

The burden of Tuberculosis in a low-incidence territory: contribution of foreign population in the disease epidemiology

Alessio Facciola^{1,2}, Giuseppa Visalli², Smeralda D'Amato², Giuseppa D'Andrea¹, Angela Di Pietro²

¹Unit of Epidemiology, Department of Prevention, Provincial Health Agency of Messina, Messina, Italy;

²Department of Biomedical and Dental Sciences and Morphofunctional Imaging, University of Messina, Italy

SUMMARY

Tuberculosis (TB) still represents one of the most important causes of death worldwide. In Italy, TB is a relatively rare disease. This research aimed to evaluate the TB cases reported in the provincial territory of Messina, Italy, in order to assess the contribution of the different groups of the local population.

We conducted a review of existing epidemiological data evaluating the trend of all TB notifications reported from 2001 to 2019. For the collection of the data, all the notifications were evaluated by analyzing the local and national computerized records.

From 2001 to 2019, 475 cases of TB were notified, 67.6% in Italian citizens and 32.4% in foreigners of which 75.3% resident and 24.7% irregularly residing (i.e., migrants landed in Messina). The incidence rate was remarkably higher in foreigners compared to Italian citizens, with average values of 31.7 and 2.7 per 100,000 inhabitants respectively. The average age was 48.4 years in Italian citizens, 32.7 years in resident foreigners and 19.6 years in irregularly residing foreigners.

In the epidemiology and maintenance of TB in our territory, the incidence of TB in foreigners surely played an important role. However, the incidence in Italian citizens remained stably low for all of the period considered, showing that there seems to be no immediate danger of spreading the infection.

Received March 03, 2020

Accepted June 30, 2020

INTRODUCTION

Tuberculosis (TB) remains a major cause of disease and one of the top 10 causes of death worldwide. About a quarter of the world's population is infected with *Mycobacterium tuberculosis* and thus is at risk of developing TB. Since 2007, TB has been the leading cause of death from a single infectious agent, ranking above HIV/AIDS (Bloom *et al.*, 2017).

In 2014-2015, all Member States of the World Health Organization (WHO) and the United Nations (UN) committed to fight and put an end to the TB epidemic. This purpose has led to the realization of a plan named "WHO's End TB Strategy," unanimously adopted at the World Health Assembly in May 2014, and to the adoption of the UN Sustainable Development Goals (SDGs) in September 2015. Specifically, SDG Target 3.3 includes ending the TB epidemic by 2030. This strategy defines milestones (for 2020 and 2025) and targets (for 2030 and 2035) to reduce both TB cases and deaths. The milestones for 2020 are a reduction of 35% in the number of TB deaths and of 20% in the TB incidence rate (new cases per 100,000 inhabitants per year) compared to 2015. The targets for 2030 are

a reduction of 90% and 80% respectively. Actually, most WHO regions and many countries with high TB burden are quite far from reaching the 2020 milestones of the End TB Strategy (Uplekar *et al.*, 2015; World Health Organization, 2014).

The last WHO Global TB Report (2019) shows that about 10.0 million people (range, 9.0-11.1 million) got sick from TB in 2018, a number that has been quite stable in recent years. Most TB cases occurred in Southeast Asia (44%), Africa (24%) and Western Pacific (18%) WHO regions, with smaller incidences are the Eastern Mediterranean (8%), the Americas (3%) and Europe (3%). Globally, the average decrease in the TB incidence rate was 1.6% per year in the period 2000-2018, and 2.0% between 2017 and 2018. The cumulative decrease between 2015 and 2018 was only 6.3%, considerably lower than expected by the End TB Strategy milestone of a 20% reduction between 2015 and 2020. The global reduction in the total number of TB deaths between 2015 and 2018 was 11%, less than one third of the End TB Strategy milestone of a 35% reduction by 2020 (World Health Organization, 2019).

The burden of the disease varies greatly among countries, from fewer than five to more than 500 new cases per 100,000 inhabitants per year, with a global average of about 130. The WHO European Region is well advanced in reaching the 2020 milestones for reductions in cases and deaths. Specifically, in 2015, TB incidence was 5.8 per 100,000 in Italy, 7.6 in Austria, 8.1 in Germany, 8.2 in France, and 7.4 in Switzerland (Tattevin *et al.*, 2012; Auer *et al.*, 2018). Between 2015 and 2018, the incidence rate decreased by 15% and the number of TB deaths de-

Key words:

Tuberculosis, Epidemiology, Foreigners.

Corresponding author:

Alessio Facciola

E-mail: afacciola@unime.it

creased by 24%. Globally, an estimated 1.2 million (range, 1.1-1.3 million) TB deaths among HIV-negative people (a 27% reduction from 1.7 million in 2000), and an additional 251,000 deaths (range, 223,000-281,000) among HIV positive people (a 60% reduction from 620,000 in 2000) occurred in 2018. TB affects people of both sexes in all age groups, but the highest burden is in adult men, who accounted for 57% of all cases in 2018, while adult women accounted for 32% and children for 11%. Among all TB cases, 8.6% were people living with HIV (European Center for Disease Control and Prevention, 2019).

In Italy, as in many other industrialized countries, TB is a relatively rare disease with an incidence lower than 10 cases/100,000 inhabitants, a threshold within which the WHO defines a country as “low endemic country”. The number of cases reported in Italy has shown a slow and progressive decrease in incidence over time, dropping from 9.5 cases per 100,000 inhabitants in 1995 to 6.5 cases per 100,000 in 2017. However, an increased irregular migratory flow, mainly from countries with high TB incidence, has been documented since 2014 (i.e., from 50,000 migrants in 2013 to >150,000 in 2014-2015 and about 200,000 in 2016) (Campogiani *et al.*, 2020). Strongly related to the increased number of migrants (i.e., people who temporarily live in Italy without a residence permit) and to resident foreigners, who amount to 5,144,440 (8.52%) in Italy in 2018 (ISTAT), from 2004 to 2014 more than 50% of the annual Italian TB notifications involved foreigners (Scotto *et al.*, 2017). Moreover, in recent years, numerous warning signs have emerged, among which an increase of up to 4 times higher TB incidence in large metropolitan cities compared to the national rate and the number of TB cases resistant to several drugs. The latter problem is slowly but progressively increasing and cases of so-called XDR-TB (extensively drug-resistant TB) have been identified in Italy, especially in foreigners, and for which the currently available drugs are not effective (Riccardi *et al.*, 2019). In 2017, 66 cases of multidrug-resistant TB (MDR-Tb, 2.5% of the total number of notified cases) were notified, of which 5 XDR Tb; 66.2% of the MDR-TB cases occurred in foreigners (Epicentro, 2019a).

This research aimed to study TB incidence in the provincial territory of Messina, Italy, in order to evaluate the modification of the temporal trend of the reported cases and to highlight the role played by the different groups of the province’s population (on average consisting of approximately 650,000 inhabitants) in the epidemiology of the disease.

MATERIALS AND METHODS

We conducted a review of existing epidemiological data evaluating the trend of all the TB notifications reported in Messina province from 2001 to 2019. The sample was made up of three categories: Italian citizens, regularly residing foreigners in our territory, and irregularly residing foreigners in Italy (i.e., foreigners without residence permit, as migrants landed on our coasts following the remarkable migratory flows that characterized our territory from 2014). In Italy, notification of TB is mandatory according to Ministerial Decree 15 December 1990 “Information system of infectious and diffusive diseases” containing rules for the mandatory notification of infectious diseases. Specifically, the decree classifies TB in the III group “Diseases for which particular documentation

are required” with AIDS, Malaria, Leprosy and non-tubercular mycobacteriosis (Ministero della Salute, 1991). The notifications are made by the local hospital or territorial healthcare workers that enter them in the Agency’s computer platform. So, for the collection of the epidemiological data, all the notifications regarding the considered period were evaluated by analyzing the computerized records of the Epidemiology Unit belonging to the Prevention Department of the Messina Provincial Health Agency (i.e., ASP n. 5 of the Sicilian Region which manages health services in the whole provincial territory). In addition to the local registers, two national computerized systems, the Infectious Diseases Information System (SIMIWEB) and the Notification System of Infectious Diseases (PREMAL) of the Italian Higher Health Institute (in Italian ISS), where all mandatory notifications of the national territory converge, were consulted.

Statistical analyses

All the obtained data were collected and analyzed with Prism 4.0 software. Descriptive statistics were used to find the percentages and the averages values with the standard deviations. The analysis of the independent variables gender and age in the different groups was performed by using t-test and Anova- respectively.

RESULTS

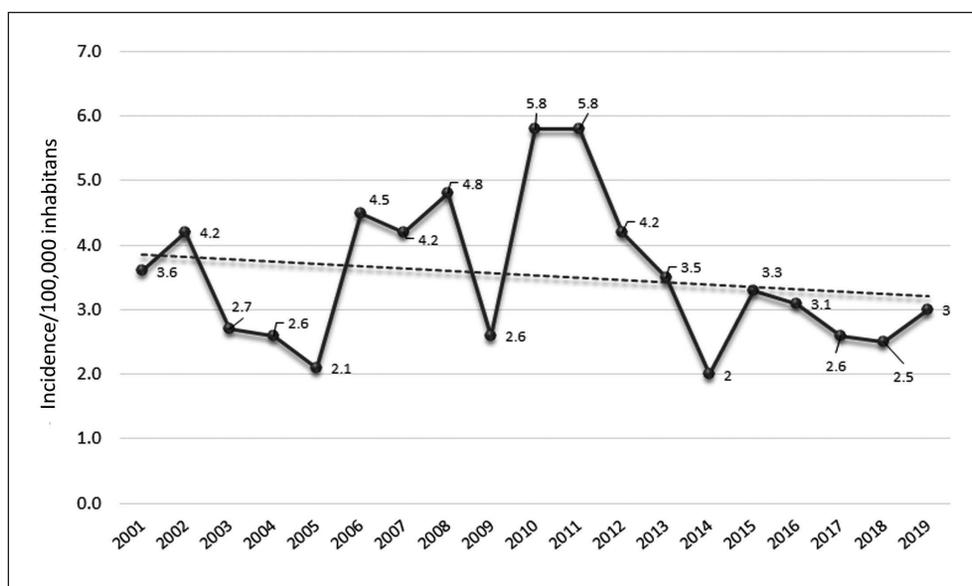
From 2001 to 2019, 475 cases of TB were notified to the Provincial Health Agency of Messina, of which the majority (86.8%) were pulmonary cases and only 13.2% extrapulmonary infections, especially renal and bone disease. Specifically, 321 (67.6%) of notified cases occurred in Italian citizens and 154 (32.4%) in foreigners, of which 116 (75.3%) were regularly residing in our territory and 38 (24.7%) were irregularly residing foreigners. *Table 1* shows the distribution of the reported cases in the three groups of people.

The total incidence of TB cases in residents (both Italians and foreigners) showed a very fluctuating trend, as shown in *Figure 1*, with two important peaks in the two-year period 2010-2011 with an incidence of 5.8/100,000 inhabitants for both years and the minimum in 2005 and 2014 with incidences of 2.1/100,000 inhabitants and 2.0/100,000 inhabitants, respectively. In recent years, several cases were reported in irregular residents (on the rise since 2014). In this category of people, 38 (8.0%) TB cases were reported from 2014 to 2018, with a peak in the three-year period 2016-2018, as shown in *Table 1*.

Figure 2 shows the TB incidence in both Italian citizens and regularly residing foreigners. The figure shows that the incidence was remarkably higher in the latter compared to Italian citizens, with average values of 31.7 ± 20.7 and 2.7 ± 1.0 , respectively. On average, in regularly residing foreigners the TB incidence was 13-fold higher compared to Italian citizens. This was true especially in some years: in 2011, 38 TB cases were reported, of which more than half (52.6%) in regularly residing foreigners. Of these 20 cases, 7 (35%) occurred in Romanians and 7 in Filipinos. Similarly, in 2012, of the 27 reported cases, 13 (48.1%) occurred in this group, of which 5 (38.5%) in Moroccans, 3 (23.1%) in Romanians and 3 (23.1%) in Filipinos.

The TB cases involved men for 63.8% with an average age of 44.9 ± 7.1 years and women for 36.2% with an average age of 39.8 ± 7.0 years. *Figure 3* shows the significant dif-

Figure 1 - Trend of TB incidence in the resident population of the Messina provincial territory from 2001 to 2019.



ferences in the average age of TB cases among Italian citizens, regularly and irregularly residing foreigners ($P < 0.001$). Specifically, the average age was 48.5 ± 6.3 years for Italian citizens and 34.6 ± 10.2 years for regularly and 19.6 ± 3.4 years for irregularly residing foreigners.

Concerning the socio-demographic characteristics of the sample, the Italian citizens affected by TB were workers (51.2%), retired (31.4%), unemployed (11.5%), and underage (<18 y/o) (5.9%). The regularly residing foreigners affected by TB were especially from Eastern Europe in 48.1% of cases (Romania 92.3%, Russia 5.1% and Poland 2.6%), South-Eastern Asia in 25.9% of cases (Philippines 80.9%, Sri Lanka 19.1%), North Africa (17.3%), all from Morocco, Sub-Saharan Africa (8.7%) (Nigeria 28.6%, Senegal 28.6%, Sudan 14.3%, Somalia 14.3% and Côte d'Ivoire

14.3%). 45.9% of them were workers, 25.2% unemployed, 12.6% underage (<18 y/o), 7.2% housewives, 3.6% prisoners; work status was unknown in 5.5% of cases. Among the workers, 23.9% were house cleaners, 28.2% construction workers, 19.6% street sellers, 13% caregivers, 6.5% agricultural day laborers, 4.4% waiters, and 4.4% traders. Concerning irregularly residing foreigners, all the cases came from Sub-Saharan Africa. Specifically, 49.9% were from countries of Eastern Africa, of which 42.0% from Eritrea, 42.0% from Somalia, 10.6% from Ethiopia and 5.4% from Sudan; 47.4% were from countries of Western Africa, of which 44.4% from Gambia, 16.6% from Senegal, 16.6% from Nigeria, 11.2% from Guinea, 11.2% from Côte d'Ivoire. Only 2.7% were from Central Africa (Burkina Faso). Regarding age, as many as 44.7% of this category

Table 1 - Number and distribution of the TB cases in the three groups of people reported to the Provincial Health Agency of Messina from 2001 to 2019.

	Total	Italian citizens (%)	Regularly residing foreigners (%)	Irregularly residing foreigners (%)
2001	24	19 (79.2)	5 (20.8)	0
2002	28	26 (92.9)	2 (7.1)	0
2003	18	15 (83.3)	3 (16.7)	0
2004	17	14 (82.3)	3 (17.7)	0
2005	14	14 (100)	0	0
2006	29	25 (86.2)	4 (13.8)	0
2007	27	22 (81.5)	5 (18.5)	0
2008	31	28 (90.3)	3 (9.7)	0
2009	17	15 (88.2)	2 (11.8)	0
2010	38	30 (78.9)	8 (21.1)	0
2011	38	17 (44.7)	21 (55.3)	0
2012	27	14 (51.8)	13 (48.2)	0
2013	23	13 (56.5)	10 (43.5)	0
2014	16	6 (37.5)	7 (43.7)	3 (18.8)
2015	24	11 (45.8)	10 (41.7)	3 (12.5)
2016	29	15 (51.7)	5 (17.2)	9 (31.1)
2017	29	10 (34.5)	7 (24.1)	12 (41.4)
2018	27	13 (48.2)	3 (11.1)	11 (40.7)
2019	19	14 (70.0)	5 (25.0)	0 (0.0)
Total	475	321 (67.6)	116 (24.4)	38 (8.0)

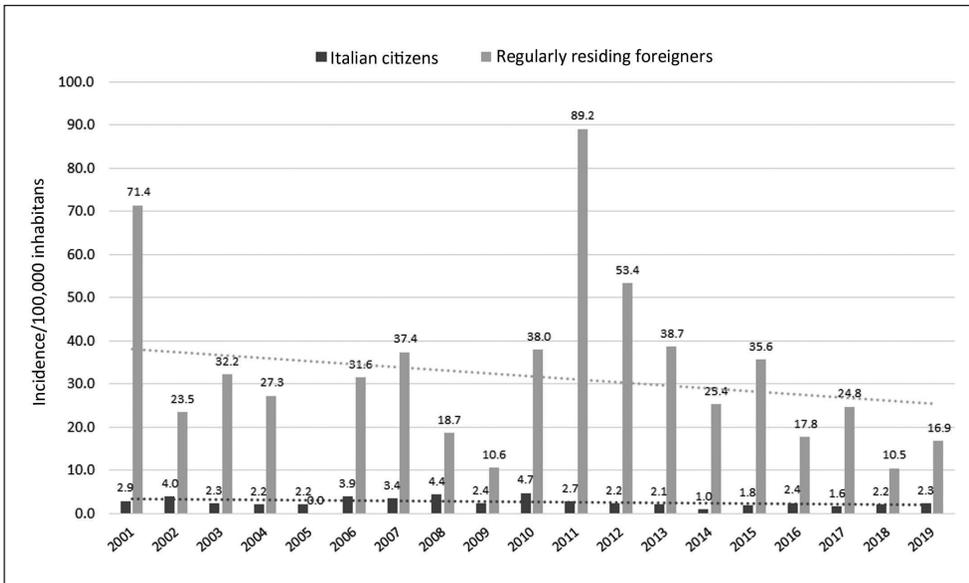


Figure 2 - Trend of TB incidence in Italian citizens and regularly residing foreigners in our territory from 2001 to 2019.

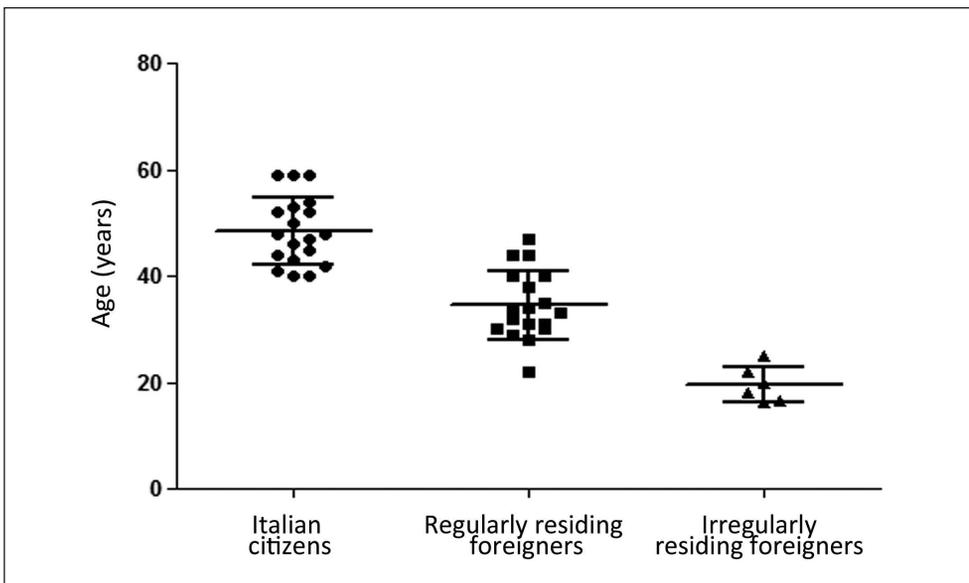


Figure 3 - Average age in Italian citizens, regularly residing foreigners and irregularly residing foreigners.

were <18 y/o. Moreover, some outbreaks among irregular residing foreigners occurred. Specifically, in 2016, 5 cases occurred among Gambian and, in 2018, 4 cases among Somali migrants.

Finally, an important issue to highlight was the lack of MDR/XDR *M. tuberculosis* detection during all the studied period, a result in contrast with the above reported statistics.

DISCUSSION

Despite the numerous and constant efforts of the international community to fight and put an end to TB, the disease keeps killing worldwide, especially in developing countries (Floyd *et al.*, 2018). This epidemiological context depends on the fact that some groups of people are at major risk of infection by TB. It was demonstrated that people with undernutrition are 3 times more at risk than people with a healthful and rich diet, and that in 2018

there were globally 2.3 million new TB cases attributable to undernutrition (Feleke *et al.*, 2019). Moreover, people living with HIV/AIDS (PLWHA) are 19 times more likely to develop active TB (see TB and HIV section below) compared to HIV uninfected people (Kwan *et al.*, 2011). Finally, alcohol use disorder and tobacco smoking increase the risk of TB by a factor of 3.3 and 1.6, respectively. In 2018, 0.83 million new TB cases worldwide were attributable to alcohol use disorder and 0.86 million were attributable to smoking (Amere *et al.*, 2018; Simou *et al.*, 2018).

From 2001/01/01 to 2019/12/31 the resident population of the Messina province decreased by 5.4%, from 662,450 to 626,876 in the two years, respectively. Conversely, regularly residing foreigners increased from 9,312 in 2003 to 29,627 (4.7% of the entire resident population) in 2019 with a percentage increase of 68.6%. Despite the increase, it is useful to underline that the proportion of foreigners residing in our province is significantly lower than the national average (4.7 vs 8.5%). Regarding nationalities,

Romanians are in first place with 25.9%, followed by Sri Lankans (15.2%), Moroccans (11.9%) and Filipinos (8.4%) (DemoIstat, 2019). About a quarter of the resident population (37.1%) lives in Messina. The territory is still endemic for some infectious diseases, such as brucellosis and measles, with numerous cases and outbreaks reported in recent years (Facciola *et al.*, 2018; Palamara *et al.*, 2018), but, concerning TB, the provincial incidence was lower than the national one. Specifically, the reported local incidence in 2017 was 2.6/100,000 inhabitants (only residents, both Italians and foreigners) compared to 6.5/100,000 inhabitants reported in the same year at the national level. Probably, in Sicily, favorable climatic factors, the positive influence of the Mediterranean diet and the lower presence of some risk factors, such as lower alcohol consumption (Epicentro, 2020) and the rate of HIV infection (Ministero della Salute, 2018; Facciola *et al.*, 2020) compared to the rest of the national territory, help to keep TB incidence low. However, our study shows that TB was present in our territory for all of the considered period with a fluctuating trend characterized by peaks, with a higher number of notified cases (38) in the two-year period 2010-2011, and valleys, with a lower number of notified cases (14) in 2005. Moreover, the incidence was remarkably higher in foreigners than in Italians (incidence ratio 31.7 ± 20.7 vs 2.7 ± 1.0). This result is consistent with studies showing that, in Italy, TB in foreigners is associated with a greater risk of both hospitalization and mortality (Baglio, 2015; Pacelli *et al.*, 2019; Cacciani *et al.*, 2019). However, the lower presence of foreigners in our province keeps the overall incidence low and therefore the contribution of foreigners to the total number of notified cases is proportionately lower (32.4 vs 67.6%). The lack of MDR/XDR *M. tuberculosis* detection in 2001-2019 in our sample is also attributable to this feature of Messina province. As reported above, drug-resistant TB occurs mainly in foreigners, increases slowly and progressively, and only 2.5% of the total number of notified cases in Italy in 2017 was formed by MDR/XDR-TB.

In Europe, foreigners seem to have a greater risk of developing active TB from a latent form contracted in their countries of origin (generally at high TB incidence) due to the marginal conditions to which they are often exposed in the host country. Since migratory flows are mainly directed to countries that offer more economic opportunities, this could partially explain the North-South gradient observed when examining the incidence ratios reported by Tattevin *et al.* (2012) and by Auer *et al.* (2018). Improved access to treatments and better living conditions can represent a crucial prevention strategy. The two higher peaks occurred in years in which there was a larger number of cases in regularly residing foreigners (coming especially from Romania and the Philippines). Indeed, Romania has always been one of the most affected European countries, with a high number of reported cases from the early 2000s and an important peak in 2002 during which an incidence of 142 cases/100,000 was reported (NiTu *et al.*, 2017; Golli *et al.*, 2019). At the same time, the Philippines is one of the most affected countries, reporting 6% of all cases worldwide, with an incidence in 2018 of 554 cases/100,000, and resulting in sixth place on the world list of the last WHO report on the global burden of TB (World Health Organization, 2019). Concerning Romanians, the result is probably consequential to the migration of many people in working age (especially women) from Romania to Italy that occurred some years after the entrance of the country

in the European Union in 2007. Probably, people affected from a latent TB infection developed an active form over time, due to new living conditions. Similarly, Filipinos are numerous in our territory, representing, as reported above, the fourth largest foreign community regularly residing in our province. Both foreign groups generally do manual works as they are, for the most part, caregivers, cleaners, waiters, porters, etc., jobs notoriously strenuous and underpaid that can generate unhealthy living conditions such as poverty and overcrowding, responsible for possible evolution of a latent TB infection.

The average age of the reported cases was quite different in the groups because, in the Italian one, the cases had a higher age than that of regularly or irregularly residing foreigners. Probably, this result occurred because among Italians the most important factors playing a role in the onset of an active infection is old age, characterized by the natural phenomenon of the immunosenescence. Moreover, the elderly often have numerous comorbidities and do multiple therapies that can weaken their immune responses. Probably, the cases of TB reported in the Italian group are the result of a reactivation of an old infection contracted when young, at a time in which the incidence of TB was much higher compared to the current one. Therefore, this finding shows a low circulation of the pathogen among the local population. Conversely, regularly residing foreigners move to our country at a young age to find a job. Therefore, as demonstrated by national statistics, the majority of the foreign population has an average age lower (35 years) than that of the Italian population (46 years) (Epicentro, 2019b). Indeed, in our territory, in 2019 half (51%) of the all regularly residing foreigners had an age ranging between 20 and 45 while the Italian citizens of the same age group accounted for the 28.8% (DemoIstat, 2019). Moreover, we have previously emphasized how the majority of the regularly residing foreigners in our territory are from countries at high incidence of TB. These are surely the causes of the lower reported average age of TB in the foreigner group.

After the peaks of 2010-2011, we observed a general decrease in TB incidence until 2014, when there was a novel important increase consequent to the cases reported in irregularly residing foreigners (i.e., migrants who landed on our coasts starting that year). Specifically, in the five-year period 2014-2018, 108 landings occurred, 17 (15.7%) in 2014, 27 (25.0%) in 2015, 35 (32.5%) in 2016, 14 (13.0%) in 2017 and 15 (13.8%) in 2018, for a total of 38,608 individuals who landed in our city (Facciola *et al.*, 2020). This event greatly affected the notification rate of TB cases, especially in the period 2016-2018, when 32 cases were reported in this group of people. Previous studies have shown that the TB cases observed in migrants generally occur due to one of three main reasons:

- 1) migrants already have an active TB infection on their arrival, or
- 2) they have a latent TB infection that reactivates after the arrival due to inadequate living conditions, or
- 3) they acquire the infection from the host population through local transmission (Pareek *et al.*, 2016).

However, studies have shown that transmission is generally low in low-incidence countries and transmission from irregular foreigners to the host population is often modest (Lönnroth *et al.*, 2017). Indeed, even in the years immediately following, the incidence in the resident population remains stably low, showing that there seems to be no immediate danger of spreading the infection. In our

study, irregular foreigners registered the lowest average age because young and very young people represented the majority of landings on our coasts. In 2019, we did not observe any TB cases in irregular foreigners, following the decrease of landings registered in our territory.

CONCLUSION

Our study demonstrates that despite the fact that TB has always been present in our territory during the last two decades, the incidence was lower than that reported in Italy, confirming that TB is not a big problem for our public health, unlike other infectious diseases. In the epidemiology and maintenance of TB in our territory, foreigners (both regularly and irregularly residing foreigners) have surely played an important role in the incidence, especially in the last decade. This result is confirmed by the much higher incidence reported in this group compared to that reported in Italian citizens during the entire period. Social inequalities, such as the prevalence of hard and underpaid work and worse living conditions, most present among foreigners, surely contributed to this picture promoting the development of a latent TB infection, the majority of foreigners suffering from TB coming from countries characterized by a high TB incidence. Many TB cases were reported in foreigners during the period of the migrant landings, explaining why the local population often considered this group a danger for local public health. However, the incidence in Italian citizens remained stably low for all the considered period, showing that the possibility of transmitting TB to local people is very rare.

Conflicts of interest

The authors declare that there are no conflicts of interest.

References

- Amere G.A., Nayak P., Salindri A.D., Narayan K.M.V., Magee M.J. (2018). Contribution of Smoking to Tuberculosis Incidence and Mortality in High-Tuberculosis-Burden Countries. *American Journal of Epidemiology*. **187**, 1846-1855.
- Auer C., Kiefer S., Zuske M., Schindler C., Wyss K., et al. (2018). Health-seeking behaviour and treatment delay in patients with pulmonary tuberculosis in Switzerland: some slip through the net. *Swiss Medical Weekly*. **148**, w14659.
- Baglio G. (2015). Tuberculosis and immigration: the answers that epidemiology can provide (and society is waiting for). *Epidemiologia e Prevenzione*. **39**, 73-74.
- Bloom B.R., Atun R., Cohen T., Dye C., Fraser H., et al. (2017). Tuberculosis. In: K.K. Holmes, S. Bertozzi, B. R. Bloom BR, & P. Jha, editors. Major Infectious Diseases. 3rd edition. Washington (DC): The International Bank for Reconstruction and Development/The World Bank.
- Cacciani L., Bargagli A.M., Marino C., Agabiti N., Canova C., et al. (2019). Ospedalizzazione: confronto tra popolazione italiana e immigrata nelle coorti della rete italiana degli studi longitudinali metropolitani. [Hospitalisation: a comparison among Italians and immigrants enrolled in the cohorts of the 43 (Suppl. 1): 1-80.
- Campogiani L., Compagno M., Coppola L., Malagnino V., Maongelli G., et al. (2020). Tuberculosis-Related Hospitalizations in a Low-Incidence Country: A Retrospective Analysis in Two Italian Infectious Diseases Wards. *International Journal of Environmental Research and Public Health*. **17**, 124.
- Demo ISTAT. (2019). Statistiche demografiche. Cittadini stranieri 2019-città metropolitana di Messina. Retrieved from <https://www.tuttitalia.it/sicilia/provincia-di-messina/statistiche/cittadini-stranieri-2019/>
- Epicentro. (2019a). Tubercolosi. Aspetti epidemiologici. Retrieved from <https://www.epicentro.iss.it/tubercolosi/epidemiologia>
- Epicentro. (2019b). Migranti e salute. I numeri in Italia. Retrieved from www.epicentro.iss.it/migranti/numeri-italia
- Epicentro. (2020). Osservatorio Nazionale Alcol. SISMA: Sistema di Monitoraggio Alcol-Correlato. Indicatori SISMA 2016. Retrieved from <http://www.epicentro.iss.it/alcol/SismaMonitoraggio>
- European Center for Disease Control and Prevention. (2019). Tuberculosis surveillance and monitoring in Europe. Solna, Sweden: European Center for Disease Control and Prevention. Retrieved from https://www.ecdc.europa.eu/sites/default/files/documents/tuberculosis-surveillance-monitoring-Europe-2019-20_Mar_2019.pdf
- Facciola A., Palamara M.A.R., D'Andrea G., Marano F., Magliarditi D., et al. (2018). Brucellosis is a public health problem in southern Italy: Burden and epidemiological trend of human and animal disease. *Journal of Infection and Public Health*. **11**, 861-866.
- Facciola A., Visalli G., Antonuccio G., Fedele F., Nunnari G., et al. (2020). Epidemiology of the new HIV infections in a large university hospital of Southern Italy: the importance of increasing the culture of the HIV screening test in the prevention of late diagnosis. *Epidemiologia e Prevenzione*. **44**, 235-242.
- Feleke B.E., Feleke T.E., Biadlegne F. (2019). Nutritional status of tuberculosis patients, a comparative cross-sectional study. *BMC Pulmonary Medicine*. **19**, 182.
- Floyd K., Glaziou P., Zumla A., Raviglione M. (2018). The global tuberculosis epidemic and progress in care, prevention, and research: an overview in year 3 of the End TB era. *Lancet Respiratory Medicine*. **6**, 299-314.
- Golli A.L., Nițu M.F., Turcu F., Popescu M., Ciobanu-Mitrache L., et al. (2019). Tuberculosis remains a public health problem in Romania. *International Journal of Tuberculosis and Lung Disease*. **23**, 226-231.
- Kwan C.K., Ernst J.D. (2011). HIV and tuberculosis: a deadly human syndrome. *Clinical Microbiology Reviews*. **24**, 351-376.
- Lönnroth K., Mor Z., Erkers C., Bruchfeld J., Nathavitharana R.R., et al. (2017). Tuberculosis in migrants in low-incidence countries: epidemiology and intervention entry points. *International Journal of Tuberculosis and Lung Disease*. **21**, 624-637.
- Ministero della Salute. (1991). Decreto Ministeriale 15 dicembre 1990. Sistema informativo delle malattie infettive e diffusive. Gazzetta Ufficiale 8 gennaio 1991, n. 6. Retrieved from http://www.salute.gov.it/imgs/C_17_normativa_1357_allegato.pdf
- Ministero della Salute. (2018). Notiziario dell'Istituto Superiore di Sanità. Aggiornamento delle nuove diagnosi di infezione da HIV e dei casi di AIDS in Italia al 31 dicembre 2017. Retrieved from http://www.salute.gov.it/imgs/C_17_notizie_3557_listaFile_itemName_0_file.pdf
- Nițu F.M., Olteanu M., Strebă C.T., Jimborean G., Postolache P., et al. (2017). Tuberculosis and its particularities in Romania and worldwide. *Romanian Journal of Morphology and Embryology*. **58**, 385-392.
- Pacelli B., Caranci N., Di Girolamo C., Broccoli S., Canova C., et al. (2019). Mortalità: confronto tra popolazione italiana e immigrata nelle coorti della rete italiana di studi longitudinali metropolitani. [Mortality: a comparison between Italian and immigrant population in the Italian Network of Longitudinal Metropolitan Studies]. *Epidemiologia e Prevenzione*. **43**, (Suppl. 1): 34-45.
- Palamara M.A.R., Visalli G., Picerno L., Di Pietro A., Puglisi G., et al. (2018). Measles outbreak from February to August 2017 in Messina, Italy. *Journal of Preventive Medicine and Hygiene*. **59**, E8-E13.
- Pareek M., Greenaway C., Noori T., Munoz J., Zenner D. (2016). The impact of migration on tuberculosis epidemiology and control in high-income countries: a review. *BMC Medicine*. **14**, 48.
- Riccardi N., Pontarelli A., Alagna R., Saderi L., Ferrarese M., et al., for StopTB Italia Onlus Group. (2019). Epidemiology and treatment outcome of MDR and pre-XDR TB in international migrants at two reference centers in the North of Italy: a cross-sectional study coordinated by Stop TB Italia Onlus. *Public Health*. **180**, 17-21.
- Scotto G., Fazio V., Lo Muzio L. (2017). Tuberculosis in the immigrant population in Italy: State-of-the-art review. *Le Infezioni in Medicina*. **25**, 199-209.
- Simou E., Britton J., Leonardi-Bee J. (2018). Alcohol consumption and risk of tuberculosis: a systematic review and meta-analysis. *International Journal of Tuberculosis and Lung Disease*. **22**, 1277-1285.
- Tattevin P., Che D., Fraisse P., Gatey C., Guichard C, et al. (2012). Factors associated with patient and health care system delay in the diagnosis of tuberculosis in France. *International Journal of Tuberculosis and Lung Diseases*. **16**, 510-5.
- Uplekar M., Weil D., Lonnroth K., Jaramillo E., Lienhardt C., et al., for WHO's Global TB Programme. (2015). WHO's new end TB strategy. *Lancet*. **385**, 1799-1801.
- Visalli G., Facciola A., Carnuccio S.M., Cristiano P., D'Andrea G., et al. (2020). Health conditions of migrants landed in north-eastern Sicily and perception of health risks of the resident population. *Public Health*. **185**, 394-399.
- World Health Organization. (2014). Tuberculosis. WHO's End TB Strategy. Geneva, Switzerland: World Health Organization. Retrieved from https://www.who.int/tb/post2015_strategy/en/
- World Health Organization. (2019). Global tuberculosis report 2019. Geneva, Switzerland: World Health Organization. Retrieved from <https://apps.who.int/iris/bitstream/handle/10665/329368/9789241565714-eng.pdf?ua=1>