Impact of travelling to high incidence countries on tuberculosis diagnostic delays among migrants: a retrospective study.

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Research article

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Abstract

Background

Most tuberculosis (TB) cases in high-income countries occur in foreign-born people, most of them coming from high incidence countries. However, migrants return more or less frequently to their birth countries. The aim of the study was to estimate the influence of travelling to high incidence countries on the diagnosis delay of tuberculosis in France.

Methods

a monocentric retrospective study of 224 consecutive cases followed at the Bas-Rhin Tuberculosis Prevention Centre.

Results

59.3% of cases were born abroad. Migrants who did not develop TB soon after arrival and, who travelled since then to high incidence countries, had a mean diagnosis delay, since their last trip, comparable to median diagnostic delay among immigrants who did not travel since their arrival (3.2 vs 4.4 years, $p = 0.42$). Diagnostic delays are shorter among those reporting an exposition to TB during their journey (1.5 years vs 3.7 years, $p = 0.2$).

Conclusion

These results suggest a targeted information on the risk of TB and LTBI among those persons and screening for tuberculosis and LTBI, in certain cases, including vulnerable patients (dialysis, under immunosuppressant drugs including anti-TNF, HIV).

Background

Tuberculosis (TB) is defined as an infection caused by a bacterium, *Mycobacterium tuberculosis* complex. Each year, around 10 million persons declare tuberculosis, and 1.5 million of them die, which make this disease, according to the World Health Organization (WHO), the top one infectious disease related mortality cause, and the 5th all-cause mortality worldwide(1). In 2014, the World Health Organization set the ambitious goal to lower the global incidence of TB to < 100 cases per million population by the year 2035, with a world free of tuberculosis(2). This incidence has already been reached in many rich countries, France for example. Currently, most cases in high income countries involve foreign-born persons(3). Data show that, in these countries, tuberculosis remains stable in foreign-born people, or sometimes might increase, whereas it decreases in native people(4). In France, Guidelines recommend a screening of tuberculosis in immigrants in the first four months since arrival

and during the first 2 years. Indeed, most cases occur during this period, suggesting that these persons might have tuberculosis at entrance or might have a latent TB infection, which progressed to active tuberculosis afterwards(5). However, among persons who do not develop tuberculosis in this period, a less studied risk factor deserves better recognition: travelling back to home countries, which frequently are high tuberculosis incidence countries. The aim of this study was to assess the influence of travelling in a high tuberculosis incidence country, on diagnostic delays.

Methods

Study population and materials

This was a retrospective monocentric study. Patients notified to Centre de Lutte Anti Tuberculeuse du Bas-Rhin (CLAT 67) with active tuberculosis between 01/01/2008 and 31/12/2010 were included. Informations on patients and their disease were collected from data of notifications and medical reports. This was : age, sex, location of tuberculosis, country of birth, nationality, date of tuberculosis diagnosis, date of arrival in France, informations related to travels (date, place, contact with a tuberculous person), past medical history of tuberculosis.

Statistical analysis

Results were analysed using Systat version 12.02 (Systat Inc, California, USA). Means, medians and proportions were calculated. Student t-test or Mann-Whitney test were used for comparison between groups.

Results

Between 01/01/2008 and 31/12/2010, 304 cases were notified to the CLAT Bas-Rhin. Records of 80 of them could not be exploited: 53 cases were living in another department, 9 cases because of refusal of the inquiry, 7 cases were living in another country, 6 cases were deceased, 1 person was diagnosed with an atypical mycobacterium, 4 persons had incomplete records (Fig. 1). In total, 224 persons were enrolled in the study for final analysis. 53.3% were men, 46.7% were women. Mean age was 46.3 years old (95% CI 43.49–49.2). Most frequent localizations were pulmonary (77,5%), followed by lymph node involvement (10.5%), disseminated form (4.4%), and pleural disease (2.6%). 59,4% of the enrolled persons (n = 133) were born abroad. According to the 2013 TB incidence, origins of migrants cases were as follows : 12.8% coming from countries with an incidence < 50/100 000, 15% from countries with an incidence between 50 and 100/100 000, 45.1% from countries with an incidence between 100 and 200/100 000, 18.8% from countries with an incidence between 200 and 300/100 000 and 8.3% from countries with an incidence above 300/100 000 inhabitants (Fig. 2). Seventy-eight foreign-born persons (58.6%) travelled outside France since their arrival. Most of them travelled back to their birth countries (n = 70, 89.7%). The majority (78,5%, n = 62) traveled to high TB incidence countries, according to the French high tuberculosis incidence definition, that is a cut-off of 40 cases per 100 000 inhabitants. Among those born in France, only 28.9% travelled abroad (n = 26). Fourteen of them travelled in a high incidence country (53.8%).

Sixty-eight persons (30%) declared having contact with a potentially contagious tuberculous person, whose 44% during their travel.

Mean delay, in the whole migrant population, was 10,7 years since arrival (95% CI : 8.3-13.15), median delay was 4 years. Among foreign-born patients, those who did not develop tuberculosis and who travelled since arrival, mean diagnostic delay since their last travel was 3.2 years (95% CI: 1.6–4.8), median diagnostic delay was 1 year. Considering foreign born persons who did not travel since arrival, mean diagnosis delay was 4,4 years (95% CI: 1.9–6.9), median delay was 1 year (Figs. 3 & 4). The difference was not statistically different ($p = 0,42$). Among cases born in France who travelled ($n = 26$), the mean delay was 7.15 years (95% CI : 1,39-12.9), the median delay was 1 year.

Among those who travelled, since their last travel, mean diagnosis delay was 7.15 years in cases born in France versus 3.19 years in foreign-born persons ($p = 0,7$).

Among foreign born persons, those who traveled in places where incidence is below 50 cases/100 000 inhabitants, diagnostic delay was 2,94 years ($n = 17$); it was 6,7 years for an incidence between 50 and 100 cases/100 000 inhabitants ($n = 9$), 1.76 years for an incidence between 100 and 200 cases/100 000 inhabitants ($n = 37$), 5,38 years for an incidence between 200 and 300 cases/100 000 inhabitants ($n = 13$) and 2 years for an incidence higher beyond 300 cases/100 000 inhabitants ($n = 2$) (Fig. 5).

Among those who traveled, since arrival, mean diagnostic delay was 1.5 years in persons who declared having a contact with a potentially contagious tuberculous person versus 3.7 years in persons who do not report having such a contact ($p = 0,2$). Diagnostic delays are shorter in foreign-born cases who travelled, with a documented TB contact (Fig. 6).

Discussion

The main aim of this study was to assess the impact of travelling in high incidence tuberculosis countries on the diagnostic delays, in foreign-born persons. Results show that, among these persons, and since arrival in France, those who travelled had a quite equivalent mean diagnostic delays than those who do not travel. These results might suggest the same mechanism, a recent latent tuberculous infection that progressed to active tuberculosis. It might also suggest that, among those who did not develop TB in the first 2 years since arrival, the risk is constant throughout years. We do not find a link between travelling in high incidence countries and diagnostic delays.

The latent tuberculosis infection risk concept after travelling to high incidence tuberculous countries has been studied several times. It has been shown that travelling to such countries is a risk factor of LTBI. In a Dutch study published in 2000(6), where authors wanted to estimate the risk of infection after travelling to high incidence countries, in non-vaccinated BCG persons with a negative tuberculin skin test (TST), a 1,8% rate of LTBI was noted 2 to 4 months after their return, and 0,3% were diagnosed active tuberculosis. Working in a health facility in these countries was associated with an increased risk of LTBI ($RR = 5.34$; $p = 0.015$). In an American study(7) where authors estimated the influence on results of TSTs in children, in

the last 12 months following a travel in high incidence countries, 7.6% of these children had a positive TST. The risk of positivity was significantly associated with an history of travelling in the last 12 months (RR = 3,9; 95% CI 1.9–7.9). Countries or regions where these children travelled were Mexico, Central America and South East Asia. Children in contact with persons from high incidence countries had an increased risk of a positive TST (OR = 2.4; 95% CI 1-5.5).

This risk is also concerning active TB. A 1984 British study(8) already noted that 20% of tuberculosis cases in Asian immigrants was associated with a travel back to their birth countries. As well, a Dutch study(9), who wanted to see, among persons born in Morocco or Turkey who travelled to their birth country in the last 12 months, but in the Netherlands for less than 2 years, the risk of diagnosing tuberculosis was 3.2 times higher than persons who did not travel (95% CI 1.3–7.7). Among Turkish patients, history of travelling was a not a significant risk factor (OR = 0.9; 95% CI 0.3–2.4). A greater incidence of tuberculosis in Morocco than in Turkey was the main explanation of the authors (which, in 2006, was 97/100 000 in Morocco versus 33/100 000 in Turkey, according to the World Bank data). The risk was even higher if the person had a long journey in this country, with a 17 times risk of developing TB if the length of stay was more than 3 years.

The statement was even more striking when distinction was made between tourists and travelers native to these countries. In a British study(10), among 1032 tuberculous patients from India declared to the health authorities between 1978 and 1997, 22% had an history of travel and 66% of them in the last 3 years preceding the diagnosis.

Our results are in line with these previous studies, mentioning the increased risk of tuberculosis following a travel in high incidence countries.

These results also raise questions about the quite similar diagnosis delays. The similarity of the distribution of data in Figs. 4 and 5 suggest that immigrants coming from high incidence countries develop tuberculosis either before the migration (early tuberculosis) or either during their journey (delayed tuberculosis). Most cases occurring in the first 2 years following their arrival in France or following a trip in a high incidence country goes clearly in that direction. Travelling to such countries should be regarded as a “reset” in the risk of tuberculosis. Unexpectedly, we did not find any relation between diagnostic delays and the TB incidence of countries, as it would have been interesting to imagine that, the higher the incidence of TB is, the higher is the risk of acquiring LTBI or active TB, and the shorter the delay could have been. In fact, it seems that a documented contact with an active TB person is a better hint for predicting the delay. Difference of delays between foreign born persons and native persons who travelled to high incidence countries might be explained by a different behavior during the journey(11). It has been shown that tourists born in these countries has a greater risk of acquiring travel related infections, including tuberculosis. It could be explained by a less cautious behavior, by more frequent contact with locals. As well, the journey is often longer.

Immigrants who plan to travel to birth countries should be, therefore, aware of risks of LTBI and active TB, especially if they have susceptibility factors. A case by case screening, depending on the person and the

country they visited, should be implemented. Our results support recent guidelines from French Public Health authorities, considering travels to high incidence countries in the indication for screening of LTBI among certain populations (susceptible persons, healthcare persons, expatriate in a high incidence country more than 6 months)(12).

This study has several limits. It did not allow us to develop certain linking of variables. However, as we consider the studied questions, most of records were complete. Some non-significant results could be explained by a lack of power, because of a low number of patients, and it might be relevant to repeat this study with a greater number. Finally, it could have been interesting to include the length of journey into the risk, which might have an influence.

Conclusion

Mean diagnostic delay of tuberculosis, following a travel to high incidence countries, among immigrants who did not develop TB after arrival, is quite similar to diagnostic delays among immigrants who did not travel since arrival, suggesting a same mechanism. The visited place could have an impact on this delay. History of contact with a potentially contagious person is an important information to consider. A close monitoring of vulnerable persons or persons working with vulnerable persons, in the 3–4 years following such a travel, might be probably relevant.

Declarations

Ethics approval: Ethics approval was obtained from the local Ethics Committee of Strasbourg's University Hospitals.

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

Authors' contribution: LK collected and analysed data regarding patients' variable of interest. PF was a major contributor in writing the manuscript. All authors read and approved the final manuscript.

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Figures

Figure 1

Diagram for study flow.

Figure 2

birth countries TB incidence of migrants

Figure 3

mean diagnostic delays in four different populations of migrants.

Figure 4

mean diagnostic delays, in years, among those born abroad.

Figure 5

mean diagnostic delays, in years, according to the incidence of the visited countries among migrants.

Figure 6

mean diagnostic delays in migrants depending on TB incidence of visited countries and a notion of exposure.