Epidemiological trend in tuberculosis in the Italian region of Liguria: Impact of immigration and AIDS

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Background: Tuberculosis (TB) uniformly decreased in all industrialized countries from 1950 to 1985. However, since 1985 an upsurge of the disease has been observed, probably due to the increases in AIDS and immigration. It is for this reason that in the last decade all industrialized countries have intensified their controls on TB and a new reduction has been recently observed. Methods: In this study we collected epidemiological data (mortalities and reported cases) for the region of Liguria over the last 15 years. We then calculated the incidence rate of TB per 100,000 residents according to age, HIV infection and nationality, making a distinction between European Union (EU) citizens and immigrants coming from countries outside the EU. Results: The rate of mortality, after the last peak at the end of the Second World War, has progressively decreased from 1946 to today, so much so that presently we record fewer than two cases per 100,000 people. We observed a consistent downward trend in the incidence rate up to 1987, but from 1988 onwards this trend stopped and, in subsequent years, we detected an increase in the incidence rate, which peaked in 1996. This led to increased interventions, which has resulted in a considerably decreased overall rate of cases of TB during the last few years. The number of TB cases specifically among foreigners increased considerably during the last 5 years, whereas there was a drastic reduction in the number of total TB cases, as well as an interesting reduction in AIDS cases. During the same period there was a progressive decrease in tuberculin skin positivity in all school classes. Conclusions: The reduction in TB notifications is probably due to an increase in surveillance and control of social and health conditions. These results show that immigrant workers are considered to be a high-risk group, whereas the risk has progressively decreased in the HIV group.

Keywords: tuberculosis, immigration, AIDS

At the time in which R. Koch isolated the tuberculosis mycobacterium in 1882, tuberculosis (TB) was the top cause of death of all infectious diseases in Europe. During the last 50 years, improved socio-economic, hygienic and therapeutic conditions, especially the discovery of streptomycin (1944), isoniazid (1952) and BCG vaccine, have allowed a progressive decrease in the incidence of TB in all industrialized countries; but this disease is still widespread in non-industrialized countries. Nevertheless, after 1985, the regular decline in TB notifications, as expected from years of observation, seems to have stopped even in industrialized countries. This phenomenon was first reported in the USA where the average annual decline of 5.7%, in the rate of notifications in the 1975–1984 period, stopped in 1985 and reversed in 1986. This could be attributed to the increase in HIV, immigration from countries where TB is common, and to the appearance of new marginalized people, especially in some urban areas. A similar trend was also observed in Europe but only in some countries and especially in urban areas. We have observed a similar trend in Italy as well, especially among 25–44 year olds (drug addicts and people engaging in unprotected sex are considered to be subjects at risk) and among immigrants coming from countries outside the EU where the incidence of TB is high.

It is for this reason that in the last decade all industrialized countries have improved their monitoring of TB and, consequently, a new downward trend, first observed in the USA, continues to be observed in other industrialized countries.

In this study we report the data that we have collected from the region of Liguria, which includes 1,606,400 inhabitants with an immigrant proportion of 3%. The largest city is Genoa, an important Mediterranean port. In addition, it is noted that Genoa has a slightly higher number of AIDS cases with respect to other Italian cities, especially for the presence of many drug addicts.

Methods

We obtained the data on mortality rate from the ‘Italian Tuberculosis Index’ published by the National Statistics Institute. The Italian Tuberculosis Index is essentially a collection of all available data on tuberculosis, in large part obtained from the Italian Ministry of Health. To evaluate the incidence rate we used TB notifications of the Regional Epidemiological Watch, which collects all the notifications from the various existing sources of information in Liguria. Each notification form recorded the patient’s personal data including age, nationality, local Health Unit, and tubercular localization (pulmonary and extra-pulmonary). The TB notifications in the region of Liguria amount to about 4% of all national notifications.

We compared the number of TB cases to the number of residents in order to evaluate the incidence rate per 100,000 people by age, nationality, making a distinction between EU citizens and immigrants coming from outside the EU.
and association with AIDS; however this last comparison was possible only from 1993 when the National Registry of AIDS cases was founded.

To evaluate the prevalence we examined the tuberculin test results among children living in Genoa: 6–7-year-old first-graders and 13–14-year-old eighth-graders from 1986 to 2002. (A similar study of 9-year-old fourth-graders was stopped in 1994 because the results were no longer necessary.) These results are of great importance because, since primary education in Italy is compulsory, the number of children tested represents a very high proportion of children in the area.

These results were obtained from all Public Health Services by means of a form specifically drafted for this study.

All tuberculin tests were initially carried out with the Mérieux test. The cut-off diameters of the tuberculin reaction were 5 mm for the Mérieux test. Monoclonal test results were considered positive if the diameter of the infiltrate was >9 mm.

The collected data were recorded in Microsoft Excel and a $\chi^2$ test was used to assess a significant difference between the cutepositivity of European and non-European immigrant children in the scholastic population during the last 3 years.

**Results**

In figure 1 we compare the mortality rates per 100 000 people in both the region of Liguria as well as Italy in its entirety, from 1935 to 2002. After one final peak at the end of the Second World War, mortality rates have dropped progressively from 1946 to the present day, so much so that nowadays we record fewer than two cases per 100 000 people.

The rate of notifications in Liguria for the period 1986–2002 is reported in figure 2. In previous years there had been a constant decrease from the Second World War up until 1987. In fact, though the rate of notification in 1950 was 140/100 000, in 1956 it dropped to 70/100 000. In 1964 it was already down to 35/100 000; while in 1971 it continued to drop down to 17/100 000; and finally, in 1987 it reached its lowest rate at 8.4/100 000. From 1988, however, this downward trend stopped and, in subsequent years, there was an increase in the incidence rate, peaking in 1996 at 17.3/100 000.

The new TB cases that occurred in Liguria among EU people, immigrants from non-EU countries and AIDS subjects are shown in figure 3. This disease, until 1993, affected mainly EU citizens while only a very small proportion of immigrants from non-EU countries were affected; from that moment on there has been an increasingly larger number of notifications of immigrants from non-EU countries. On the contrary, the association between TB and AIDS, after an increase in the early 1990s, has progressively decreased in the last few years (1996–2002). Therefore, in these last few years, whereas the number of AIDS patients has decreased, the number of new TB cases among immigrants from non-EU countries has increased (~30%).

Moreover, whilst during the period 1970–1987 most of the cases were concentrated among the elderly population, in the last few years a substantial number of new cases has occurred in a younger age group (25–45-year-olds) in addition to those already noted among the elderly. Furthermore, table 1 shows the number of TB notifications by age group among the two subpopulations, EU citizens and non-EU citizens, in 2002.

The tuberculin skin positivity in children living in Genoa from 1986 to 2002 is reported in figure 4. During this 15-year period the rate of prevalence among school children dropped from 1.3% in 1987 to 0.3% in 2002 among 6-year-old children, from 6.5% in 1987 to 0.7% in 2002 among 14-year-old children. The third study group (9-year-old children) was stopped in 1994 due to the dramatically reduced difference in percentages between the 6-year-old group and 14-year-old age group. Table 2 shows the impact of immigrant children from non-EU countries in these age groups in the last 3 years.

**Discussion**

The dramatic decline in tuberculosis in developed countries over the last century is attributed to not only the introduction of effective drugs against TB, but also many other factors, including better social and health conditions, better nutrition, reduced crowding and hospitalization of infected cases in sanatoriums. Even in Italy, as seen in Liguria, the mortality rate, after a final peak at the end of the Second World War, has progressively dropped from 1946 to the present day. So much so, in fact, that in the last 5 years fewer than two cases per 100 000 people are documented; and there is no reason to suspect that they might increase in the immediate future.
of AIDS notifications was one of the highest in Italy (after the regions of Lombardy, Lazio and Emilia Romagna); but in the last 5 years, this association seems to have had less importance.\textsuperscript{16,17} On the contrary, our results suggest that immigration is responsible for the continuous upward trend in TB notifications. In fact, Genoa, the largest city in Liguria, is an important Mediterranean port through which a large number of immigrants coming from South America, Eastern Europe, Africa and Asia reach Italy and Europe. The zone surrounding the port is the old city, where immigrants generally stop before reaching their final destination. The type of life they lead is often unhealthy and poor and so it is very easy for them to succumb to endogenous reactivation or exogenous re-infection. Actually, we have found that it is precisely the arrival of immigrants from non-EU countries that is the most important factor in the inversion of the trend in TB, because the development of the incidence of the disease from 1990 onward is almost entirely correlated with the immigrant population from non-EU countries,\textsuperscript{18} though the indigenous population shows a stable rate. This phenomenon has been described in other Italian cities as well, particularly in Milan and Turin.\textsuperscript{19,20} Furthermore, the predominant immigration of young people explains the modification in age groups; whilst most of the cases were concentrated in the elderly population during the 1946–1985 period, in subsequent years a consistent number of new cases have occurred in a younger age group (25–45-year-olds) in addition to those in the elderly.\textsuperscript{10}

It is for this reason that in 1995 the ‘Organising Committee of the Region of Liguria for the Prevention and Control of Tuberculosis’ approved an operational protocol for the surveillance, prevention and control of TB in Liguria, which has been gradually applied in Genoa and in the entire region of Liguria. This programme has improved the flow of notifications (comparing the notifications with data coming from the laboratories), the control of contacts (establishing a strict cooperation between the Departments), the monitoring of treated patients with active surveillance and a voluntary tuberculin screening for all new immigrants from non-EU countries at their first arrival in Italy.

In addition, new therapeutic methodologies for the treatment of HIV infection, which add newly introduced antiretroviral drugs, have drastically reduced the incidence of AIDS complications, such as TB.\textsuperscript{21}

Actually, our analysis shows a marked reduction in TB notifications among AIDS patients in the last 5 years, but it is interesting to note that in the same period the corresponding number of new TB cases increased among immigrants from South America, extremely high mortality rates are constantly being recorded.\textsuperscript{11–13} Conversely, in many developing countries of Africa, Asia and South America, extremely high mortality rates are constantly being recorded.\textsuperscript{11–13}

The rate of notifications, which had constantly decreased in Liguria from 1946 to 1987, started to increase in 1988 and is still continuing. This trend is similar to the epidemiological data observed from 1984 onwards in the USA and in many other European countries. Many studies have been carried out to explain this inversion in the trend and the most important risk factors that have been observed can be summarized as: association of TB with HIV, immigration from countries where TB is endemic, and the risk of new underprivileged population complications, such as TB.\textsuperscript{21}

The association of TB and HIV has probably contributed only to the upward trend in Liguria, where the rate of notifications among AIDS patients in the last 5 years, this association seems to have had less importance.\textsuperscript{16,17} On the contrary, our results suggest that immigration is responsible for the continuous upward trend in TB notifications. In fact, Genoa, the largest city in Liguria, is an important Mediterranean port through which a large number of immigrants coming from South America, Eastern Europe, Africa and Asia reach Italy and Europe. The zone surrounding the port is the old city, where immigrants generally stop before reaching their final destination. The type of life they lead is often unhealthy and poor and so it is very easy for them to succumb to endogenous reactivation or exogenous re-infection. Actually, we have found that it is precisely the arrival of immigrants from non-EU countries that is the most important factor in the inversion of the trend in TB, because the development of the incidence of the disease from 1990 onward is almost entirely correlated with the immigrant population from non-EU countries,\textsuperscript{18} though the indigenous population shows a stable rate. This phenomenon has been described in other Italian cities as well, particularly in Milan and Turin.\textsuperscript{19,20} Furthermore, the predominant immigration of young people explains the modification in age groups; whilst most of the cases were concentrated in the elderly population during the 1946–1985 period, in subsequent years a consistent number of new cases have occurred in a younger age group (25–45-year-olds) in addition to those in the elderly.\textsuperscript{10}

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<table>
<thead>
<tr>
<th>Age groups</th>
<th>EU %</th>
<th>Non-EU %</th>
<th>Total %</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5</td>
<td>2</td>
<td>1.9</td>
<td>2.5</td>
</tr>
<tr>
<td>5–14</td>
<td>7</td>
<td>6.6</td>
<td>6.9</td>
</tr>
<tr>
<td>15–24</td>
<td>19</td>
<td>17.9</td>
<td>26.4</td>
</tr>
<tr>
<td>25–44</td>
<td>26</td>
<td>24.5</td>
<td>34.1</td>
</tr>
<tr>
<td>45–64</td>
<td>50</td>
<td>47.2</td>
<td>54.9</td>
</tr>
<tr>
<td>&gt;65</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

EU, European Union citizens; Non-EU, non European Union citizens; % = (notifications by age group/total notifications) × 100.

Table 2 Impact of immigrant children from non-EU countries in the two studied age groups during the 3-year period 1999–2002

<table>
<thead>
<tr>
<th>Primary school (6–7-year-old children)</th>
<th>Non-EU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Examined</td>
<td>Positives</td>
</tr>
<tr>
<td>1999–2000</td>
<td>3886</td>
</tr>
<tr>
<td>2000–2001</td>
<td>4853</td>
</tr>
<tr>
<td>2001–2002</td>
<td>4622</td>
</tr>
<tr>
<td>Total</td>
<td>14 361</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Secondary school (13–14-year-old children)</th>
<th>Non-EU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Examined</td>
<td>Positives</td>
</tr>
<tr>
<td>1999–2000</td>
<td>4205</td>
</tr>
<tr>
<td>2000–2001</td>
<td>4788</td>
</tr>
<tr>
<td>2001–2002</td>
<td>4461</td>
</tr>
<tr>
<td>Total</td>
<td>13 454</td>
</tr>
</tbody>
</table>

EU, European Union citizens; Non-EU, non European Union citizens; % = (cutipositive children/examined children) × 100.

Figure 4 Cutipositivity in Genoan schoolchildren from 1986 to 2002

Examined Positives % Examined Positives %

EU Non-EU

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non-EU countries. These results are similar to those reported in the USA, in most developed Western European countries and in some Eastern European countries, where the rate of incidence of TB has noticeably decreased.\(^{16,17}\) Conversely, in the last few years the worldwide incidence of TB has increased.\(^{22,23,24}\)

Regarding the lower age groups, up to 2002, the data on TB control among children confirm a downward trend that suggests a low risk of transmission in this category. Nevertheless, the rate of skin positivity in children of immigrants from non-EU countries is higher than in EU children. This tendency mainly affects eighth-graders (13–14-year-olds, \(P < 0.001\)) where skin positive results are 15 times higher. However, even among the younger children (6–7-year-olds, \(P < 0.02\)), skin positive results are almost 10 times higher in children of immigrants from non-EU countries.

In conclusion, our analysis indicates that many factors have had an effect on the decline in tubercular morbidity over the last century; but this downward trend stopped in many countries during the 1980s. This change was attributed to several factors, such as the HIV epidemic, new migration flows, the growing problem of the homeless and a reduction in control programmes. Due to the growing number of TB cases that have occurred in the last few years, officials have focussed their attention on better surveillance, prevention and control of this disease. This has resulted in a decrease in notifications both in Italy and in western countries. Nevertheless, the developed nations need to invest more resources in TB control in the high TB incidence countries where many immigrants originate, for reasons of both self-interest and solidarity.\(^{25}\)

**Acknowledgements**

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**Key points**

- TB epidemiological data (mortalities and notifications) in the region of Liguria during the last 15 years are reported.
- From 1987 onwards TB incidence rate increased from 8.4/100,000 to 17.3/100,000 in 1996.
- Authorities in 1995 have approved an operational protocol to improve surveillance, prevention and control of TB in Liguria.
- From 1997 to today, a marked reduction in all TB notifications and among AIDS patients was recorded, but new TB cases has increased among immigrants.
- An improvement in surveillance and control of social and health conditions of high-risk groups like immigrant workers is encouraged.

**References**


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