Tuberculosis among South American immigrants in São Paulo municipality: an analysis in space and time

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S U M M A R Y

O B J E C T I V E : To identify spatial and temporal, and spatial variation in temporal trends in clusters of tuberculosis (TB) among South American migrants residing in São Paulo municipality, SP, Brazil, between 2006 and 2013.

D E S I G N : An ecological descriptive study was conducted using data obtained from official TB reports and the 2010 Brazilian demographic census. Clusters were identified using scan statistics and SaTScan software; those with $P < 0.05$ were considered statistically significant. Social and economic characteristics of residents within the clusters were investigated.

R E S U L T S : One high-risk spatial cluster (relative risk [RR] 4.46, $P < 0.001$) for TB was identified. Bolivian immigrants comprised the majority of immigrants residing in this area. One purely temporal high-risk cluster was identified between 2011 and 2013 (RR 1.55, $P = 0.001$). In one of the spatial variation in temporal trends clusters, the annual increase in TB incidence was 17.54% inside the cluster and 5.17% outside.

C O N C L U S I O N S : We found areas of high risk for TB among South American immigrants. These areas and those with increasing trends of TB incidence must be prioritised by TB control programmes.

K E Y W O R D S : epidemiology; geographical analysis; low- and middle-income countries

OVER THE PAST FEW DECADES, middle-income countries such as Brazil have attracted an increasing number of immigrants.[1] In these developing areas, immigration, together with rapid industrialisation and high population density, has worsened the problem of tuberculosis (TB) as a public health issue.[2] In Brazil, the São Paulo municipality receives the majority of immigrants from other South American countries,[3] most of whom work and live in a precarious situation and are unable to afford a balanced diet, making them vulnerable to contracting TB.[4] The annual incidence of TB in São Paulo is high (51.1 per 100 000 population), with most new cases occurring among vulnerable populations such as immigrants.[5] The detection of high-risk areas for TB is therefore an essential tool in surveillance, and for planning control and prevention interventions.[6]

We hypothesised that TB distribution among South American immigrants follows heterogeneous spatial and temporal patterns. The present study therefore aimed to identify spatial and temporal clusters and spatial variation in temporal trends clusters of TB in the immigrant population of São Paulo during 2006–2013.

METHODS

Study area and population

This ecological descriptive study was conducted in São Paulo, the capital of São Paulo State, located in the south-east region of Brazil (Figure 1). In 2016, the municipality had an estimated population of 12 038 175,[7] making it the most populous municipality in the southern hemisphere and the most economically important in Brazil.[8] São Paulo is a very heterogeneous metropolis with many contrasts and substantial social and health inequalities.[9]

The study population comprised all new cases of TB reported from 2006 to 2013 occurring in South American immigrants residing in São Paulo. It is worth noting that 91.5% of the total number of immigrants diagnosed with TB in this period were from South America.

A new case of TB was defined as a patient with no history of previous TB who was either newly diagnosed with TB or was identified as being within a 30-day period of having initiated anti-tuberculosis medication.[10] South American immigrants were identified as those being of 'South American' nationality on the TB notification form. Patients whose diagnosis was changed from TB to another diagnosis were excluded. As prison inmates are subject to
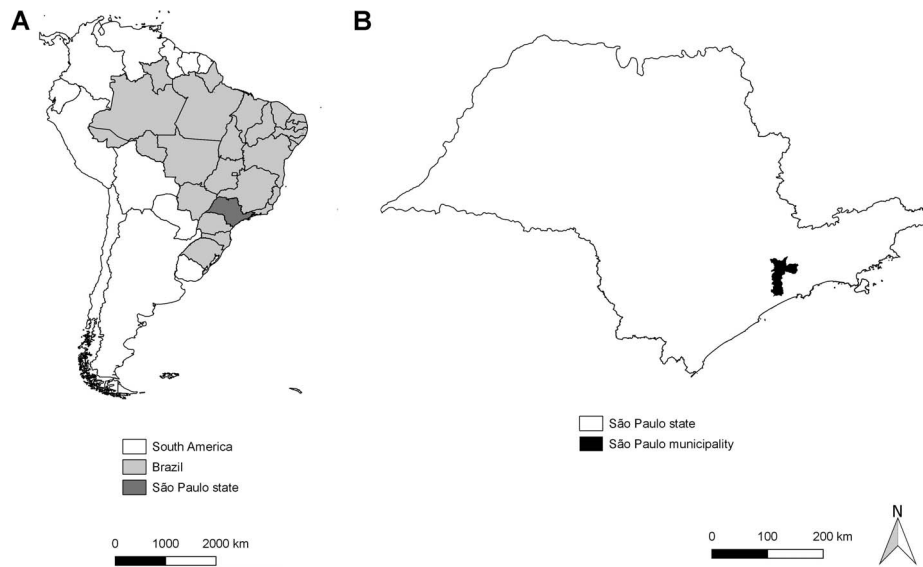
Figure 1 Geographic location of the study area. **A)** Location of São Paulo State in relation to Brazil and South America. **B)** Location of São Paulo municipality within São Paulo State.

conditions that increase the risk of illness, TB incidence among inmates is much higher than in the general population.[11] Only one case was found among inmates; this patient was excluded from the study to obtain the most homogeneous population.

Data sources

Data were obtained from TB-WEB, an online database of TB notifications from the State of São Paulo Tuberculosis Control Programme that was implemented in 2006, the first year of the present study. The population of South American immigrants residing in São Paulo was extracted from the sample results of the 2010 Demographic Census, which contained information on population mobility; these data are freely available at the Brazilian Institute of Geography and Statistics (Rio de Janeiro, RJ, Brazil) website (http://www.ibge.gov.br/english/).

Immigrants were identified using a weighting area. This comprised a group of census tracts from which the estimates obtained were applied to the entire population and the smallest geographical unit in which it would be possible to obtain information on the population of South American immigrants. São Paulo has 310 weighting areas,[12] each of which has an average of 40 000 inhabitants. The study variables comprised TB cases among South American immigrants: sex, age, and ethnicity of these patients; year of diagnosis; treatment address; and level of schooling.

Data analysis

Case geocoding and thematic mapping were performed using QGis v2.16 (Nodebo, QGis Development Team, Open Source Geospatial Foundation, Chicago, IL, USA, 2016). For geocoding, the street name, number, and zip code of the treatment address was used. Geocoding was performed using metric interpolation of the cartographic base adjusted in the Global Coordinate Reference System European Petroleum Survey Group code: 4326, projection latitude/longitude WGS84 units in degrees. The bases of sites (2014) and areas of weighting (2010) were obtained free of charge from the website of the Center for Metropolis Studies (São Paulo, SP) website (http://www.fflch.usp.br/centrodametropole/en/).

Purely spatial, purely temporal and spatial variation in temporal trends clusters were determined using SaTScan™ v9.3 (Martin Kulldorff, Harvard Medical School, Information Management Services, Boston, MA, USA). Purely spatial and temporal analyses identify clusters only in space and time, respectively. However, the spatial variation in temporal trends identifies clusters with growth rates (or decreases) in and out of these clusters, and evaluates whether the difference between them is statistically significant. This method allows the identification of areas with a tendency to grow over time, and also provides an estimate of the temporal trend throughout the study area.

This free software computes a scanning statistic based on the number of events and the exposed population (the population of South American immigrants) according to each weighting area, based on a Poisson distribution. It determines the relative risk (RR) for each cluster, which represents the relationship between the incidence rates inside and outside the cluster. The software covered the entire study region, calculated the RR for each of the weighting areas, identified the RR of clusters above and below the null and determined statistical significance ($P < 0.05$) using the Monte Carlo
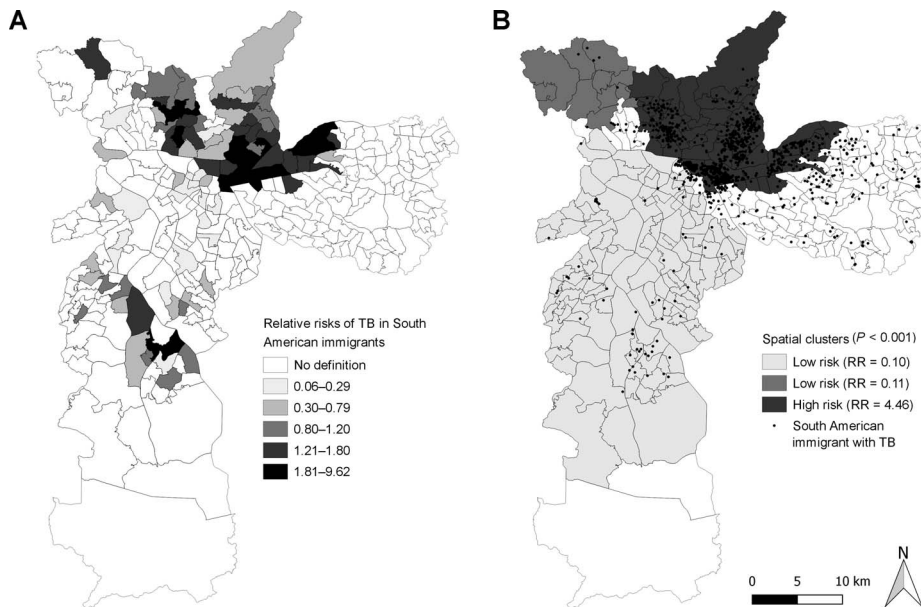
Figure 2   TB in South American immigrants in São Paulo municipality. **A)** RRs by spatial analysis.
B) Spatial clusters identified and TB cases, 2006–2013. TB = tuberculosis; RR = relative risk.

method with 999 simulations. To analyse spatial variation in temporal trends, the programme opened spatial scanning windows and calculated the temporal trend inside and outside each locality. If the time trend inside the window was statistically different from the trend outside the window, a cluster was identified.[13] Once clusters were identified, the socio-demographic characteristics of South American immigrants with TB residing inside the clusters were analysed using proportions (i.e., each characteristic was analysed using absolute and relative frequencies).

Ethical considerations

This project was approved by the Scientific Committee of the Faculty of Medical Sciences of the Santa Casa de São Paulo, São Paulo, SP (006/2014), and was exempt from the need for ethics committee approval because it used secondary data. The use of the database was authorised by the Epidemiological Surveillance Center of the State of São Paulo, São Paulo, SP, which provided anonymised patient data.

RESULTS

Between 2006 and 2013, 1916 new cases of TB were reported among South American immigrants residing in São Paulo, which represented 4.2% of all new TB cases in the municipality during this period. The majority of cases occurred in men (63.2%) and in individuals aged 15–29 years (72.1%). There was a preponderance of indigenous (33.7%) and brown (33.1%) ethnicities in the sample; a minority (2.8%) was illiterate. Of the total reported cases, 1815 (94.7%) were geocoded, 87 (4.8%) of whom were located in weighting areas with no registration of a

South American immigrant population according to 2010 census data; it was thus not possible to use the scanning statistic for these 87 cases. Data from the remaining 1728 cases (90.3% of the total number of notified cases from the population of interest) were thus used to calculate the RR of the weighting areas and to identify clusters.

The weighting areas with an RR representative of an excess risk for TB (>1.20) among South American immigrants were located mainly in the central, northern and north-eastern regions (Figure 2A). The purely spatial analysis revealed a high-risk spatial cluster (RR 4.46, $P < 0.001$) covering the central, north-eastern and northern regions of the city (Figure 2B). Two low-risk spatial clusters were also identified. The larger of these (RR 0.10, $P < 0.001$) was in the southern region (although it also included small areas of the western and central regions), and the other (RR 0.11, $P < 0.001$) was wholly inside the western region. Nevertheless, these two clusters also presented some weighting areas with an excess of risk for TB (Figure 2A).

Two clusters of spatial variation in temporal trends with statistically significant increases were found. The first, in the city's central region, had an RR of 2.35; however, the trend of increasing TB incidence was lower inside (1.4% of annual increase) than outside (15.4% of annual increase) the cluster. The RR of the second cluster, situated in the eastern and north-eastern regions, was 1.37. The trend of annual increasing TB incidence was 17.5% inside this cluster and 5.2% outside. The annual percentage increase in reported cases of TB in the whole municipality was 9.8% (Figure 3). Furthermore, a purely temporal
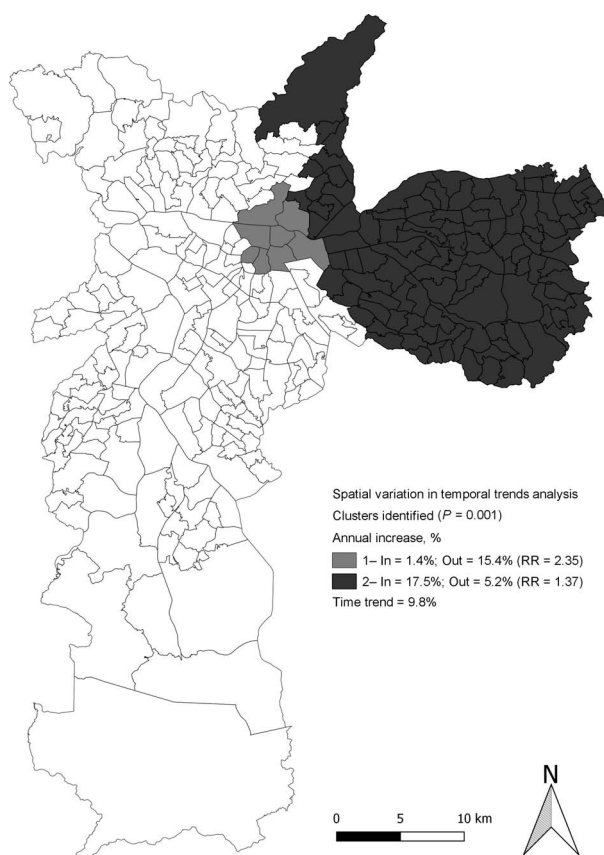
Figure 3 Spatial variation in temporal trends clusters of tuberculosis among South American immigrants by weighting area, São Paulo municipality, 2006–2013. RR = relative risk.

high-risk cluster (RR 1.55, $P = 0.001$) was identified in the last 3 years of the study period (2011–2013).

Bolivians comprised the majority (54.9%) of South American immigrants living within São Paulo. The presence of a majority of this group was even more evident in the high-risk spatial cluster (79.9%) and in the two increasing spatial variation in temporal trends clusters (64.3% and 73.8%). In contrast, in the low-risk spatial clusters, the largest resident migrant population group comprised Argentinians (26.6%), followed by Chileans (19.5%). These results demonstrated the difference between low- and high-risk clusters (Table 1).

In terms of sociodemographic profile, South American immigrants living in high-risk clusters differed from those living in low-risk clusters. Among South American immigrants with TB residing in the high-risk cluster, the majority (80.8%) were aged <30 years, whereas in low-risk clusters this group represented 51.6% of the corresponding population. People of indigenous ethnicity constituted 37.3% of immigrants in high-risk clusters and 14.5% in low-risk clusters. With regard to schooling, the proportion of immigrants who had achieved ⩾8 years of education was higher among those living in low-risk (60.8%) than in high-risk clusters (51.6%) (Table 2).

DISCUSSION

Our study identified high-risk regions with a high tendency for expansion of TB among South American immigrants in São Paulo. The location of these high-risk clusters overlapped with the areas of the city with large numbers of Bolivian immigrants and people with vulnerable sociodemographic characteristics. Although the spatial aggregation pattern of TB identified in our study has been described in other studies carried out in Brazil,[6,14] the participation of immigrants in such clusters has not been investigated in Brazil. Immigration and overcrowding are determinants of the formation of TB clusters.[15–17]

Bolivians constituted the main immigrant group residing in high-risk TB clusters in São Paulo. Most Bolivians migrate seeking professional placement in the city's textile sector,[4] where they are required to perform hard work in poorly ventilated spaces, which exposes them to a high-risk environment for contracting TB.[18] Due to the large number of sewing workshops, the central region of São Paulo is the most attractive destination for South American immigrants.[4] It is also an area with a high concentration of TB cases among Bolivians.[19] In the present study, this region contained the high-risk clusters identified, consistent with findings from Beijing, China, where the city centre had a high incidence of TB and harboured a high proportion of immigrants.[20] The downtown part of São Paulo is also an important

Table 1 Immigrants according to country of origin (results of the Brazilian demographic census, São Paulo municipality, SP, Brazil, 2010) by whole municipality and cluster

Country of origin	São Paulo municipality n (%)	High-risk spatial cluster n (%)	Low-risk spatial cluster n (%)	Spatial variation in temporal trends cluster 1 n (%)	Spatial variation in temporal trends cluster 2 n (%)
Argentina	4 699 (11.9)	467 (2.4)	3 870 (26.6)	119 (1.5)	644 (3.1)
Bolivia	21 680 (54.9)	15 812 (79.9)	2 716 (18.7)	5 221 (64.3)	15 485 (73.8)
Chile	3 864 (9.8)	580 (2.9)	2 830 (19.5)	163 (2.0)	637 (3.0)
Paraguay	3 170 (8.0)	1 541 (7.8)	1 125 (7.7)	979 (12.0)	1 815 (8.7)
Peru	2 949 (7.5)	954 (4.8)	1 855 (12.8)	1 359 (16.7)	1 622 (7.7)
Other countries	3 130 (7.9)	432 (2.2)	2 131 (14.7)	284 (3.5)	787 (3.7)
Total	39 491	19 786	14 527	8 124	20 990

Table 2 Epidemiological profile of South American immigrants with tuberculosis in the São Paulo municipality and in the clusters identified, 2006–2013

Variable	Low-risk spatial clusters n (%)	High-risk spatial cluster n (%)	São Paulo municipality n (%)
Sex			
Female	37 (38.1)	520 (37.0)	705 (36.8)
Male	60 (61.9)	885 (63.0)	1211 (63.2)
Age, years			
<15	2 (2.1)	89 (6.3)	107 (5.6)
15–29	48 (49.5)	1046 (74.5)	1380 (72.1)
30–44	31 (32.0)	233 (16.6)	347 (18.1)
45–59	10 (10.3)	27 (1.9)	55 (2.9)
⩾60	6 (6.2)	9 (0.6)	26 (1.4)
Ethnicity			
Asian	2 (2.4)	64 (5.9)	91 (6.0)
White	32 (38.6)	272 (24.9)	397 (26.2)
Indigenous	12 (14.5)	407 (37.3)	511 (33.7)
Black	37 (44.6)	349 (31.9)	516 (34.1)
Schooling, years			
⩽7	29 (39.2)	504 (48.4)	677 (46.9)
⩾8	45 (60.8)	537 (51.6)	767 (53.1)

place of residence for other marginalised groups such as street dwellers and those who depend on shelters,[9] which imposes greater difficulties for the implementation of public health policies. The central area showed a growing trend in TB incidence among South American immigrants, although the trend outside the cluster was greater. The eastern region, however, had a much higher growth rate inside than outside the cluster, and has the potential to become a high-risk area in the near future if adequate TB prevention and control measures are not adopted.

Indications that the eastern region may harbour a cluster of TB among South American immigrants suggests that such immigrants are moving to the suburbs of São Paulo, which may result in even more social exclusion. Migrant mobility is intrinsically related to economic and labour issues.[21] Within the study area, the search for new places of residence is associated with the intention of evading the frequent labour inspections in the central region and of reducing rental expenses.[18] Movement of immigrants within the city allows exchange of pathogens between migrant and native populations, which generates changes in the epidemiology of the disease.[22]

The development of purely temporal clusters has been recent, indicating that the impact of South American immigration on TB in São Paulo is a current and growing phenomenon. Considering that most cases of TB among immigrants are due to reactivation of latent tuberculous infection,[23] the Municipal Disease Control Programme should guide strategies for active TB surveillance for these sites, such as searching for people with symptomatic respiratory disease, screening, contact tracing and investigation.[16]

The profile of South American immigrants residing within the identified high-risk clusters differed from those residing in low-risk clusters. The fact that they were younger seems to confirm the relationship between TB and placement of immigrants in the unhealthy spaces of the sewing workshops. There was also a high proportion of indigenous people, a group that seems to experience difficulties related to treatment adherence; this can lead to multidrug resistance and contributes to TB-related mortality.[24] The low educational level of this population is relevant given that this is associated with delays in TB diagnosis.[25] TB control strategies aimed at immigrants should therefore take into account the inequality of their situation; it may be beneficial to consider introducing social protection measures.[26]

Our study had four main limitations. First, the use of secondary data from passive TB surveillance could have led to an underestimation of the true situation. Second, the nationality field of the notification form had a low proportion of completion (56%) over the study period, indicating that the actual number of TB cases in South American immigrants was underreported. Third, the country of origin of immigrants could not be distinguished due to the lack of nationality information in the version of the notification form used until 2013. Finally, the demographic census data on the number of South American immigrants living in São Paulo City did not reflect the true number of such immigrants; approximately 64 953 regular Bolivian immigrants are estimated to be living in the municipality.[3] Nevertheless, the data were extracted from a trustworthy official database, and we assume that at least the spatial distribution of this population was reliable.

Study strengths were the high proportion of TB cases (>90.0%) that were geocoded and the cluster detection method used to determine the RR according to area units (somewhat circumscribing the inaccuracy of the population count of immigrants). This method allows adjustment for population density,

avoids the selection bias of clusters, and allows investigation of the existence of clusters in space, time and space-time. Moreover, we investigated an issue that is not very well addressed in middle-income countries, namely the relationship between immigration and TB.

In conclusion, TB among South American immigrants is not homogeneously distributed within São Paulo. This study identified areas that, due to the high risk of TB among immigrants, should be the focus of efforts by TB disease control programmes in terms of active surveillance of cases with the aim of disrupting the chain of transmission. In addition, we identified that the majority population in the high-risk clusters is Bolivian, mobile within the territory and has its own characteristics; public policies should take these factors into account.

Acknowledgements

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_____ **RÉSUMÉ**

OBJECTIF : Identifier les variations spatiales, temporelles et les variations spatiales des tendances temporelles des groupes de tendances de la tuberculose (TB) parmi des migrants sud-américains résidant dans la municipalité de São Paulo entre 2006 et 2013.

SCHÉMA : Une étude descriptive écologique a été réalisée grâce aux données obtenues dans les rapports officiels sur la TB et dans celles du recensement démographique du Brésil en 2010. Les regroupements ont été identifiés grâce aux logiciels d'analyse statistique et SaTScan ; ceux dont la valeur de P a été <0,05 ont été considérés comme statistiquement significatifs. Les caractéristiques sociales et économiques des résidents au sein des groupes ont été examinées.

RÉSULTATS : Un groupe à haut risque spatial (risque relatif [RR] 4,46 ; $P < 0,001$) de TB a été identifié. Les immigrants boliviens constituent la majorité des immigrants résidant dans cette région. Un groupe à haut risque purement temporel a été identifié entre 2011 et 2013 (RR 1,55 ; $P = 0,001$). Dans l'une des variations spatiales des groupes à tendance temporelle, l'augmentation annuelle de l'incidence de la TB a été de 17,54% au sein du groupe et de 5,17% en dehors.

CONCLUSION : L'étude a découvert des zones de risque élevé de TB parmi les immigrants sud-américains. Ces zones et celles où l'incidence de la TB tend à augmenter doivent avoir la priorité des programmes de lutte contre la TB.

_____ **RESUMEN**

OBJETIVO: Detectar la variación espacial y temporoespacial en los conglomerados de tuberculosis (TB) con evolución temporal de migrantes sudamericanos que residían en la municipalidad de São Paulo del 2006 al 2013.

MÉTODO: Se llevó a cabo un estudio ecológico descriptivo a partir de los datos obtenidos de los registros oficiales de la TB y del censo demográfico del Brasil del 2010. Se analizó la presencia de conglomerados mediante técnicas de rastreo estadístico y el programa SaTScan; la significación estadística se definió con una $P < 0,05$. Se investigaron las características sociales y económicas de los residentes en cada conglomerado.

RESULTADOS: Se puso en evidencia un conglomerado espacial con alto riesgo de padecer TB (riesgo relativo [RR] 4,46; $P < 0,001$). La mayor parte de inmigrantes que residían en esta zona eran bolivianos. Se encontró un conglomerado puramente temporal de alto riesgo entre el 2011 y el 2013 (RR 1,55; $P = 0,001$). En una variación espacial de los conglomerados con tendencias temporales, el incremento anual de la incidencia de TB fue 17,54% dentro del conglomerado y 5,17% al exterior del mismo.

CONCLUSIÓN: El estudio puso de manifiesto zonas de alto riesgo de padecer TB en los inmigrantes sudamericanos. Es necesario que los programas de control de la TB den prioridad a estas zonas y a las zonas que exhiben una tendencia hacia el aumento de la incidencia de la enfermedad.