5	431 (32.82)	65 (24.71)	15.08		
	18.6-24-99	746 (56.81)	147 (55.90)	19.70	32.67	0.000
BMI (kg/m²)	25-29.99	111 (8.45)	41 (15.59)	36.93		
	≥30	25 (1.92)	10 (3.80)	40		
	Employee	47 (3.57)	10 (3.79)	21.27		
	Driver	41 (3.12)	8 (3.03)	19.51		
	Housewife	108 (8.22)	45 (17.05)	41.66	36.32	0.000
	Farmer	239 (18.16)	47 (17.80)	19.66		
	Unemployed	97 (7.37)	13 (4.92)	13.40		
Occupation	Retired	218 (16.56)	40 (15.15)	18.34		
	Other	566 (43)	101 (38.26)	17.84		
	25-34	380 (28.87)	27 (10.23)	7.10		
	35-44	290 (22.03)	50 (18.93)	17.24		
Age group (year)	45-54	191 (14.51)	59 (22.34)	39.89	105.19	0.000
	55-65	152 (11.55)	60 (22.73)	39.47		
	65-74	135 (10.25)	42 (15.91)	31.11		
	75-84	122 (3.27)	22 (8.34)	18.03		
	≥85	46 (3.49)	4 (1.52)	8.69		

Multivariate regression was used for the variables less than 0.20 in single-variable and chi-square analyses to eliminate confounding variables in the data analysis and to determine the factors affecting the prevalence of type-2 diabetes in pulmonary TB patients. Multivariate logistic regression model revealed a significant relationship between BMI and the prevalence of type-2 diabetes in pulmonary TB patients. The relevant odds ratios and p values are demonstrated in table 2. Based on the findings, the highest OR was identified for BMI 25-29.99 (OR=2.66, CI%95= 1.07-6.57, P = 0.03). Increasing of BMI among patients with pulmonary TB showed a positive and significant relationship between age group and the prevalence of type-2 diabetes in pulmonary TB patients and increasing of age was significantly associated with the prevalence of diabetes among TB patients (table 2).

There was an increasing trend for the prevalence of type-2 diabetes among pulmonary TB patients from 2013 to 2017 (Graph 1).



Graph 1: The prevalence of type-2 diabetes in pulmonary TB patients from 2013 to 2017

	Variable	The frequency of pulmonary TB (%)	Frequency of Type-2 Diabetes N (%)	OR (CI%95)	Р
Gender	Female	307 (23.32)	82 (26.71)	1.20 (0.76-1.90)	0.4
	Male	1009 (76.68)	182 (18.03)	1.00 (Ref)	
	Married	839 (63.86)	194 (23.12)	0.59 (0.34-1.01)	0.05
Marital status	Single	248 (18.87)	20 (8.06)	0.95 (0.57-1.59)	0.8
	Divorced	124 (9.44)	23 (18.54)	1.05 (0.60-1.82)	0.8
	Widow/widower	103 (7.85)	26 (25.24)	1.00 (Ref)	
	≤18.5	431 (32.82)	65 (15.08)	1.41 (1.01-1.98)	0.4
BMI	18.6-24-99	746 (56.81)	147 (19.7)	2.65 (1.59-4.40)	0.000
(kg/m <sup>2</sup> )	25-29.99	111 (8.45)	41 (36.93)	2.66 (1.07-6.57)	0.03
	≥30	25 (1.92)	10 (40)	1.00 (Ref)	
	25-34	380 (28.87)	27 (7.10)	2.52 (1.54-4.22)	0.000
	35-44	290 (22.03)	50 (17.24)	4.62 (2.71-7.88)	0.000
Group	45-54	191 (14.51)	59 (30.89)	5.09 (2.86-9.07)	0.000
Age (year)	55-65	152 (11.55)	60 (39.47)	4.48 (2.31-8.69)	0.000
	65-74	135 (10.25)	42 (31.11)	2.71 (1.07-6.89)	0.03
	75-84	122 (3.27)	22 (18.03)	1.27 (0.34-4.73)	0.7
	≥ 85	46 (3.49)	4 (5.69)	1.00 (Ref)	

Table 2: Relationship between type-2 diabetes prevalence in pulmonary TB patients in multivariate analysis in Mazandaran from 2013 to 2017

#### Discussion

The purpose of this study was to determine the prevalence and relationship between type-2 diabetes and pulmonary TB in Mazandaran province, Iran from 2013 to 2017. In this study, 1316 patients with pulmonary TB were identified during study period and the prevalence of type-2 diabetes in all patients with pulmonary TB was 20.06% and this rate increased by 6% from 2013 to 2017. In a study conducted in Mazandaran province in 2012, the prevalence of type-2 diabetes in these patients was reported as 16.9% (Biranvand et al., 2012). An increasing trend in the prevalence of diabetes has been reported in most Iranian and foreign studies (Haghdoost et al., 2009; Azimi-Nezhad et al., 2008). In studies by Larijani and Zahedi in Tehran and Isfahan, the prevalence of type-2 diabetes in participants over 30 years of age in the general population was reported in urban and rural areas as 8 and 5% respectively. Diabetes increases the risk of TB prevalence by 2-3 times (Asante-Poku et al., 2019; Harries et al., 2011). It is very difficult and almost impossible to determine the precedence of TB or type-2 diabetes, but a study from 1965 to 2007 found that type-2 diabetes mellitus had a threefold risk of developing TB (Jeon and Murray, 2008). Another study by Glusha et al. in Golestan in 2009 showed that the prevalence of diabetes in pulmonary TB patients was 23.05% (Rezaei Shirazi et al., 2009). Moreover, in a study by Bermejo et al. (2009) in Spain, 42% of diabetic patients had a positive tuberculin skin test, showing a high prevalence of TB in diabetic patients (Mansilla et al., 1995). Diabetes has a significant contribution to TB (Stevenson et al., 2007), and type-2 diabetes is considerably increasing in developing countries (Harries et al., 2011), which can lead to recurrence and increase in the prevalence and complications associated with TB.

In the present study, the prevalence of type-2 diabetes in women was 1.5 times higher than that of men, in line with other studies in Iran (Biranvand et al., 2012) and Malaysia (Nissapatorn et al., 2005). However, in a study by Walker et al. in England (2010), the prevalence of type-2 diabetes was 1.5 times higher in men than in women. The higher prevalence of diabetes in women is also seen in the general population (Larejani and Zahedi, 2001). In a study by Aziminejad et al. in the Northern, Southern and Razavi Khorasans, the incidence of diabetes in the general population of women was 5.8% and in males was 5.1%. In a meta-analysis study conducted by Haghdoust et al. in 2009, the prevalence of type-2 diabetes in women was higher, and regression analysis showed that the prevalence of type-2 diabetes in TB patients and the prevalence of diabetes among females was a risk factor for increasing pulmonary TB. In a study by Siddiqui et al. (2017) in India, the prevalence of type-2 diabetes in pulmonary TB patients was more common in women. In a study by Mave et al., the prevalence of TB and diabetes in women was 1.5 times that of men. Nonetheless, in the study of Wang et al. in China (2010-2012), the incidence of type-2 diabetes in men was almost twice that of women. These discrepancies may be associated with the methodology, number of participants, general health conditions and /or the geographical variables associated with TB involvement, or diabetes prevalence.

The current study found that the prevalence of type-2 diabetes in illiterate people and those with primary education was higher than that of those with secondary and university education. In the study by Aziminejad et al. in Eastern Iran, the highest prevalence was reported among the illiterate people. In a study by Nickbakht et al. in Babol in 2016 and among TB patients, illiterate and elementary students were more at risk. However, given the high level of education and study power in people with higher education, these people can better respond to health issues and prevent the spread of diseases, especially TB and diabetes.

In this study, the highest prevalence of type-2 diabetes among the patients with pulmonary TB was among homemakers significantly (41.66%). In a study by Rastgari et al. (2014), the highest prevalence of diabetes in women with TB was among the homemakers (57.3%). In a study by Hashemi Benjar et al. (2016) in Zabol, the higher rate of simultaneity of pulmonary TB and type-2 diabetes were reported among the workers, housewives and retired people, respectively. Another study in Tanzania by Faurholt-Jepson et al. (2012) reported the highest incidence of diabetes among TB patients in farmers and fishermen. In Viwantan's study (2012) from India, the highest prevalence of diabetes was among the workers and the lowest was among retired people, and housewives were in the third ranking. As is seen in most studies and in the current research, housewives are at a higher risk for both type-2 diabetes and pulmonary TB. However, due to the large number of hours spent in the house's open space, lack of adequate ventilation and inadequate mobility and exercise, and usually a high-calorie diet can justify this subject.

In the present study, the prevalence of type-2 diabetes among the married couples and those with dead spouses was three times more than single and divorced (23.12% for married and 25.24% for widows/widowers versus 8.06% for single and divorced). This high prevalence can be due to the older age of most married couples and those with dead spouses versus single and divorced people. In the study by Faurholt-Jepsen et al. in Tanzania, the prevalence of type-2 diabetes in married people was twice as high as singles. In the study by Kermansaravi et al. in Zahedan, the highest incidence of pulmonary TB and type-2 diabetes was in married couples and then in those with dead spouses. In Mave et al. (2017) in India, the simultaneity of type-2 diabetes and pulmonary TB in married individuals was three-quarters of the total population of pulmonary TB. However, in the study by Aziminejad et al. in east of Iran, the highest prevalence of diabetes was seen in widows/widowers and divorced people.

In the present study, the highest prevalence of type-2 diabetes among the patients with pulmonary TB was found at the age group of 45-54 years old and 55-64 years old people (39.89% and 39.47% respectively). Moreover, the lowest incidence was in the age group of 25 to 34 years and older than 85 years (7.10% and 8.69%, respectively). In Demlow et al. study (2010), in California, the most common comorbidity of type-2 diabetes and pulmonary TB was in the age group of 45-64 years. In the study by Kermansaravi et al. in Zahedan, the highest prevalence of type-2 diabetes was reported in pulmonary TB patients in the age group of 45-60 years. In another study by Walker and Unwin in England in 2009 among black, white and Asian races, the highest prevalence of type-2 diabetes in pulmonary TB patients was among the age group of 45-64 years. In a study by Po-yen ko et al. (2017), an increase in the prevalence rate of type-2 diabetes in pulmonary TB patients was seen in the age groups over 55 in Taiwan, but unlike our study, the highest prevalence was reported in age group older than 75 years of age. This difference could be due to more effective care and treatment and a higher life quality for these patients in Taiwan, leading to the survival of patients at high ages or may be associated with the different methodology.

In the present study, there was a significant relationship between the prevalence of type-2 diabetes and the age of individuals in patients with pulmonary TB. Moreover, the highest significance was in the age group of 45-54 years. In addition, in the age group 25-34 years, and from 74 years on, the prevalence of type-2 diabetes in people with pulmonary TB was reduced, where the reason for this reduction at younger ages (25-34 years) could be related to lower incidence of type-2 diabetes in this age groups. Moreover, probably at the older ages, many of these people do not survive over the age of 74 years, due to complications caused by the synchronization of pulmonary TB and type-2 diabetes. The timely diagnosis of diabetes and its examination of pulmonary TB can play an important role in prevention of mortality among those with TB and type-2 diabetes (Mave et al., 2017). In Siddiqui study (2017) from India, the prevalence rate of among people with pulmonary TB was higher in the age group 45 years and older. Similar to our results, the highest prevalence rate of type 2 diabetes among TB patients in Kermansaravi study from Zahedan was reported in the age group of 45-60 years and the prevalence rate gradually decreased among those before and after this age group. Stevenson, in his study, grouped people separately by their age group to men and women, and indicated that there were no differences in the incidence of type-2 diabetes in pulmonary TB patients in the corresponding age groups (male and female), and in both genders the incidence of diabetes increased with age (Stevenson et al., 2007).

In the present study, the prevalence of type-2 diabetes in urban areas was approximately 1.5 times higher than rural areas. In the study by Baqayee et al. (2015) in Tehran and Stevenson et al. (2007) in India, the prevalence of diabetes among similar participants was higher in urban areas. The prevalence of diabetes in the general population was also higher in urban areas than in rural areas (Larejani and Zahedi, 2001), which could be related to and the higher risk factors in the urban areas, such as stress, high-fat and high-calorie foods (fast food) and stagnancy.

In the present study, the prevalence of type-2 diabetes in pulmonary TB patients was directly correlated with the increase in BMI, so that in subjects with a BMI greater than 25, it was approximately 2 times higher than that of those less than 18.5 and 18.6-24.99. This results were in accordance with the study by Wang et al. in China, which was conducted in 2013 among 6,382 pulmonary TB patients (Wang et

al., 2013). In Wivanthan et al. study (2012) in India, the incidence of type-2 diabetes increased with the increase in BMI among TB patients. This study revealed a significant correlation between BMI and the prevalence of diabetes in pulmonary TB patients. Moreover, those with a BMI higher than 24.99 (including overweight and obese subjects) were 2.6 times more likely to have type-2 diabetes than those with low BMI and thin profile. According to the results of this study, one of the factors contributing to the increase in the prevalence of TB could be the increasing prevalence of type-2 diabetes. According to the report by International Federation for Diabetes, people with diabetes were 171 million people in 2000 that would reach 366-440 million people in 2030, and three-quarters of the patients with type-2 diabetes will live in less developed countries. In the absence of suitable interventional issues, the increasing trend of type-2 diabetes will increase the prevalence of pulmonary TB and related complications in Iran.

#### Conclusion

According to the results of this study, a significant number of TB patients suffered from concomitant type-2 diabetes and this increasing in the prevalence rate was higher in some variables such as female gender, higher BMI and higher age groups. This showed that diabetes screening among the patients with pulmonary TB is a vital and effective measure and this could help those simultaneously suffering from these two diseases. Moreover, it is recommended that in health education and tuberculosis screening programs, type-2 diabetes should be considered as a major contributor for increasing the risk of TB incidence.

#### Acknowledgment

This paper was the result of a part of the first author's dissertation entitled "The prevalence of type-2 diabetes among pulmonary TB patients in Mazandaran during 2013-2017," conducted with the support of Ilam University of Medical Sciences with the research project No. IR.MEDILAM.REC.1397.117. We appreciate all those who contributed in the study.

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