

ORIGINAL ARTICLE

Impact of immigration on burden of Tuberculosis in Umbria: a low-incidence Italian region with high immigrants rates

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Key words

Tuberculosis • Surveillance • Epidemiology

Summary

Introduction. In Italy, Tuberculosis (TB) has increasingly become a disease for specific population subgroups such as immigrants. The objective of this paper is to describe the trend in TB incidence from 1999 to 2008 in Umbria: a low-incidence Italian region with high immigrants rates.

Methods. Data were obtained from the Regional Information System for Infectious Diseases. Using a linear regressions model we estimated trends for number of cases and incidence rates; with a logistic regression model we estimated the effect of a set of covariates on the probability of being affected by TB.

Result. 590 TB cases were reported of whom 254 (43%) were foreign. In 2008 39.7 new cases per 100.000 were registered

among foreign-born subjects. TB incidence among Italians was 3.8/100.000 Italians. But a linear regression analysis showed a statistically significant decreasing trend in the notification rate among foreign-born people (coef: -7.32, $r^2:0.57$, $p < 0.05$). The probability to be affected by extra-pulmonary is significantly larger in foreign patients (OR = 0.72, CI = 0.48-1.07). Foreign unskilled workers report a higher probability to be affected by TB (OR = 19.05, CI = 6.01-60.4).

Discussion. Increasing immigration rates may affect TB epidemiology. The analysis of incidence trends is an important tool for monitoring tuberculosis disease control and to identify specific sub-group at risk.

Introduction

During the last 50 years, the improvement of socio-economic, hygienic and therapeutic conditions have allowed a progressive decrease in the incidence of Tuberculosis (TB) in industrialized countries [1, 2]. However, the increase in HIV, the appearance of new marginalized people, especially in some urban areas and, in particular, immigration from high TB incidence countries have recently contributed to reverse this downward trend [3, 4]. In 2006, in the United States 57% of all reported TB cases were among foreign-born persons and in 2007 the TB case rate for foreign-born persons was 9.9 times greater than the rate for US-born persons [5, 6]. In most European countries there was a steady decline in the number of notified cases of native-born between 2001 and 2008, whereas case notifications of foreign-born generally increased, especially in lower-incidence countries [7]. In 2008 TB incidence among Italians was 3.8/100.000 Italians, TB incidence among foreign born persons was 52.1/ 100.000. The annual proportion of foreign-born cases on the total TB notifications increased from 20.3% in 1999, to 48.7% in 2008 [8, 9]. As the global burden of TB falls principally on developing countries, estimates of the role of immigration on the epidemiology of TB in low-prevalence countries are important for the design of appropriate strategies in disease control.

In this paper, the aim is to describe the trend in tuberculosis incidence from 1999 to 2008 in the central Italian region Umbria, highlighting the main differences in TB incidence between native-born and not Italy-born in this Region featured by a high immigration rate.

Methods

We conduct a retrospective study within the Surveillance System for Infectious Diseases in Umbria, a region with about 900.000 inhabitants and about 10% of resident immigrants, the second highest Italian Region for presence of foreign [8]. Data were obtained from the Regional Information System for Infectious Diseases, based on mandatory physician notifications. From the database, we extracted year of notification, gender, age, citizenship, occupational status, professional position, sector of activity of patients and the site of the disease (pulmonary, extra-pulmonary and disseminated). Data on HIV co-infection of incident cases could contribute significantly to TB surveillance, but it would be required record linkage between two independent data sources. Foreign-born were differentiated in “regularly registered” and “not regularly registered”. Not regularly registered have been estimated according to the procedure reported in the report on foreigners’ health status in 2007 of the National Observatory of health at regional level [10], that

Tab. I. TB total cases and shares according to origin of patients by site of disease, Umbria region, Italy: 1999-2008.

Year	Italy		Not Italy		Total	Pulmonary			Extra-pulmonary			Disseminated		
	nr.	%	nr.	%		nr.	%	%	%	nr.	%	%	nr.	%
1999	55	79.7	14	20.3	69	70.9	57.1	68.1	25.5	42.9	29.0	3.6	0.0	2.9
2000	52	63.4	30	36.6	82	75.0	56.7	68.3	25.0	40.0	30.5	0.0	3.3	1.2
2001	38	54.3	32	45.7	70	78.9	78.1	78.6	21.1	15.6	18.6	0.0	6.3	2.9
2002	23	52.3	21	47.7	44	78.3	61.9	70.4	21.7	38.1	29.6	0.0	0.0	0.0
2003	30	50.9	29	49.1	59	50.0	89.7	69.5	50.0	10.3	30.5	0.0	0.0	0.0
2004	30	57.7	22	42.3	52	70.0	81.8	75.0	23.3	13.6	19.2	6.7	4.6	5.8
2005	20	45.5	24	54.5	44	80.0	95.8	88.6	20.0	0.0	9.1	0.0	4.2	2.3
2006	31	59.6	21	40.4	52	67.7	81.0	73.1	25.8	14.3	21.2	6.5	4.8	5.8
2007	26	45.6	31	54.4	57	88.5	80.7	84.2	11.5	12.9	12.3	0.0	6.5	3.5
2008	31	50.8	30	49.2	61	67.7	76.8	72.1	25.8	23.3	24.6	6.5	0.0	3.3
Total	336	56.9	254	43.1	590	72.3	76.8	74.2	25.3	20.1	23.1	2.4	3.2	2.7

considered irregular immigrants to be 20% of regular ones for every year, except for 2003, when a national decree massively legitimized irregular immigrants, where it was considered to be 10% of the regular ones. We compared odd-ratios according to origin of patients by age group (0-19, 20-39, 40-59, 60-79 and 80 years or more), type of profession (skilled and unskilled workers) and occupational status (occupied, unemployed and retired). For each comparison we performed a chi-squared test to check for the presence of heterogeneous odd-ratios. Moreover, we calculated: number of TB cases, shares of pulmonary, extra-pulmonary and disseminated TB, and incidence rates (/100.000 population per year) for both the groups of patients. We also estimated trends for number of cases and incidence rates using a linear regressions model. We report the estimated coefficients, their confidential intervals (95% Confidence Interval [CI]) and a p-value labelling the observed significance level for the t-statistic. Since information about individuals not affected by TB was not collected in our original sample, we also use the “Everyday Life Aspects” (ELA), conducted by the National Statistical Institute (ISTAT) to retrieve information for healthy individuals. We extracted from the entire dataset only those observations corresponding to Umbria region for the years 2002-2008, with exception for 2004, year in which the ELA survey was not conducted. Using a logistic regression model, we estimated the effect of a set of covariates on the probability of being affected by TB for native-born and foreign-born groups. Statistical analysis was performed using Stata (Version 12).

Results

Over the decade examined (1999-2008) a total of 590 TB cases notified were reported. Overall 333 (56.4%) of 590 patients with TB are male, 219 (37%) are ≥ 60 year old and the median age is of 47 years in the entire sample; 254 (43.1%) cases were foreign-born. The

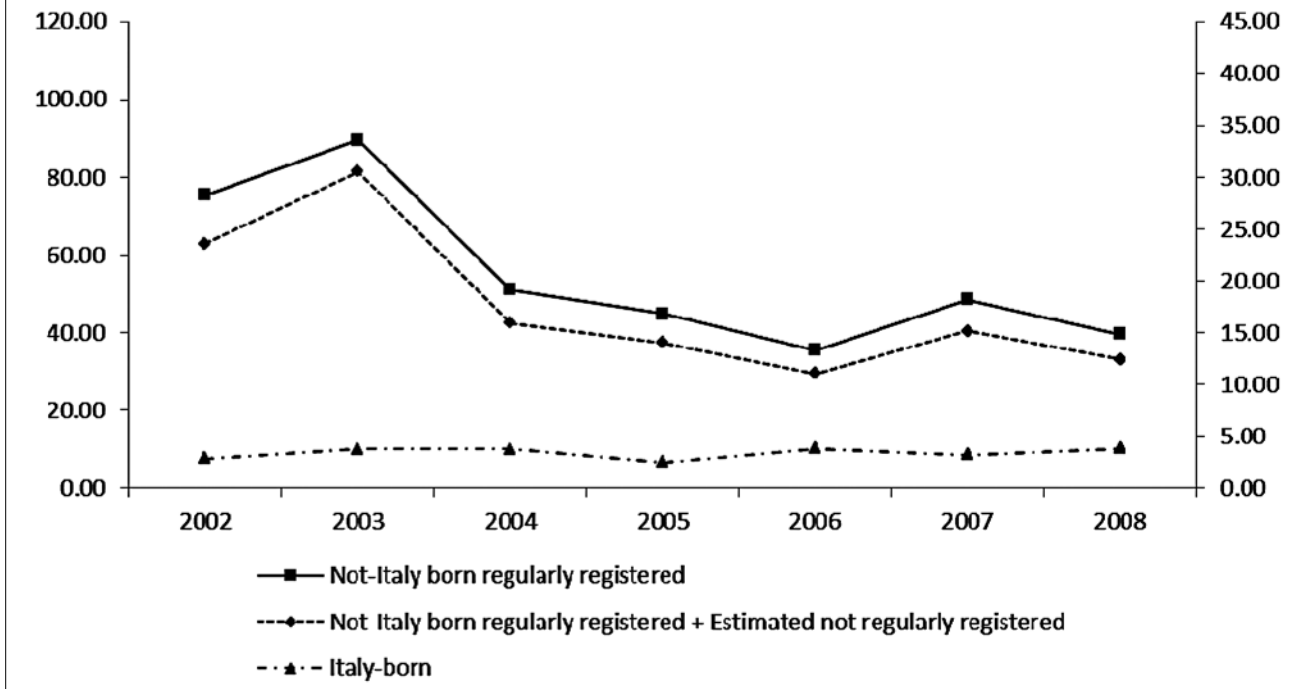
Tab. II. Trend of TB cases and incidence rate according to origin of patients.

	TB case		TB Incidence rate	
	Coef	R ²	Coef	R ²
Italy-born	-2.68** (1.00)	0.49	0.07 (0.073)	0.50
Not Italy-born	0.59 (0.741)	0.09	-7.32** (2.144)	0.57
Total	-2.08 (1.157)	0.27	0.12 (0.125)	0.38

Standard errors in parentheses
 *** p < 0.01, ** p < 0.05, * p < 0.1

median age of foreign-born individuals is of 31 years, much lower than that reported by Italy born subjects, 66 years. 73.7% of not-Italy-born cases were aged 15–39 years, compared to 17.9% of native-born cases. 74.2% of reported TB cases was diagnosed with pulmonary disease, 23.1% had a diagnosis of extra-pulmonary TB and only 2.7% with disseminated TB. Extra-pulmonary TB was light common among Italian patients (Tab. I). Total TB cases were, on average, 59 per year and no significant time trends were found. Foreign-born TB subjects showed an increase of 114.3% during the study period (from 14 in 1999 to 30 in 2008). The annual proportion of not Italy-born cases on the total TB notifications increased from 20.3% in 1999, to 49.2% in 2008. Over the last four years the proportion of foreign born cases has reached that of native-born and in 2005 and 2007 also reported higher values (54.6% and 54.4% respectively) (Tab. I). But a linear regression analysis showed a statistically significant decreasing trend in the number of not Italy-born cases (coef: -2.68, r²:0.09, p < 0.05) and a concurrently statistically significant decreasing trend in the incidence rate among foreign-born people (coef: -7.32, r²:0.57, p < 0.05) (Tab. II).

Fig. 1. TB incidence rates (/100.000 population per year) in the Italy born (left scale) and not-Italy born (right scale) population: denominators with and without estimated not regularly registered presences. Umbria region, Italy: 1999-2008.



TB incidence rate for the whole population decreased from 8.4 new cases /100.000 inhabitants in 2002 to 6.9 in 2008. TB incidence was found to be higher for the not-Italy born population. In 2008, 39.7 new cases per 100.000 were registered among foreign-born subjects and 33.1/100.000 adding 20% of estimated irregular presences to the denominator. TB incidence among Italians was 2.9 /100.000 population in 2002 and 3.8 in 2008 (Fig. 1). This difference remained when rates were standardised for age group and sex ranging from 3.6 to 5.0/100.000 for native born males and 76.0 to 29.9/100.000 for foreigner males and from 1.9 to 2.4/100.000 for native females and 69.1 to 44.8/100.000 for foreigner females (data not showed).

In tables 3 we report odd-ratios for site of disease according to origin of patients by age group, type of profession and occupational status. It shows that native-born subjects aged 0-19 present a significantly higher probability to contract pulmonary TB compared to foreigners (Odds Ratio [OR]: 0,17; CI 95% 0,02-1,55). Extra-pulmonary TB, instead, seem to be more associated with young age classes of immigrants (0-19 and 20-39), where number of cases is also consistently larger (OR: 6,00; CI 0,64-55,95). We also report odd-ratios for site of disease according to origin of patients by type of profession (manual and non-manual). For each site, the majority of TB cases are recorded by manual workers. The probability to be affected by pulmonary TB is smaller, but not significantly different, for Italian patients (OR = 1.29, CI = 0.88-1.91). The probability to be affected by extra-pulmonary TB, instead, it is found to be significantly larger in foreign patients (OR = 0.72, CI = 0.48-1.07). Finally we distinguish between employed, unemployed and retired individuals. In this case, no significative

differences are found between Italy born and not-Italy born subjects, but the retired group confirmed, as previously highlighted for the age classes, that the elder Italian population is more likely affected by pulmonary TB compared to foreigners (OR = 0.43, CI = 0.12-1.56) and that the opposite result holds in case of extra-pulmonary TB (OR = 2.55, CI = 0.71-9.14). For the other groups, respectively employed and unemployed, only the unemployed seem to report some differences in the probabilities to be affected by pulmonary (OR = 1.46, CI = 0.67-3.19) and extra-pulmonary TB (OR = 0.59, CI = 0.26-1.32). Moreover, we compared TB cases, for native-born and foreign-born separately, with the average individual living in Umbria. Table IV reports the coefficients from the logit model on the probability to be affected by TB conditioned on some socio-demographics characteristics and the associated odds-ratio. The coefficients estimated using the Italy born sub-sample increase their magnitude with age of patients and turn from negative to positive in correspondence of the reference age class (40-59) with associated odds-ratio respectively lower than one for age classes below and greater than one for age classes above the reference age class. Italian patients belonging to age classes 0-19, 60-79 and ≥ 80 years have respectively a probability of 0.15, 2.05 and 5.32 times higher to contract TB, respect to the reference age class. Only the 20-39 age class shows a non-significant coefficient. Foreign born subjects present a quite different relation between age classes and the probability to be affected by TB. In this case, the coefficients associated with age classes tend to decrease with age, the highest probability of contracting the disease is estimated in correspondence of individuals with 20-39 years, 2.69 times higher to be affected by TB. After this threshold the probability

Tab. III. Odd ratios for site of disease according to origin of patients (not Italy born/Italy born) by age group, type of profession and occupational status.

Age group (years)	Pulmonary TB			Extra-Pulmonary TB			Disseminated TB		
	Not Italy born	Italy-born	OR 95% CI	Not Italy born	Italy-born	OR 95% CI	Not Italy born	Italy-born	OR 95% CI
Age group									
	N	N		N	N		N	N	
0-19	14	12	0.17* (0.02-1.55)	7	1	6.00* (0.64-55.95)	0	0	-
20-39	131	38	0.80 (0.35-1.79)	31	8	1.09 (0.46-2.56)	8	1	2.27 (0.28-18.6)
40-59	40	58	1.48 (0.55-3.95)	7	14	0.74 (0.27-1.99)	0	1	-
60-70	9	93	1.14 (0.33-3.89)	4	41	1.07 (0.31-3.68)	0	6	-
≥ 80	1	42	0.25 (0.02-2.92)	2	21	4.00 (0.34-46.68)	0	0	-
Total	195	243	1.29 (0.88-1.91)	51	85	0.79 (0.54-1.16)	8	8	1.33 (0.49-3.60)
Type of profession									
	N	N		N	N		N	N	
Non-manual	4	29	-	0	6	-	0	1	-
Manual	191	214	1.3 (0.89-1.91)	51	79	0.72* (0.48-1.07)	8	7	1.38 (0.49-3.87)
Total	195	243	1.29 (0.88-1.91)	51	85	0.79* (0.54-1.16)	8	8	1.33 (0.49-3.60)
Occupational status									
	N	N		N	N		N	N	
Employed	101	69	1.26 (0.64-2.51)	19	16	0.82 (0.4-1.71)	3	3	0.71 (0.14-3.59)
Unemployed	76	26	1.46 (0.67-3.19)	23	13	0.59 (0.26-1.32)	5	1	1.97 (0.22-17.4)
Retired	5	136	0.43 (0.12-1.56)	5	55	2.55* (0.71-9.14)	0	4	-
Total	182	231	1.26 (0.87-1.84)	47	84	0.74* (0.50-1.10)	8	8	1.33 (0.49-3.60)

Note: Non-manual workers category: managers and white collars, entrepreneurs and self-employed. Manual workers category: blue collars, other employed and self-employed workers.

Tab. IV. Logit model Coefficients and Odds Ratio for TB cases.

VARIABLES	(1) Not Italy-born			(2) Italy-born		
	Coeff.	Odds-ratio	CI 95%	Coeff.	Odds-ratio	CI 95%
Male	0.17 (0.189)	1.18 (0.22)	[0.82;1.71]	1.96*** (0.237)	7.13*** (1.689)	[4.48;11.34]
0-19	-0.90** (0.375)	0.41*** (0.152)	[0.19;0.85]	-1.89*** (0.497)	0.15*** (0.075)	[0.06;0.4]
20-39	0.99*** (0.221)	2.69*** (0.596)	[1.75;4.16]	-0.50 (0.315)	0.61 (0.191)	[0.33;1.13]
60-79	-1.37*** (0.425)	0.25*** (0.107)	[0.11;0.58]	0.72*** (0.252)	2.05*** (0.516)	[1.25;3.36]
≥ 80	-2.09** (1.021)	0.12*** (0.125)	[0.02;0.92]	1.67*** (0.291)	5.32*** (1.551)	[3.01;9.43]
Unskilled worker	2.95*** (0.589)	19.05*** (11.215)	[6.01;60.4]	0.30 (0.302)	1.35 (0.408)	[0.75;2.45]
Retired	-1.39** (0.597)	0.25*** (0.148)	[0.08;0.8]	3.56*** (0.251)	35.21*** (8.851)	[21.61;57.72]
Unemployed	1.42*** (0.202)	4.13*** (0.833)	[2.78;6.13]	1.74*** (0.353)	0.74 (0.225)	[2.86;11.39]
Constant	-7.06*** (0.629)			-6.80*** (0.388)		
Observations		7,909			7,912	
Pseudo R-squared		0.187			0.259	

Standard errors in parentheses

*** p < 0.01, ** p < 0.05, * p < 0.1

decreases to 0.25 and 0.12 times for elder individuals (50-79 and ≥ 80 respectively). According to the other socio-demographics characteristics considered we can highlight the following differences: male individuals are more likely to be affected by TB in the Italy-born sample (OR = 7.13, CI = 4.48-11.34), while in the not-Italy born sample have the same probability as females; unskilled workers present a higher probability to be affected by TB than skilled ones. Moreover, not-Italy unskilled workers report a higher probability (OR = 19.05, CI = 6.01-60.4) than Italy born ones (OR = 1.35, CI = 0.75-2.45). The retired group has a much higher probability of contracting the disease in the Italy born subjects (OR = 35.21, CI = 21.61-57.72) than in the not-Italy born subjects (OR = 0.25, CI = 0.08-0.8). Unemployment is significant only for the foreign-born group, reporting a higher probability to be affected by TB (OR = 4.13, CI = 2.78-6.13).

Discussion

Regional TB incidence rate estimation (in 2008: 6.9 cases per 100.000 population in Umbria) is quite lower than other northern and central region and Italy (Italian mean 7.4 cases per 100.000 population) [11-13]. In developed countries, TB has increasingly become a disease for specific population subgroups; in particular, immigrants are a population group at risk and their presence may affect the TB epidemiologic situation in host countries [4, 12, 14]. The increase of foreign-born TB cases in Umbria region appears to be correlated with progressively increased immigration, while in aggregate TB incidence has shown a progressive reduction. Our results are in accordance with trends at the national level [10, 13] and the demographic characteristics of non- Italy-born and Italy-born cases differed, reflecting the differing epidemiology of disease in these populations. This study provides a clear description of the current epidemiology of TB in foreign-born people in Umbria, which will help inform appropriate public health action and health service provision. During 2005-2008, 49.5% of TB cases in Umbria were foreign born, yet this group constituted only 7.3% of the population. This trend is partly explained by the decreasing number of cases in the indigenous population, but also by migration patterns and the changing global epidemiology of TB. Given that the immigrants increase in Umbria by 171% from 2002 to 2008, it is possible to explain the increasing risk of TB in this area of Italy. This effect is not even completely under control although in Umbria TB incidence in foreign born population decreased in the last years. It is known that incidence among the not-Italy born is likely to largely reflect the prevalence of disease in their country of origin. Other factors such as the conditions of migration and socio-economic conditions could make ethnic-minority groups living in less-deprived areas still at higher risk of disease. Immigration conditions in the host country is often indicative of living in crowded places, being homeless or in prison, all well-known risk factors for TB infection, reactivation, transmission and TB disease progression [15, 16].

Limitations in estimating TB incidence must be mentioned. Denominators for the immigrant population which only considers documented foreign-born subjects in Umbria (not including immigrants without a legal residence permit) leads to overestimate TB incidence. TB incidence rates decreased, in fact, adding the estimate of irregular presences to the denominator (Fig. 1).

But not regularly registered immigrants are not easily quantified and no official data are available in the Umbria region. In addition, differentiating between native-born and foreign-born cases doesn't allow including young foreigners who were born in Italy. This study being based on notified cases, as a unique source of information, is another limiting aspect. Although the surveillance system is considered efficient in Italy, it can be hampered by under-reporting and inconsistency. Most interestingly, even if healthcare assistance is offered also to "not regularly registered" immigrants, foreign-born subjects without legal residence permit might be reluctant to access to healthservice, this attitude leading to underestimation of TB cases and being a matter of public health concern [17]. In our study, as reported in other developed areas [15, 18, 19], TB among immigrants is mostly found in young adults. This could be partially linked to the immigration of predominantly young people but it also reflects true epidemiologic differences in TB patterns of transmission in low-incidence countries like Italy and countries of origin of immigrants. In this context, it is more complex to demonstrate whether TB in immigrants is a consequence of an infection acquired in the country of origin [18, 20] or in the host country [21, 22], as specific molecular investigations are needed but were not available for this study.

Relating to TB disease sites, differences in the likelihood of extra pulmonary TB depending on immigration status remain largely unclear [23]. Available data show a significant higher risk of extra pulmonary TB for immigrants in the age group 0-19 and 20-39 years (Tab. III). One aspect for concern is that extra pulmonary TB forms are more likely to be under-reported or not suspected by health specialists often inadequately trained in TB diagnosis.

According to European Action Plan to fight Tuberculosis, new recommendations for TB control activities were also developed in Italy and in Umbria Region. It aimed to tackle the increase in tuberculosis, and to outline measures for control including better clinical services, screening and surveillance. The delayed effect between infection and progression to disease means that cases detected by screening for tuberculosis in migrants before (pre-entry) or upon entry to Italy are likely to account for only a small proportion of all cases diagnosed in foreign-born populations. The evidence from numerous studies suggests that a one-off approach of new entrant screening for active disease is likely to be of limited value. This emphasises the need for communities and health care practitioners to maintain awareness of the risk of TB, not only in recent entrants, but also among those who have been resident for many years and minority ethnic groups. Prompt diagnosis and effective treatment remain priorities in terms of TB control for all persons, irrespective of their country of origin or migration status.

Conclusions

TB surveillance among specific at-risk subgroups should be made a priority as immigration flow to Italy is increasing at a fast rate. In Umbria despite the clear gap,

we recorded an impact of TB lower than the national average both in the native population than in foreigners. This is probably due to the particular demographic aspects of Umbria region (such as absence of metropolitan areas) and to its organization of the public health system.

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