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The correlation between tuberculosis and diabetes incidence and the impact of mass migration on the development of tuberculosis and drug-resistant tuberculosis on the example of India and England

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Abstract

Introduction: Tuberculosis is still a major health concern around the world, especially in developing countries with very large populations. Diabetes may be responsible for the progression of *Mycobacterium tuberculosis* infection. According to the research of some authors, the development of an active form of tuberculosis is associated with the earlier

development of diabetes, which is called the epidemic of the 21st century due to the very large number of patients around the world and worrying predictions of the incidence of diabetes for the upcoming years. Diabetes May also predispose to drug-resistant tuberculosis as well as worse and slower anti-tuberculosis treatment effects. In European countries where the prevalence of drug-resistant and TB is Lower than in developing countries, most cases of tuberculosis have been reported among immigrants.

The aim of the study is to analyze the current epidemiological situation of tuberculosis, multi-drug resistant tuberculosis and diabetes in Great Britain (with particular attention directed to England) and in India in correlation with the influx of migrants from India to Great Britain.

Materials and method: The data used in this analysis come from the Global Tuberculosis Reports published by The World Health Organization and National Diabetes Audit Reports published by The Health and Social Care Information Center, as well as from Rother publications made available in 2001-2019.

Results: There has been a significant increase in the incidence of diabetes in England and India in recent years, the incidence of tuberculosis in England Has been decreasing, while in India it Has remained more or less stable. An increase in the incidence of drug-resistant tuberculosis was observed in the population of India and in the population of migrants of Hindu origin in England, while the Total number of MDR cases in England Romains more or less stable with a downward trend in 2011-2014 and slightly rising in 2015-2017.

Conclusions: Due to the strong association between diabetes and tuberculosis, the probable association of diabetes and multi-drug resistant tuberculosis, and the increasing incidence of diabetes, the control of TB incidence may be disturbed, and there is a risk of an increase in the incidence of MDR tuberculosis. This phenomenon can threaten not only developing countries, where tuberculosis is more common than in other regions of the world, but also highly developer countries that akcept large numbers of migrants.

Keywords: tuberculosis; diabetes; MDR; migration;

Introduction

Despite the strategies implemented over the last several years to reduce the occurrence of a tuberculosis pandemic, it remains a serious public health problem. It is considered that *Mycobacterium tuberculosis* is the most common cause of death from a single infectious agent. In 2017, about 10 million pe ople developer tuberculosis, of which 27% of cases were in India. Tuberculosis has contributed to the deaths of 1.3 million HIV-negative patients and 300,000 HIV-positive patients worldwide [1]. The fight against high tuberculosis incidence is based on the elimination of factors that favor infection, such as smoking, drinking alcohol, air pollution, overcrowding, transmission of infection from the source case. Factors causing progression of *M. tuberculosis* infection to active disease are usually conditions that weaken the immune system, e.g. HIV infection, malnutrition, alcoholism, diabetes [2]. Although HIV infection is considered to be the strongest risk factor for the development of active tuberculosis [3], numerous studies indicate that the high and steadily increasing rate of diabetes in the world can predispose to the development of tuberculosis more than human immunodeficiency virus infection [4].

It is estimated that 451 million people (aged 18-99) worldwide suffered from diabetes in 2017, 374 million people had abnormal glucose tolerance, and nearly 21.3 million newborns were expected to be born by mothers who had hyperglycemia during pregnancy [5]. In developing countries with low incomes and large populations such as India or China, there has been a rapid increase in the number of people with diabetes. At the same time, these are countries where tuberculosis is endemic and is more common than in other populations [6]. Poor glycemic control can cause a decrease in interferon gamma production, impaired macrophage function [7], development of pulmonary microangiopathy and renal failure [8], which increases the risk of tuberculosis in diabetics.

The abnormal blood glucose level also affects the course of anti-mycobacterial therapy - the response to initial intensive four-drug therapy is slower [6]. Some studies have shown a higher risk of tuberculosis treatment failure in patients with diabetes and have suggested the possibility of up to six times higher risk of tuberculosis death in patients with diabetes [3], as well as an increased risk of developing multi-drug resistant tuberculosis (MDR) [9]. MDR / RR-TB is widespread worldwide, with a total of around 480,000 cases in 2014 [10], and in 2017 24% of MDR cases were registered in India [1].In European countries

belonging to the EU, the incidence of tuberculosis is low, on average 73.4% of MDR-TB cases were registered among immigrants [10].

The aim of the study is to analyze the current epidemiological situation of tuberculosis, drug-resistant tuberculosis and diabetes in India and Great Britain, with particular emphasis on England in the years 2011-2017 including correlation between diabetes and tuberculosis occurrence and migration of the Indian population to the UK.

Materials and method: the data used for epidemiological analysis come from data provided by WHO, British and Indian government institutions and scientific societies for the control of tuberculosis and diabetes in the world, as well as data available in articles shared on the PubMed website.

Results

The analysis show significant increase in the number of MDR-TB cases in India. Tuberculosis incidencerate in India is variable, there is no downward trend, but nevertheless an increase in all cases in recent years is noticeable (Diagram 1).

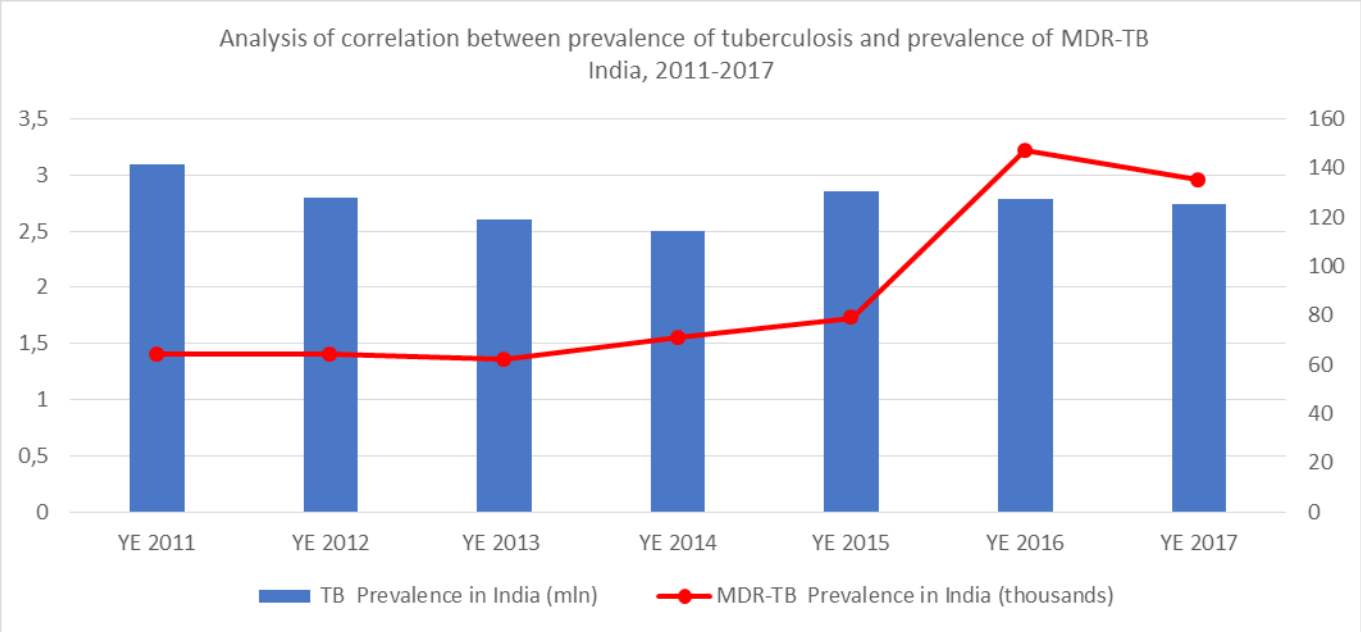

Diagram 1. Analysis of correlation between prevalence of tuberculosis and prevalence of MDR-TB. India, 2011-2017

India has show an increase in the overall number of TB cases in correlation with the increase in the overall number of diabetes cases in 2013–2015, suggesting that diabetes are susceptible to TB infection [Diagram 2].

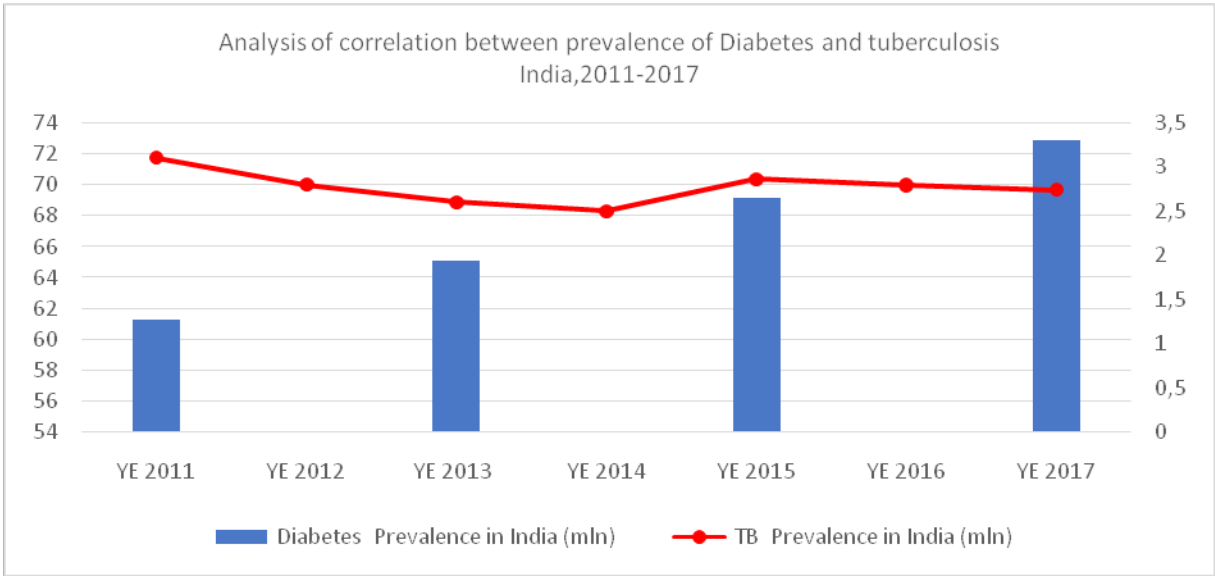

Diagram 2. Analysis of correlation between prevalence of diabetes and tuberculosis. India,2011-2017

In England, an increase in the incidence rate and number of cases of diabetes Has been demonstrated with a simultaneous reduction in the number of tuberculosis cases [Diagram 3].

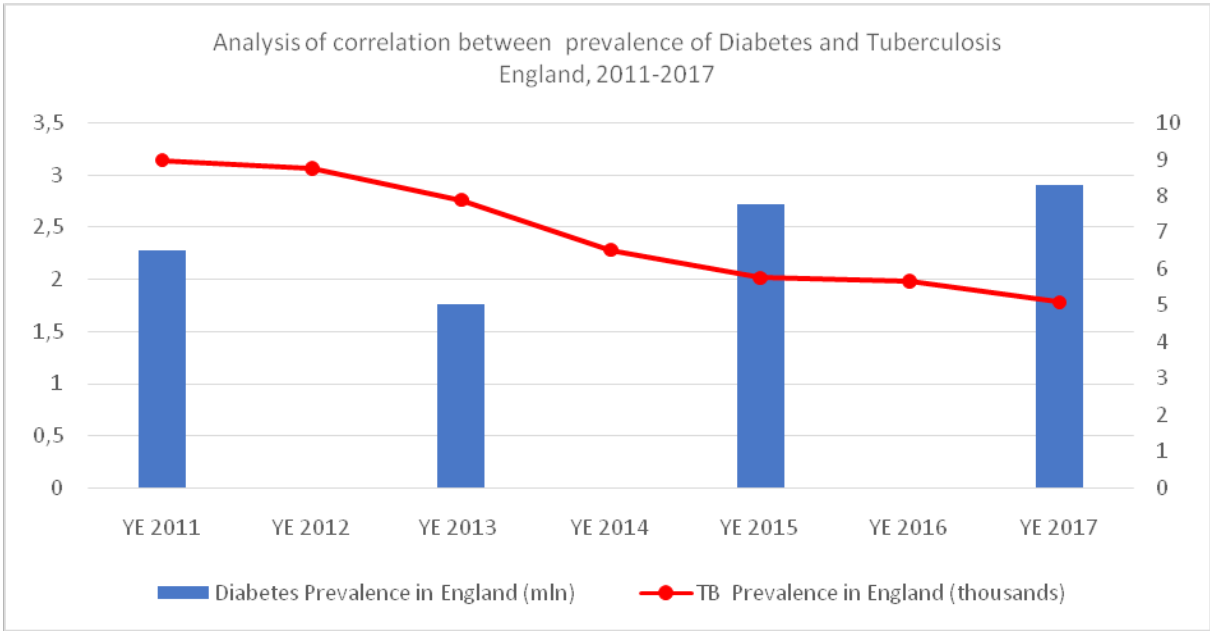

Diagram 3. Analysis of correlation between prevalence of diabetes and tuberculosis. England, 2011-2017

Comparison of the results of the analysis of both countries: the relationship between the occurrence of tuberculosis and diabetes is definitely more visible in the case of India.

The analysis below show that for years, the vast majority of the Total number of TB cases in England were people outside of Great Britain. [Diagram 4.]

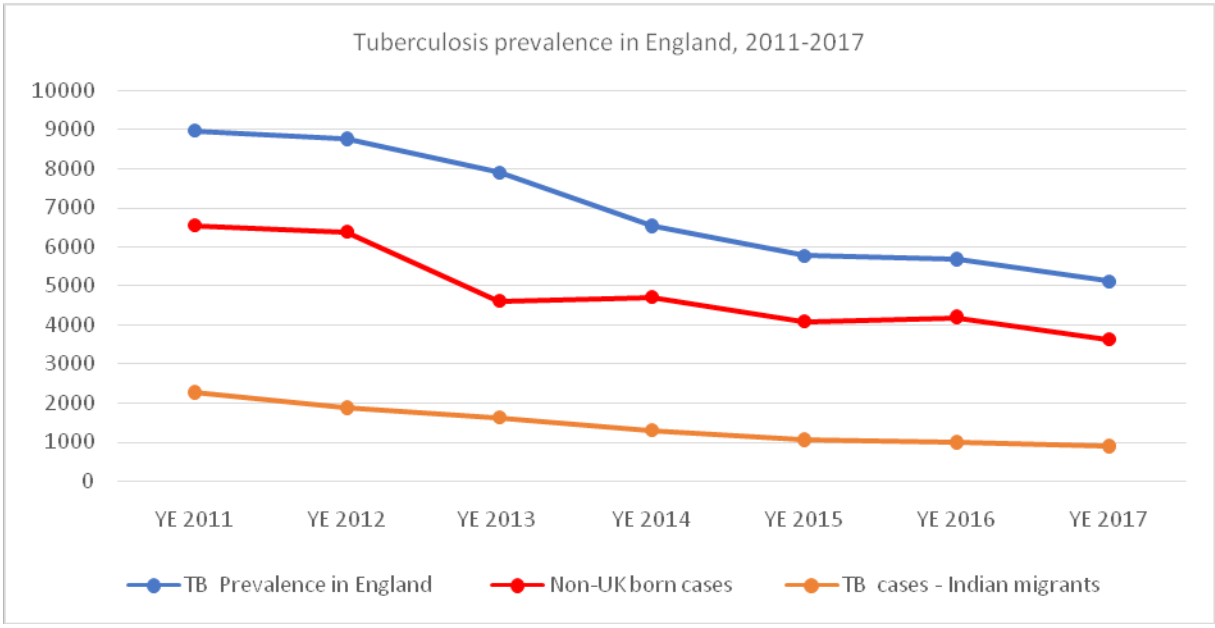

Diagram 4. Tuberculosis prevalence in England, 2011-2017

The data presented show that, over the years, an average of 25% of MDR-TB cases have been detected in migrants from India in England. An increase in the prevalence of MDR-TB cases in England was demonstrated in 2015-2017. [Diagram 5.]

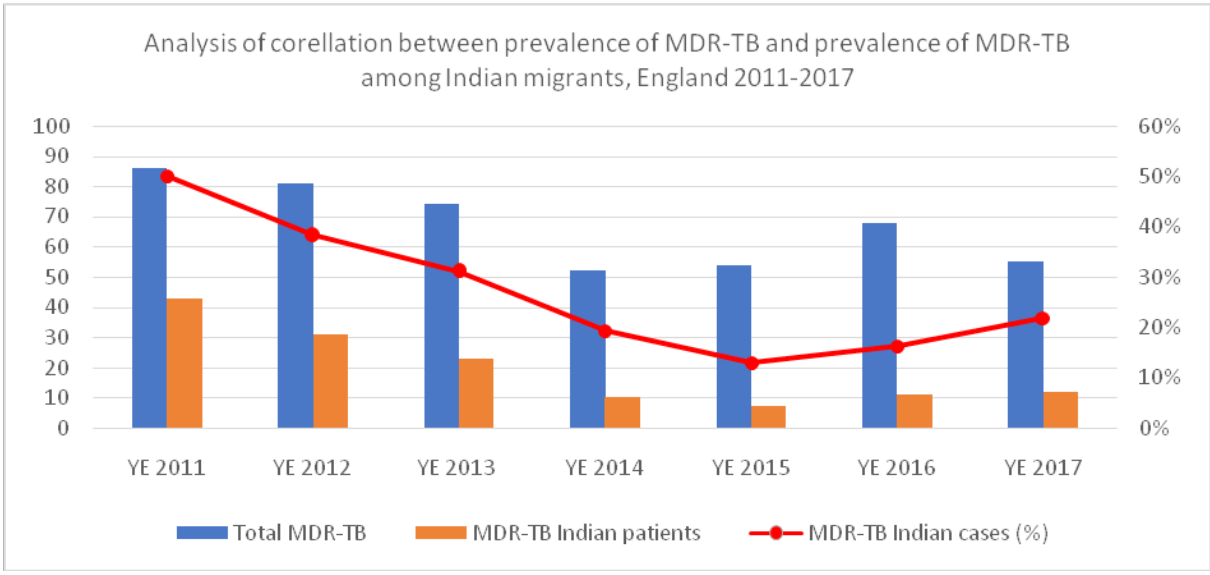

Diagram 5. Analysis of corellation between prevalence of MDR-TB and prevalence of MDR-TB among Indian migrants, England 2011-2017

The analysis showed a steadyt increase in the number of immigrants from India to the UK. England as a destination is particularly popular among migrants, with little influx of immigrants over the years in other Kingdom countries. [Diagram 6.]

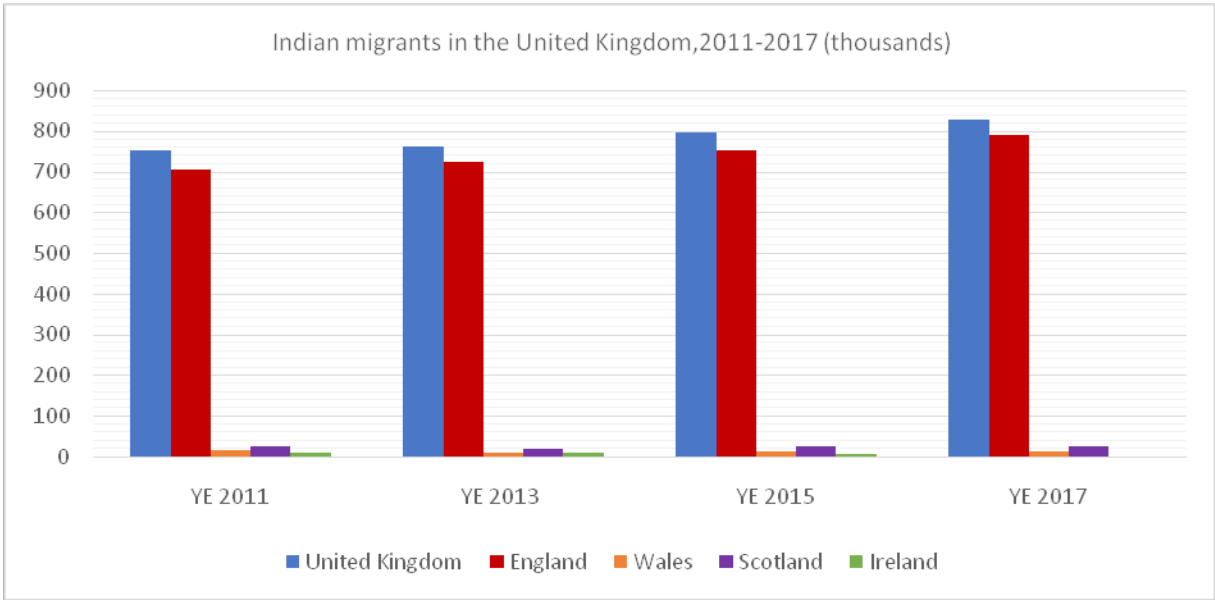

Diagram 6. Indian migrants in the United Kingdom, 2011-2017 (thousands)

The data presented show that over the years, the largest number of tuberculosis cases Has been reported in England. Cases of tuberculosis in England are counted in thousands compared to hundreds or fewer cases in other countries of Great Britain. [Diagram 7.]

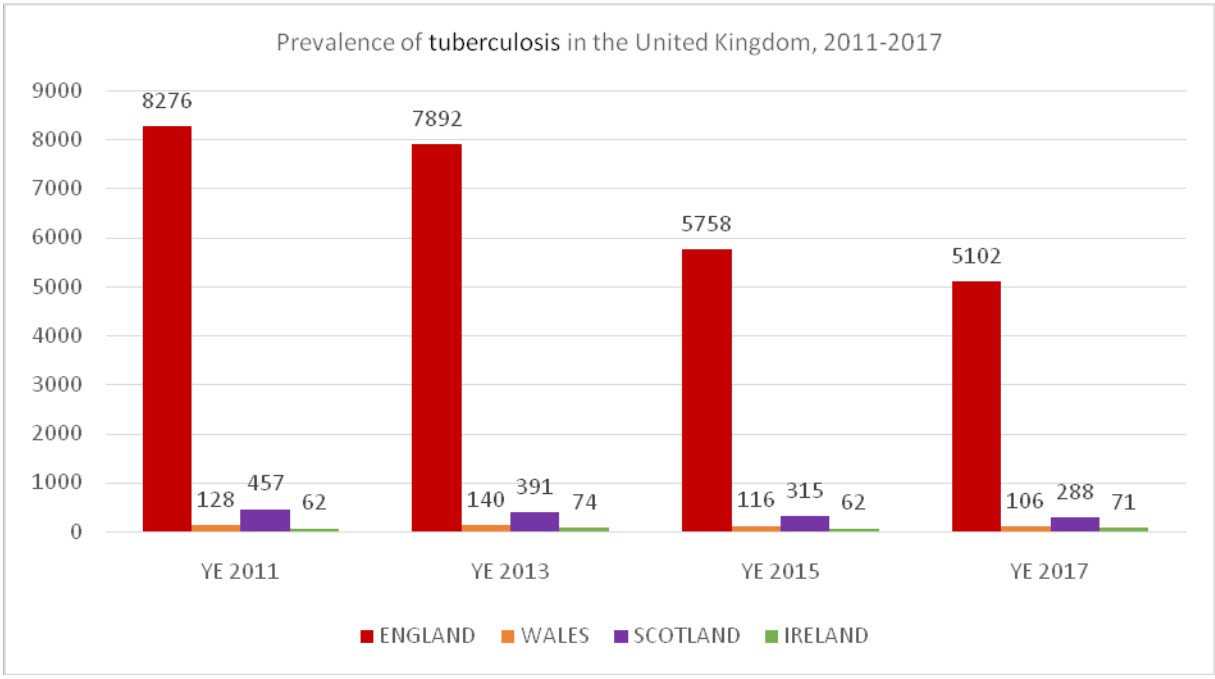

Diagram 7. Prevalence of tuberculosis in the United Kingdom, 2011-2017

Discussion

The connection between tuberculosis and diabetes has been documented many times. It is still unclear, however, whether only diabetes predisposes to active tuberculosis or whether tuberculosis leads to the development of diabetes. It is only certain that both these diseases tend to occur together [19] and this is most evident in developing countries, such as India, which in this analysis was treated as a representative of countries belonging to the group of countries with a large population and medium or low income [6]. A high increase in the incidence of diabetes is associated with rapidly progressing socioeconomic change, industrialization and urbanization [20], despite this society is still characterized by low level of health awareness, unavailability of drugs and trained medical personnel [21]. The result is poor diabetes control in India, where the average hemoglobin A1c is 9.0% [22]. Numerous studies emphasize the specifics of diabetes in India - it mainly affects young people with low BMI, rural residents are increasingly sick [20,21]. These data are worrying when compared with the results of independent studies, which state that the relationship between tuberculosis and diabetes is more pronounced in young people, people with poor glycemic control (risk ratio 1.39, 95% CI 1.18-1.63 glycated hemoglobin [HbA1c]) [7], patients with type 1 diabetes and patients treated with insulin [3]. This interaction between infectious and non-infectious diseases should be a challenge for global healthcare. It seems that due to the epidemic of

diabetes, the control of tuberculosis in countries with a high burden of this disease may be at risk [23]. Model studies have estimated that a 25% increase in the incidence of diabetes worldwide would increase the incidence of tuberculosis by 8% by 2035 [19].

The connection between diabetes and tuberculosis is definitely less visible in the analysis of the incidence of these diseases in England [diagram 3], which in this publication was treated as a representative of a large European region and part of a country belonging to highly developed countries, with efficient health protection. A poorly visible correlation may be the result of better glycemic control than in developing countries - in England and Wales a satisfactory HbA1c level of 7.5% or less was reported in 27.3% of patients with type 1 diabetes and 64.8% of patients with type 2 diabetes and HbA1c less than 6.5% in 7.5% of patients with type 1 diabetes and 26.4% of patients with type 2 diabetes [24]. In addition, the United Kingdom has introduced diabetes control and eradication programs such as cohort reviews, active tuberculosis screening. These additional measures were necessary due to the higher incidence of tuberculosis in the UK than in other high-income European countries and more than four times higher incidence of tuberculosis than in the US [25]. What is more, the relationship between tuberculosis and diabetes does not have to be simultaneous - according to presented studies, hypothetical slow but systematic increase in the incidence of diabetes may contribute to a noticeable increase in the incidence of tuberculosis in about 10 years or may contribute to difficulties in its reduction [19, 23]. Continuous increase in the incidence of diabetes is visible in England and the whole of Great Britain [14], and additional concern may be caused, among others, by a lower level of glycemic control in people with type 1 diabetes [24], having a stronger correlation with the occurrence of tuberculosis [3, 7] and high influx of immigrants from around the world, including regions where tuberculosis is endemic [6, 16].

As a result of environmental disasters, conflicts and humanitarian crises on other grounds, the number of forced displaced persons has increased significantly in recent years, reaching 6.5 million at the end of 2017, with most of them living in the urban environment [26]. The relationship between the number of TB cases and the number of immigrants arriving in England is highly worrying. These figures are incomparably higher for England than for other parts of Great Britain and represent the overwhelming percentage of the whole country [16]. A study was conducted on migrants from 15 countries with a high incidence of tuberculosis, applying to enter Great Britain. Over 470,000 people were tested for

bacteriologically confirmed tuberculosis and received a result of 92 (95% CI 84-101) per 100,000 people. Most cases of confirmed tuberculosis were obtained from people from countries where the WHO estimated incidence of tuberculosis is 150-349 per 100,000 [27].

Because bacterial resistance to antibiotics is an increasingly serious problem worldwide, it was also decided to include the association of diabetes with drug-resistant *M. tuberculosis* in this analysis. However, the studies differ significantly in results - some authors did not find a relationship between the occurrence of diabetes and multi-drug resistant tuberculosis, while other studies showed a significantly (even 8.6 times) risk of developing isoniazid and rifampicin resistant TB among diabetics. It seems necessary to conduct further extensive research on this issue and the possible mechanism leading to drug resistance in patients with diabetes. Currently, there are only hypotheses, and one of them states that in type 2 diabetes, the production of reactive oxygen species that damage bacterial strains may be impaired, and tuberculosis strains with mutations of the katG gene may show better drug tolerance, since this gene encodes enzyme that converts isoniazid to the active form [3].

Conclusions

Diabetes is a predisposing factor for the development of tuberculosis, therefore, despite the decline in tuberculosis in England and India, there is a high risk of a further increase in the incidence rate of tuberculosis in the future due to the growing numbers of diabetes in both populations. Moreover increase in diabetes incidence rate is strongly associated with the MDR tuberculosis incidence rate increase in the population of India, England and Hindu immigrants population living in England. Comparison of data also shows the relationship between the growing number of immigrants arriving from India to England and the recent increase in the incidence rate of MDR tuberculosis in England. The increasing trend of diabetes in England and the large influx of immigrants from India may cause an increase in the number of TB and drug-resistant TB patients in the UK in the coming years.

Health care professionals around the world face the challenge of reducing diabetes and fighting infectious diseases, which are still a problem, especially in the era of drug resistance, the popularity of anti-vaccine movements in Europe, and the humanitarian crisis in Asian and African countries. More extensive research on the effects of diabetes on the development of drug-resistant tuberculosis and on the transmission of infections appears to be necessary, as well as prevention of diabetes and tuberculosis.

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