

PAPER DETAILS

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RESEARCH ARTICLE

A Systematic Review and Data Analysis on the Epidemiology of Tuberculosis and Diabetes Mellitus

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ABSTRACT

Objectives: This study aims to analyze epidemiological data that diabetes leads to increased susceptibility to initial tuberculosis infection or if diabetes leads to increased progression from latent tuberculosis to active tuberculosis.

Methods: A simplified MEDLINE search method has been used in this study. The PubMed's Clinical Queries, which have "research methodology filters" to study the patterns, causes, and clinical effects of health and the disease conditions in defined populations, were explored and extracted.

Results: Using the keyword-based queries in PubMed/ Medline and Embase, 38 relevant published studies were collected from 1970 to 2020. Published studies from the literature search were combined with the observational studies of summary statistics which can further be used for clinical trials.

Conclusion: The high prevalence of diabetes is a factor that increases the incidence of tuberculosis and is considered in the fight against tuberculosis worldwide. There have been many significant recent advances in knowledge regarding diabetes-associated tuberculosis's epidemiology, management, and control. *J Microbiol Infect Dis* 2021; 11(4):191-200.

Keywords: *Mycobacterium tuberculosis*, Diabetes, Epidemiology, Review analysis

INTRODUCTION

The relation between tuberculosis and diabetes has been known for centuries. Presently, tuberculosis prevalence remarkably decreased in high-income countries. However, occurrence remains high in countries with high rates of diabetes, the high commonness of malnutrition, and mass living conditions or insufficient tuberculosis control infrastructure. In addition, many studies showed that diabetes is an important risk factor for tuberculosis and might affect the disease presentation and treatment response.

Moreover, tuberculosis might induce glucose intolerance and inflaming glycaemic control in

people with diabetes. Also, the drugs used in treating tuberculosis disease interact with oral anti-diabetic drugs [1]. In recent years, many important advances have been made in elucidating the epidemiology of diabetes-related tuberculosis and in methods to diagnose, treat, and prevent tuberculosis and reduce mortality in tuberculosis/diabetes co-infected patients.

In sub-Saharan Africa, tuberculosis is a serious problem and is the leading cause of death in diabetic people. Diabetes is one of the paramount factors in the development of active and latent tuberculosis. Drug-resistant tuberculosis is a severe yet unsolved public

health problem, especially in Southeast Asia, Africa. This study attempted to evaluate this primary source of information from where we collected already available data of the patients. This paper highlights the related findings in tuberculosis and diabetes co-infection epidemic, particularly globally.

Past studies are important in order to understand the present study. An early study reported in Germany in the year 1950s, where diabetic patients with tuberculosis treatment have been evaluated, after the completion of post-treatment of prophylaxis with isoniazid for 6-24 months, reported the lower rates of repetition in the intervention group [2]. Early studies showed that glucose intolerance occurs in the background of tuberculosis without diabetes when changes in carbohydrate metabolism during the primary attack of tuberculosis with enhanced insulin secretion and signs of respective insulin deficiency with persistent hyperglycemia as a forerunner to severe diabetes. Some specific tuberculosis studies showed the production of anti-insulin antibodies in mice, and mycobacterial proteins directly cause insulinitis, hyperglycemia, and diabetes, which predict mainly autoimmune destruction of pancreatic islets in Type-1 diabetes.

In the previous, the studies conducted were expensive as well as time-consuming. These studies were problematic because of the absence of randomized details regarding interventions. Some studies showed several developments of severe diabetes in patients with pulmonary tuberculosis, relatively increased in the disease duration with deficiency associated with the higher secretory function of the insular pancreatic apparatus, which decreased its functional reserves [3]. In 1995, a study reported that pulmonary tuberculosis might predispose to glucose intolerance or endocrine abnormality [4]. It was found that 49% of the cases with pulmonary tuberculosis had bad glucose intolerance, which indicated that the patients with pulmonary tuberculosis should be screened positive with glucose intolerance.

Countries have different control strategies for tuberculosis. For example, a survey of State Tuberculosis Control Laws and Regulations showed that the US states differ in their approach to controlling tuberculosis [5]. The major goal of tuberculosis programs is to

eliminate tuberculosis by appropriately treating persons infected with tuberculosis, safeguard the confidentiality and civil liberties of the persons who have tuberculosis, and protect them from unlawful discrimination because of their disease. Keeping in mind the epidemiology co-existence of tuberculosis/diabetes, we have carried out the data analysis of the two diseases.

METHODS

Search strategy

The information was retrieved from the literature sources using specific PubMed/MEDLINE and Embase queries. The search results were not limited to abstracts published in English. The abstracts were downloaded for further information extraction, and the full articles were studied that met the inclusion criteria. The articles retrieved using different queries are tabulated in tables (Table 1).

After searching the published relevant articles, population-based studies reporting the incidence and prevalence of tuberculosis and diabetes were evaluated. Studies were considered population-based if they employed a sampling method meant to represent the entire population and were completed in a defined geographical area of known population size. The studies were excluded if they did not provide an estimation of incidence or prevalence and the collected data before 1997 and whether the study reported non-original data (i.e., reviews, letters, or editorials).

Data collection

For this epidemiological study with respect to data analysis, PubMed/Medline and Embase (Excerpta Medica Database) were searched to identify all relevant published data from 1970 to 2020 on the prevalence of "*Mycobacterium tuberculosis*" pathogen for causing tuberculosis in patients with diabetes and vice versa worldwide. The search strategy included "tuberculosis", "diabetes", "anti-tuberculosis", "hyperglycemia", "epidemiology" and "data analysis".

A total of 2,304 studies from MEDLINE and EMBASE were collected, which includes all the search strategies to fulfill our research criteria. Duplicated articles, studies without population-based or incidence data were excluded, studies with abstracts only were

excluded, only full-text articles were scanned. Thus, we finally included thirty-eight studies related to our study.

Data Extraction

Data extraction was done with each adult population-based cohort study published from 1997 till 2020, where prevalence could be calculated from available data and then taken for consideration. We have excluded the studies that presented estimation based on small subsets of a population, e.g., hospital outpatient, clinical patients. We did not exclude the selected populations that were considered to be illustrated in the general population of a particular geographical area. A complete list of inclusion and exclusion criteria is given in (Figure 1). After reading the articles, the information was extracted from the publications based on the year, country, author, time frame, age range, diagnostic criteria, data source, prevalence date, number of cases, gender, population size, and the potential replicating of data.

Data Analysis

It was used a graphical plot to show results from individual studies based on year-wise analysis and provide graphical information about estimates of the statistical significance of the cited publications (Figure 2).

Table 1. Number of citations retrieved using the various search terms

PubMed/MEDLINE and Embase Search Query	Number of abstracts
((Tuberculosis) AND (Diabetes))	1941
((Pharmacokinetics) AND (anti-tuberculosis) AND (enzymes))	69
((Tuberculosis therapy) AND (Diabetes) AND (hyperglycemia))	168
((Tuberculosis) AND (Diabetes) AND (hyperglycemia) AND (epidemiology))	126

RESULTS

The data of tuberculosis/diabetes was combined yearly in a list (Table 2).

Table 2. Tuberculosis and Diabetes stratified yearly since the year 1997 to 2020.

Year of Publication	Sum of citation per year	Mean citation for each year
1997	1263	1263
2005	69	69
2006	258	258
2007	489	244.5
2008	1519	1519
2009	189	189
2010	622	311
2011	108	108
2012	220	73.3
2013	245	61.25
2014	120	30
2015	40	13.3
2016	95	31.6
2017	328	54.6
2018	9	9
2019	40	13.3
2020	6	6

Calculations:

Score= (Sum of citations of publications/Number of publications)/number of years passed.

Incidence studies of tuberculosis with known blood sugar status:

The studies used incidence based on the hospital or clinical records, administrative databases, and/or surveys of physicians to estimate incidence within the geographical boundaries of their service area from the literature search. The major parts of these studies were prevalence estimates based on systematic reviews.

Prevalence studies

In total, 38 studies were examined for the prevalence of tuberculosis with diabetes. Eight studies were from the USA, eight studies China, four studies Korea, thirteen studies different Asian countries, two studies African countries, and three from global population studies included in this study (Table 3).

Risk factors for tuberculosis/diabetes comorbidity

The risk factors associated with tuberculosis/diabetes comorbidity were heterogeneous. The studies used different measures to analyze the factors coalition with the disease. Some studies reported tuberculosis/diabetes risk consortium factors using odds ratio, relative risk ratio, or hazard ratio. Conversely, other studies did not report either interrelation or risk factors for tuberculosis/diabetes co-existence. This might be due to that the studies did not have enough sample size, and almost all studies mentioned neither in their objective nor in the controlled part about the risk factors of tuberculosis/diabetes comorbidity.

Numerous studies concluded that both males and females [6-10] of all ages were at high risk for tuberculosis/diabetes comorbidity regarding socio-demographic and socioeconomic factors. At the same time, men were more likely to develop tuberculosis/diabetes comorbidity than women [11]. Furthermore, 22 studies reported that older aged people are mostly the ones who are at increased risk of tuberculosis/diabetes comorbidity [8-28].

When we look at the behavioral risk factors, illegal drug consumption and inactive lifestyle were among the most reported behavioral factors related to tuberculosis/diabetes comorbidity [11,29]. In addition, smoking [7] and being an alcoholic [15] are reported as increased risk factors for tuberculosis/diabetes co-existence. On the other hand, practicing a good active lifestyle and various frequent outdoor activities were less behavioral risk factors for tuberculosis/diabetes comorbidity [19].

Body mass index (BMI), whether higher or lower, human immune-deficiency virus (HIV)

DISCUSSION

Diabetes is the most potent risk factor for tuberculosis. Diabetes co-infection with tuberculosis collate with diabetes

hyperglycemia, anatomy of which recorded in diabetes prevalence countries. March 2019, WHO declared a new intent to end tuberculosis in the world by 2030. In many developing countries where healthcare resources are limited, diabetes and tuberculosis comorbidity is a public health concern. co-infection, bodyweight loss or gain in body weight, hypertension, and hyperglycemia were reported as associated factors for tuberculosis/diabetes comorbidity [7,8,11,17,18]. Pre-existence as well as long duration of diabetes [8], poor glycemic control reported during tuberculosis diagnosis, patients with liver cirrhosis [7], and high blood pressure [17] were identified as some of the main reasons for increased risk factors for the development of tuberculosis/diabetes comorbidity. Diabetes with positive [11] and negative HIV conditions was linked and increased risk factors for tuberculosis/diabetes comorbid condition, whereas HIV co-infection and malnutrition were also suggested as low-risk factors for tuberculosis/diabetes comorbidity [10]. On the other hand, being extra-pulmonary tuberculosis (EPTB) case was reported as a low-risk factor for tuberculosis/diabetes comorbidity [28].

In some studies showed that direct contact with the tuberculosis patient within the family was reported as an increased risk factor for tuberculosis/diabetes comorbidity. Being a prisoner was associated with tuberculosis/diabetes comorbidity [11]. TBDM patients were more expected to die from tuberculosis/diabetes comorbidity [28]. On the other hand, retained in some institutions (prisons, shelters, orphanages, and psychiatric hospitals) were reported as low-risk factors for tuberculosis/diabetes comorbidity [28].

According to World Health Organisation (WHO) treatment guidelines, tuberculosis suspected patients should be treated with a four-drug rule regimen, which is a breakup in a starting two months intensive phase, i.e., isoniazid, rifampicin, ethambutol, pyrazinamide, and a four months two drugs continuing phase (isoniazid and rifampicin). In comparison, the patients with poor response and evidence of drug resistance are advised quickly to initiate treatment with second-line drugs. In this study, potential interactions with second-line drugs are not reported.

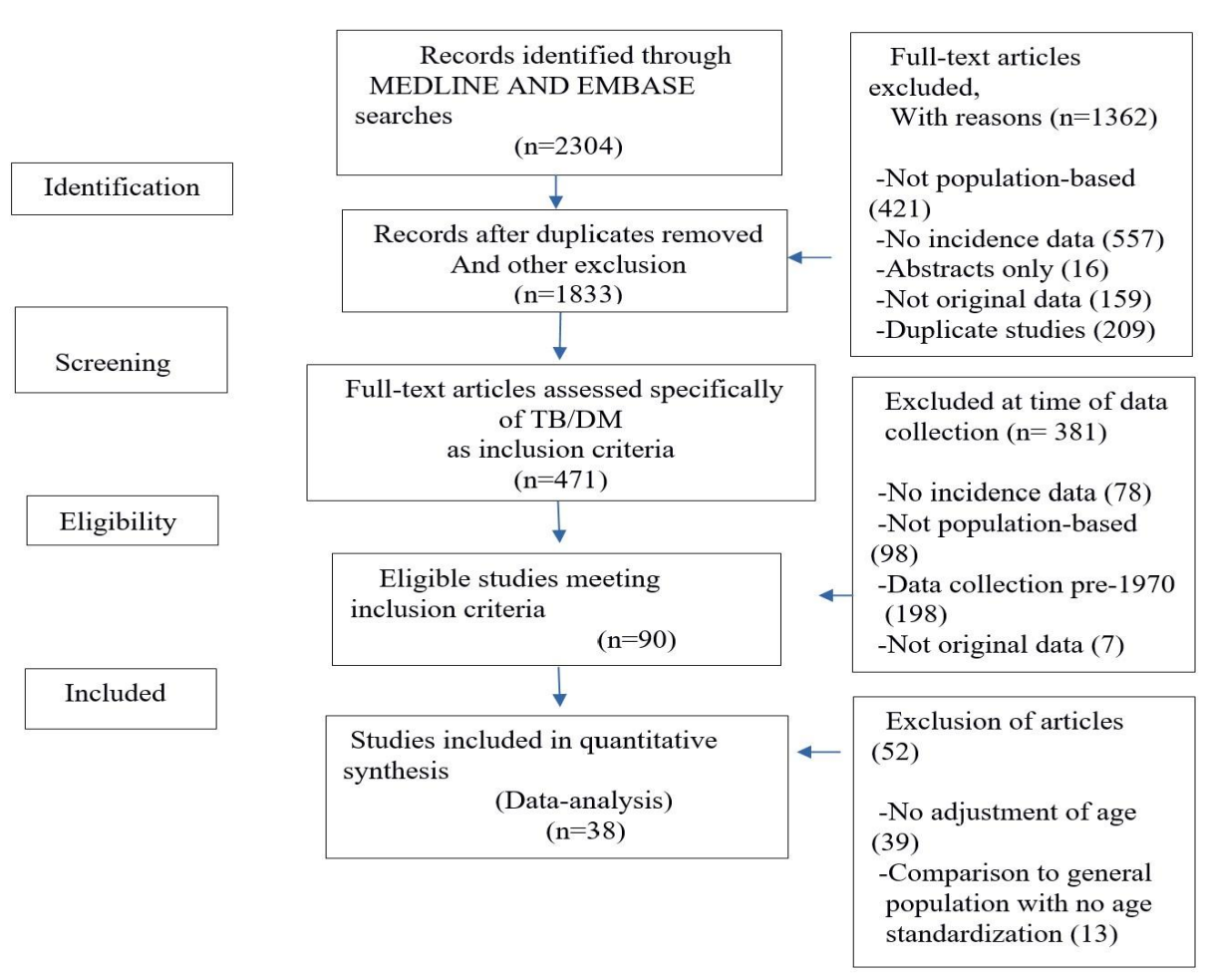


Figure 1. Study selection criteria via flow chart.

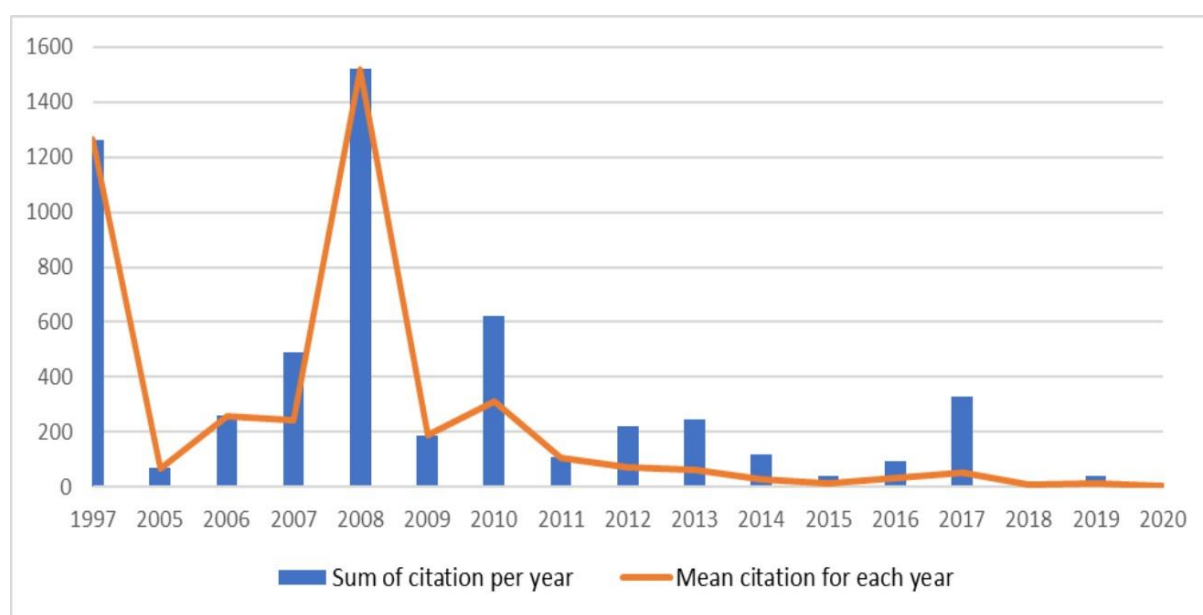


Figure 2. Year-wise citations of Tuberculosis and Diabetes cases (1997-2020)

Table 3. Studies were examined for the prevalence of TB with DM.

S.No	Author	Publication year, country	Time frame and age range	Inclusion Criteria	Prevalence date	Number of cases	Gender	Population size (Millions)
1.	Ariel Pablos-Mendez	1997, California, USA	1997, all ages	Hospital, clinic chart review	1991	5290	Both	32.2
2.	Lawrence Broxmeyer	2005, US	1934-2004, all ages	Review	1934-2004	not specified	Both	295.5
3.	Nijland et al	2006, Jakarta, Indonesia	2006, all ages	clinic chart review	2006	36	Both	229.3
4.	Alisjahbana et al	2007, Indonesia	2000-2005, all ages	Hospital, clinic chart review	2000-2005	737	Both	232.4
5.	Nigel Unwin	2007, India	2000, all ages	"administrative data	2000	116000	Both	1183.2
6.	Christie Y. Jeon	2008, (USA)	1965-2007	clinic chart review	1965-2007	17698	Both	304.1
7.	NA	2009, global	2009, all ages	clinic chart review	2009	36	Both	Not specified
8.	Rovina Ruslami	2010, Indonesia	2009, all ages	administrative database, chart review	2009	36	Both	241.8
9.	A. D. Harries et al	2010, Paris, France	May 2009-August 2009	age-adjusted, quantitative, observational studies	May 2009-August 2009	not specified	Both	104.6
10.	Christopher Dye	2011, India and Korea	1998-2008, all ages	administrative data	1998-2008	not specified	Both	1250.3
11.	Claudia Caroline Dobler	2012, Australia	2001-2006, all ages	administrative database, clinical chart	2001-2006	6276	Both	19. 855 283
12.	Diana I. Gomez	2012, South Texas	2012, all ages	clinical chart, review	2012	not specified	Both	313.9
13.	Liaqat Ali Chaudhry	2012, Saudi Arabia	2003-2010, all ages	clinical chart, Review	2003 and 2010.	1388	Both	29.2
14.	Lyudmila Boyanova	2013, Bulgaria(USA)	2009-2013, all ages	Review	2009-2013	not specified	Both	7.28
15.	Aylin Babalik	2013, Istanbul, Turkey	2013, all ages	clinic chart review	2013	70	Both	13.658
16.	V.	2013, South	2007-2013,	Hospital, clinic	2007-2013	245	Both	210

	Viswanathan	India	all ages	chart review				
17.	Boillat-Blanco et al.	2013, Kinondoni District, Taiwan	2013, all ages	Hospital, clinic chart review	2013	250	Both	1.357 4
18.	Fengling Mi	2014, Beijing, China	2011-2012, all ages	clinic chart review	2011-2012, all ages	621	Both	13
19.	M. J. Magee et al.	2014, Georgia	2009-2012, all ages	administrative database, clinic chart review	2009-2012	1325	Both	10.1
20.	M. J. Chang et al.	2014, Korea	2014, all ages	administrative database, clinic chart review	2014	54	Both	50.7
21.	Marit Eika Jørgensen	2014, Denmark	1990-2013, all ages	clinical trial database	1990-2013	4959	Both	5.6
22.	Yu-Cheng Chen	2015, Taiwan	2000–2010, all ages	hospital/clinic chart review, administrative data	2000–2010	2492	Both	1
23.	Saurabh Mehta	2015, Andhra Pradesh, India	2012-2013, all ages	clinic chart review, administrative data	2013	304	Both	276
24.	Wang	2015, Taiwan (China)	1996-2010, all ages	Mailed survey, hospital/clinic chart review, administrative data	2010	151571	Both	234,920,000
25.	Nathella Pavan Kumar	2016, India	2016, all ages	Clinical charts, Graphs plot"	2016	57	Both	1324.5
26.	Malabika Sarker	2016, Bangladesh	2016, all ages	Hospital, clinic chart review	2016	1910	Both	158
27.	Hsien-Ho Lin	2016, Taiwan	2016, all ages	administrative database	2016	38 263	Both	23.6182
28.	Yu-Cheng Chen	2017, Taiwan	2000-2010, all ages	Hospital, administrative database, clinic chart review	2000-2010	9833	Both	23.6745 460
29.	Zheng et al.	2017, China	2017	administrative database, clinic chart review	2017		Both	1386.4
30.	Rami H. Al-Rifai	2017, USA	1945-2015, all ages	Database review	1945-2015	5,84,72,375	Both	325.1
31.	Mahteme Haile	2017, Asia, North America,	1900-2016,	Database review	1900-2015	1845	Both	Not specified

	Workneh	Oceania	all ages					
32.	Hemant Deepak Shewade	2017, USA	1996-2017, all ages	electronic databases	1996-2017	2326	Both	325.1
33.	Song Yee Kim	2017, Seoul, South Korea	2010-2012, all ages	Patients Registry	2010-2012	1044	Both	9.78
34.	Fasil Wagnew	2018, African and Asian countries	1980-2017, all ages	clinic chart review, administrative data	1980-2017	23068	Both	Not specified
35.	Jean Joel Bigna	Worldwide	1986-2017, all ages	Administrative database, Plots	Jan 1, 1986, and June 15, 2017	2-3 million	Both	230
36.	Mtabho et al	2019, Tanzania	2019, all ages	hospital/clinic chart review, administrative data	2019	40	age 18 years, Both	58.005 463
37.	J. E. Golub	2019, Korea	1997-2000, all ages	hospital/clinic chart review, administrative data	1997-2000	1 267 564	Both	5.126 436
38.	Jianming Wang	2020, Jiangsu Province, China	2016-2018, all ages	hospital/clinic chart review, administrative data	2016-2018	14 869	Both	14,393.

The prevalence of diabetes is estimated to increase from about 382 million in 2013 to around 592 million in 2030. In 2013 about 80% of diabetes patients lived in developing countries where healthcare resources were limited. The more significant concern is that about 48% of the patients with diabetes were undiagnosed. Diabetes patients amid in low-income countries are increasing in number; thus, tuberculosis/diabetes comorbidity could inevitably increase. This might hamper the WHO target to decrease global tuberculosis incidence by 90% or less than 10 cases per 100,000 populations in 2035. Furthermore, it is more difficult for the world's long-term vision to eliminate tuberculosis as a public health concern by reducing tuberculosis incidence to less than 1 case per million of the population by 2050. The study collected here has its pros and cons. This study included many studies covering almost all worldwide data, which is the pros of this study. Cons of this study are the exclusion of studies written in language rather than English. Inclusion study criteria

which were taken here accommodated in the studies associated/risk factors of tuberculosis/diabetes comorbidity; therefore, the effect of excluding languages other than English written articles as of which findings of an empirical investigation grab for a variety of populations would be minimal. Some reported studies showed the population and gender of patients associated with tuberculosis and diabetes. The studies were observational studies and descriptive studies. Thus, we have used prevalence and incidence rate as our total effort to relate it with what the reviewed articles reported worldwide. This study is combined with the data analysis of summary statistics which were frequently used in citations. Our main objective was to understand the global epidemiology of tuberculosis/diabetes comorbidity having a less moderate risk of bias in a more comprehensive manner.

Conclusion: However, although they have appeared in limited numbers and are supportive, they have come at what, for

diabetics, has been a painfully slow rate. Latent tuberculosis infection occurs when tubercle bacilli are in the body; the immune system keeps them under control. Nevertheless, suppose the immune system weakens in people with high diabetes ubiquity. In that case, tuberculosis can become active, and during its active state, it can cause the death of tissue in the organs they infect. We collected the evidence from an increased risk of tuberculosis patients with diabetes despite the variations in study design, with joint founders to control severe disease and control it with the exposure of its outcome of the burden of tuberculosis geographical boundaries. Data analyses which showed the human studies of different age groups and other factors are consistent with rising information on the biological mechanisms which may affect the host immune response to tuberculosis, including hyperglycaemic conditions. Among various factors that contributed to internet information exploring the data are: using a web browser and databases connected to web browser front ends.

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