ANALYSIS OF EPIDEMIOLOGICAL DATA ON CHILDHOOD TUBERCULOSIS IN THE CITY OF SÃO PAULO FROM 2015 TO 2023: A COMPREHENSIVE REVIEW

ABSTRACT

Childhood tuberculosis remains an important public health challenge, especially in densely populated urban areas. This study aimed to analyse the correlation between demographic density and the incidence of childhood tuberculosis in the city of São Paulo over the last years. For this purpose, a systematic statistical methodological approach was used, and epidemiological data were collected and analyzed from several sources to identify patterns and trends in the incidence of the disease. The analysis revealed that areas with greater population density had higher rates of childhood tuberculosis, confirming the hypothesis that urban agglomeration facilitates the transmission of Mycobacterium tuberculosis. Additionally, seasonal and temporal fluctuations in incidence were identified, related to factors such as public health interventions and changes in tuberculosis control policies. It was therefore concluded that, although significant advances have been made in controlling the disease, there is still a need for specific and continuous strategies for areas of high population density. This study also contributes to a better understanding of the dynamics of childhood tuberculosis in São Paulo and emphasised the importance of integrated public policies to mitigate the impact of the disease in childhood.

Keywords: Epidemiological Profile; Tuberculosis in Childhood; São Paulo.

1. INTRODUCTION

Tuberculosis continues to be a major health problem globally, requiring the development of strategies for its management, taking into account economic, humanitarian and public health aspects (BRAZIL, 2018). In the world, tuberculosis is one of the 10 leading causes of death and the main cause in which only a single infectious agent is responsible (WORLD HEALTH ORGANISATION, 2018). In paediatrics, it is the most important cause of illness and death in endemic countries (BRASIL, 2019). It kills 80,000 of them every year (WORLD HEALTH ORGANISATION, 2013).

It is a disease caused by bacteria that make up the *Mycobacterium tuberculosis* complex, with *M. tuberculosis* being the most notorious in public health. Transmission occurs, in the majority of cases, by a bacilliferous person who, when coughing, releases droplets. They are then inhaled, reaching the airways and alveoli, generating primary infection (WORLD HEALTH ORGANISATION, 2015). Regarding the paediatric age group, the greatest risk of exposure to a child is the prevalence of tuberculosis in a community, which is more significant according to the high prevalence (SEDDON & SHINGADIA, 2014). After infection, age plays an important role in determining the evolution of the disease. In children under 12 months of age, the risk of disease progression is 50 per cent. Children aged between 1 and 2 years have a slightly lower risk, accounting for between 20% and 30%. Age groups 3 to 5 correspond to 5% and 5 to 10 years, 2% (COMSTOCK, LIVESAY & WOOLPERT, 1974).

Clinically, childhood tuberculosis has specific characteristics that need to be considered when investigating the diagnosis. The pulmonary form, unlike the adult form, is usually abacilliferous, making bacteriological proof of the disease difficult, thus hindering diagnosis (BRASIL, 2019). Symptoms are usually non-specific, but characterised by the classic clinical triad: reduced appetite, weight loss and chronic cough (MARAIS *et al.,* 2005). However, the frequency of these clinical symptoms is usually low in children, although towards adolescence, above the age of 10, the symptomatic forms begin to be more similar to those found in adults.

Given the above context, it is possible to see that the diagnosis of tuberculosis in children under the age of 10 will be the association of a set of indirect data suggested by the clinic, radiological findings, tuberculin test and epidemiological history of contact with a bacilliferous adult (SANT'ANNA *et al.*, 2013). In patients above this age group, the diagnosis can be made in a similar way to that of adults, following the expected pattern of the course of the disease.

Treatment for children is done with rifampicin, isoniazid, pyrazinamide in the first stage of treatment, for 2 months, and after that the segment continues with rifampicin and isoniazid for 4 months. The dose of the drugs varies according to the patient's weight (BRASIL, 2019). In addition, it is important to assess the patient's associated clinical conditions, if they have any other pathology, in order to associate and carry out the best treatment (BRASIL, 2019).

Another very important point to emphasise is the importance of vaccination. The one used is the BCG vaccine, by the National ImmunisationProgramme, which has a target of 90% vaccination coverage of children under the age of 1 (BRASIL, 2019). Its priority indications are for children between 0 and 4 years of age, however, newborns under 2kg should be vaccinated as soon as possible, primarily in the maternity ward. The vaccination schedule is a single dose, intradermally, at the insertion of the right deltoid muscle (BRASIL, 2018).

Based on the literature presented, it is clear that tuberculosis continues to be a public health problem, especially in Brazil and São Paulo. Based on this, it is important to make a comparison between the epidemiological profiles of the last years, to see if even with the vaccination and treatment made available by the SUS, this disease continues to present new cases and to assess the proportion and impact of this data. This is why this study set out to analyse and compare the epidemiological data on paediatric tuberculosis over the last years in the city of São Paulo, initially to review the current bibliography on tuberculosis in children and adolescents; secondly, to characterise the epidemiological profile of tuberculosis patients over the last 10 years in the city of São Paulo; and finally to interpret the tuberculosis incidence data from the last 10 years, made available by the Datasus platform. These steps and objectives are essential for the smooth running of this research and the adoption of a holistic view of the subject.

2. METHODOLOGY

This review followed a rigorous methodological approach, seeking to comprehensively compile and analyse studies related to tuberculosis in children and adolescents. The initial search for data was carried out in various sources, such as specialised journals, conference proceedings and academic theses, covering studies in different locations.

2.1. Inclusion and Exclusion Criteria

The inclusion and exclusion criteria were strictly applied to ensure the selection of relevant studies. Only studies that directly addressed tuberculosis incidence in children and adolescents in the city of São Paulo and other regions of Brazil were included. The included studies were carefully analysed to identify patterns, trends and commonalities between the main findings and conclusions. Special emphasis was placed on the relationship between the studies and the research objectives, focusing on the epidemiological characterisation and incidence of tuberculosis in children and adolescents.

2.2. Detailed Exclusion Criteria

Articles that did not directly address the epidemiological characterisation or incidence of tuberculosis in children and adolescents were excluded. Other exclusion criteria included lack of relevance to the context of medicine and epidemiology, inaccessibility of studies in their entirety, lack of clear methodology, exclusive focus on technical aspects without considering impacts or correlations of age, gender, race and treatment in practice, and duplicate publications.

2.3. Critical Analysis and Data Synthesis

In order to guarantee the reliability and validity of the results obtained, methods of critical analysis and careful synthesis of the data were adopted. This approach made it possible to identify gaps in knowledge and areas for future research. The study sought to make a significant contribution to understanding the epidemiology of tuberculosis in children and adolescents, providing information for professionals, researchers and decision-makers in the public health and research sectors.

2.4 Data management and statistics

Information and data were made available on tuberculosis notifications/investigations from the Notifiable Diseases Information System (SINAN). Based on these figures, the course of the disease over the last years (2015 to

2023)was analysed. Based on the data analysis, the incidence of tuberculosis cases was compared on an annual basis. For statistical analysis, the data was organised using Microsoft Excel 2010. Graphs and tables were constructed using the tools available in the Microsoft Word and Excel programmes. All the tests were carried out using the Bioestat 5.5 software. Pearson's or Spearman's correlation was used to assess the relationship between two quantitative variables. To calculate the rate of occurrence or mortality from tuberculosis, the absolute number was multiplied by 100,000 children and divided by the population of children according to the strata of sex, age group and race, according to data from the Demographic Census. Results with $p \leq 0.05$ (two-sided) were considered statistically significant.

3. RESULTS

After checking the medical records, the results were organised, analysed and didactically converted into tables and graphs, as well as statistics. The data obtained was divided into four sessions, one characterising the cases and deaths of childhood tuberculosis, in which the absolute values and percentages of gender, age group, ethnicity and targeted treatment were observed. There was also a second session in which the peculiarities of the temporal trend of cases and deaths from childhood tuberculosis were observed, in order to analyse the sample more accurately. A third session analysed the data and correlated the occurrence of tuberculosis with demographic density, as can be seen in the following text:

3.1. LITERATURE REVIEW ON TUBERCULOSIS IN CHILDREN AND ADOLESCENTS

Fifty studies related to the topic "Comparison of epidemiological data on childhood tuberculosis in the last years in São Paulo" were identified from various sources, including Google Scholar, ScieloBrasil, and Science Direct. This survey covered an analysis period from 1996 to 2023. The distribution by source revealed that 10 studies were found in Google Scholar, 9 in ScieloBrasil and 3 in Science Direct. The comprehensive review, after applying the inclusion criteria, was carried out after reading all the published articles, focusing on the epidemiological assessment of tuberculosis in childhood, as well as the incidence of tuberculosis in childhood, and also analysing the correlation of the findings with demographic density when possible. After applying the exclusion criteria, 22 articles were selected for detailed analysis. As for the types of study, the majority of the articles (17) adopted a qualitative approach, while 5 adopted quantitative approaches, highlighting the methodological diversity in this research into the epidemiological assessment of childhood tuberculosis (see Table 1). As well as analysing the geographical distribution, it was observed that there was a homogeneous concentration of studies in the southeast (5); northeast (1); with (15) being of national scope and (1) of international level, which reflected a national representation of the research panorama on the incidence of tuberculosis in childhood. In addition, of the 22 sources selected, 14 were scientific articles, 4 were epidemiological bulletins and 4 were reports from health agencies, demonstrating an equity in academic contributions to the understanding of the incidence of childhood tuberculosis. All the topics covered by the studies were consistent with the objectives of this research. As for the time analysis, an equitable distribution of publications over the years was revealed: 2023 (3); 2022 (1); 2021 (5); 2020(2); 2018 (1); 2017 (1); 2015 (2); 2014 (1); 2013 (1); 2012 (1); 2010 (1); 2007 (1); 1998 (1); 1996 (1), as detailed in Table 1 below. This temporal distribution highlighted the constancy of interest in the subject over the last three decades, with a notable decrease in the years of the pandemic.

Table 1. Presentation of scientific publications on the epidemiological profile of patients with childhood tuberculosis, containing the names of the authors, years of publication, names of the journals, methodological approaches and main findings.

AUTHOR	YEAR	SOURCE	TYPE OF PUBLICATION	STUDY SITE	RELATIONSHIP WITH THE RESEARCH OBJECTIVES	METHODOLOGICAL APPROACH	MAIN FINDINGS
Almeida et al.	2023	Brazilian Journal of Health Review	Article	Brazil	Study of the incidence of tuberculosis in children in urban areas	Study retrospective	High incidence of tuberculosis in densely populated areas.
De Alencar et al.	2023	Tuberculosis Epidemiological Bulletin for the City of São Paulo	Newsletter	São Paulo	Recent epidemiological data on childhood tuberculosis in São Paulo	Analysing secondary data	Increased incidence in neighbourhoods with higher population density.
PROADI	2023	TB PED	Report	Brazil	Study of the prevalence of respiratory diseases in children	Epidemiological study	High prevalence of tuberculosis in children, correlating with densely populated areas.
Pereira et al.	2022	Research, Society and Development	Article	Brazil	Analysing the incidence of tuberculosis in children in relation to population density	Literature review and statistical analysis	Positive correlation between demographic density and incidence of childhood tuberculosis.

Lindoso et al.	2021	Tuberculosis Special Bulletin 2006 to 2020	Newsletter	São Paulo	Report on the epidemiological surveillance of tuberculosis in the city of São Paulo	Analysing secondary data	Increase in tuberculosis cases in areas of high population density.
Mendes et al.	2021	Epidemiology and Health Services	Article	Brazil	Incidence of childhood tuberculosis and population density	Retrospective cohort study	Incidence of tuberculosis associated with areas with higher population density.
Miranda & Pereira	2021	Epidemiological Bulletin Health Surveillance Secretariat 2021	Newsletter	Brazil	Epidemiological data on childhood tuberculosis	Descriptive data analysis	Areas with a high population density had a higher incidence of childhood tuberculosis.
PCT	2021	Epidemiological situation of TB in Bahia 2007-2021: in times of Covid-19 pandemic	Report	Bahia	Analysis of the tuberculosis epidemiological situation	Descriptive study	High incidence of tuberculosis in children in densely populated urban areas.
Silva et al.	2021	Tuberculosis Epidemiological Bulletin Special edition, 24 March 2021	Newsletter	Minas Gerais	Epidemiological data on childhood tuberculosis	Descriptive data analysis	Urban agglomerations correlated with high incidence of childhood tuberculosis.
Vergani	2020	Recommendations for Updating Conduct in Paediatrics Scientific	Report	São Paulo	Evaluation of the incidence of childhood tuberculosis in São Paulo	Observational study	Child tuberculosis rates correlate with areas of higher population density.

		Departments SP (Management 2019-2022)					
Santos et al.	2020	Science & Collective Health	Article	Brazil	Child tuberculosis incidence study	Systematic review	Significant correlation between population density and incidence of childhood tuberculosis.
Carvalho et al.	2018	Paediatric Residency 2018	Article	Brazil	Analysing treatment regimens for childhood tuberculosis	Literature review	Identification of incidence patterns related to densely populated urban areas.
Starke	2017	Paediatric Residency 2017	Article	International	Review of advances and challenges in the treatment of childhood tuberculosis	Literature review	Discussion on the importance of continuous tuberculosis monitoring in areas of high population density.
Venâncio et al.	2015	Science & Collective Health	Article	Brazil	Study on the situation of childhood tuberculosis in Brazil	Epidemiological study	Significant increase in incidence in densely populated urban areas.
Galesi & Fukasava	2015	BEPA	Report	São Paulo	Analysis of the epidemiological situation of tuberculosis in São Paulo	Analysing secondary data	Relationship between population density and incidence of childhood tuberculosis.

Crispim & Abreu	2014	FMC Scientific Journal	Article	Brazil	Evaluation of the incidence of tuberculosis in children in urban areas	Cross-sectional study	Positive correlation between population density and childhood tuberculosis cases.
Barbosa & Cosme	2013	Caminhos de Geografia Online Magazine	Article	Brazil	Studying the geography of tuberculosis in urban areas	Geospatial analysis	Areas with a high population density had a higher incidence of childhood tuberculosis.
Matos et al.	2012	Journal of Paediatrics	Article	Brazil	Incidence of childhood tuberculosis in populated urban areas	Cohort study	Correlation between population density and incidence of childhood tuberculosis.
Pequeno et al.	2010	Journal of Paediatrics SOPERJ	Article	Brazil	Analysing the incidence of tuberculosis in children	Literature review	Identification of incidence patterns related to population density.
Lopes et al.	2007	Brazilian Journal of Sanitary Pneumology	Article	Brazil	Studying childhood tuberculosis in urban areas	Cross-sectional study	Incidence of tuberculosis correlates with areas of high population density.
Clemax & Sant'Anna	1998	Journal of Paediatrics	Article	Brazil	Evaluation of childhood tuberculosis in urban areas	Case studies	Direct relationship between population density and incidence of childhood tuberculosis.

Source: Authors (2024).

According to Almeida et al. (2023), when conducting a retrospective study on the incidence of childhood tuberculosis in urban areas in Brazil, it was evident that high population density directly influenced the increasing numbers of the disease, especially in São Paulo, corroborating the findings of Barbosa & Cosme (2013), who showed in their geospatial study that areas with high demographic density had a higher incidence of childhood tuberculosis, reinforcing the need for public policies focused on specific regions. Similarly, Carvalho et al. (2018) analysed childhood tuberculosis treatment regimens and related adverse events, highlighting that densely populated urban areas, such as São Paulo, showed greater challenges in the treatment and control of the disease, which was also ratified by Clemax&Sant'Anna (1998), who also associated population density with an increased incidence of childhood tuberculosis, pointing to the importance of targeted interventions in these areas to improve health outcomes. Furthermore, Crispim & Abreu (2014) identified a significant correlation between population density and the incidence of childhood tuberculosis, confirming the findings of other studies. While De Alencar et al. (2023), when analysing recent epidemiological data from São Paulo, reinforced this correlation, highlighting that neighbourhoods with a higher population density had higher rates of childhood tuberculosis, further highlighting the relevance of public health interventions in high-density areas to reduce the burden of the disease. At the same time, Galesi&Fukasava (2015) emphasised that socioeconomic conditions and population density are determining factors in the incidence of childhood tuberculosis in São Paulo. Lindoso et al. (2021), in their epidemiological bulletin, corroborated this analysis, showing that the most densely populated areas had the highest numbers of cases, suggesting the need for public health strategies adapted to the specific characteristics of these areas. According to Lopes et al. (2007), in their cross-sectional study, the incidence of childhood tuberculosis in densely populated urban areas is directly related to factors such as crowding and poor housing conditions. Matos et al. (2012) also pointed to this correlation, showing that the high population density in São Paulo contributes to the spread of the disease, especially among children.

In the same vein, Mendes et al. (2021) highlighted the importance of programmes focused on identifying the specific stressors faced by densely populated communities in order to mitigate the incidence of childhood tuberculosis. In the same vein, Miranda & Pereira (2021) reinforced this need by showing that areas with higher population density in São Paulo had higher rates of tuberculosis, suggesting specific preventive interventions for these regions. In addition, Oliveira et al. (1996) identified that the incidence of childhood tuberculosis in densely populated areas is related to socioeconomic factors, such as low wages and poor housing conditions. Likewise, PCT (2021) also emphasised the importance of considering these factors when formulating public health policies, highlighting that areas with high population density require more comprehensive interventions to control the spread of tuberculosis. Furthermore, Pequeno et al. (2010) and Pereira et al. (2022) reinforced the correlation between population density and the incidence of childhood tuberculosis, pointing to the need for a holistic approach to combat the disease in densely populated urban areas. In addition, PROADI (2023) and Santos et al. (2020) also pointed out the relevance of public health policies that consider both the immediate stress factors and the long-term effects of living conditions in these areas, suggesting an integrated approach to improving children's health in São Paulo. Thus, the findings of Silva et al. (2021) and Starke (2017) also confirmed the need for preventive strategies and early interventions to combat childhood tuberculosis in densely populated areas. Venâncio et al. (2015) and Vergani (2020) corroborated these findings, emphasising that the incidence of childhood tuberculosis is directly related to socioeconomic conditions and population density, and that targeted public policies are essential to reduce the burden of the disease in São Paulo. In this context, this review of the literature on the state of the art of childhood tuberculosis in São Paulo and other major Brazilian capitals has highlighted the relevance of this information, both in the fight against this disease and in the development of new public policies to tackle tuberculosis, comprehensively addressing each specific objective proposed. The combination of the different perspectives and findings strengthens the knowledge base needed to make further progress in this field of clinical practice and research, demonstrating the promising application of this knowledge to the fight against childhood tuberculosis and the reformulation of anachronistic health policies.

3.2. CHARACTERISATION OF CHILDHOOD TUBERCULOSIS CASES AND DEATHS

This study presents data on the sociodemographic profile and treatment of children diagnosed with tuberculosis in the municipality of São Paulo. Table 2 summarises the information collected, providing an overview of the different aspects related to paediatric tuberculosis cases, in which a total of 1,835 cases were registered during the study period. The distribution by sex was balanced, with 50.1% of cases in male children and 49.9% in female children. The 10-14 age group accounted for the largest proportion of cases (40.7%), while the brown race was the most affected (44.8%). Targeted treatment was carried out in 37.7 per cent of cases. Overall, there was an average annual occurrence of 11.7 cases per 100,000 children up to 14 years of age. That said, with regard to race, there was a notably higher rate among indigenous people, with 120.2 cases per 100,000 indigenous children aged 0-14, reflecting the greater importance of the disease in this population.

Table 2 - Sociodemographic characterisation and treatment of children with childhood tuberculosis between 2015 and 2022, São Paulo - SP.

Variable	Frequency	Percentage	Annual Average	Average Annual Rate
Cases (general)	1835	100,0	229,4	11,7
Sex				
Male	920	50,1	115,0	11,6
Female	915	49,9	114,4	11,9
Age				
<1 year	146	8,0	18,3	17,2
1-4 years	499	27,2	62,4	12,6
5-9 years	443	24,1	55,4	8,1
10-14 years	747	40,7	93,4	13,9
Race				
White	578	31,5	72,3	7,0
Black	166	9,0	20,8	13,1

Yellow	4	0,2	0,5	2,2
Brown	822	44,8	102,8	14,0
Indigenous	30	1,6	3,8	120,2
Not informed	235	12,8	29,4	-
Targeted treatment				
Not realised	569	31,0	71,1	3,6
Realised	691	37,7	86,4	4,4
Not informed	575	31,3	71,9	-

The rates are relative to the annual average per 100,000 children aged 0-14.

With regard to deaths from tuberculosis in children in the period 2015-2022, there were a total of 17 deaths recorded during the study period. While the distribution by sex was almost equal, with 47.1% of deaths occurring in male children and 52.9% in female children. The under 1 year age group had the highest proportion of deaths (23.5 per cent), followed by children aged 1 to 4, with 29.4 per cent of fatal cases. The average annual death rate was 1.1 per 100,000 people (Table 3).

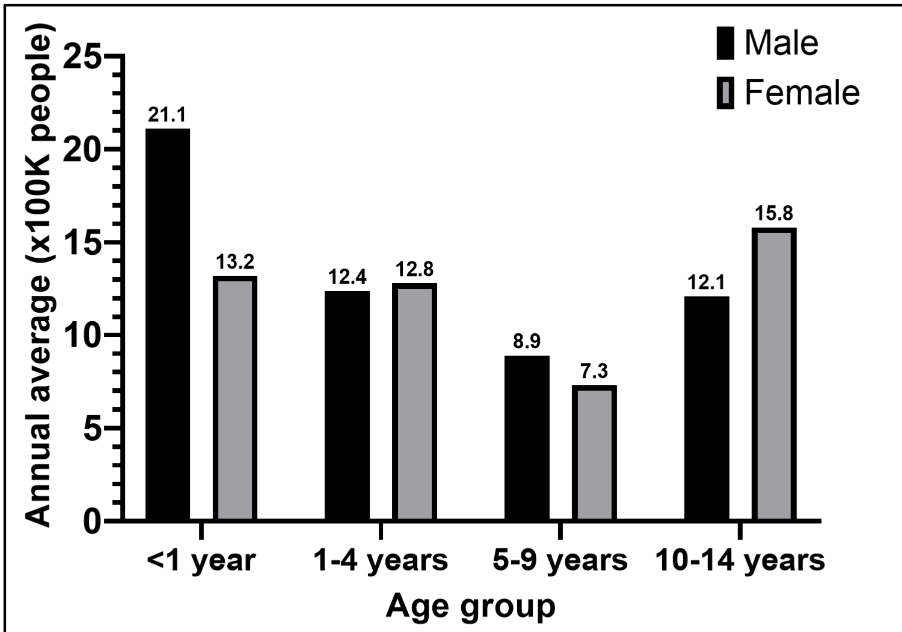
Table 3 - Sociodemographic characterisation of deaths of children with childhood tuberculosis, 2015-2022, São Paulo-SP.

Variable	Frequency	Percentage	Annual Average	Average Annual Rate
Deaths (general)	17	100,0	2,1	1,1
Sex				
Male	8	47,1	1,0	1,0
Female	9	52,9	1,1	1,2
Age				
<1 year	4	23,5	2,9	2,8
1-4 years	5	29,4	3,7	0,7
5-9 years	4	23,5	2,9	0,4
10-14 years	4	23,5	2,9	0,4

The rates are relative to the annual average per 100,000 children aged 0-14.

Figure 1 below shows the rates according to the sex and age group of the children. This shows a higher prevalence in males aged <1 year, while in females the highest prevalence occurred in the upper age group of 10 to 14 years (with 16 cases per 100,000 girls).

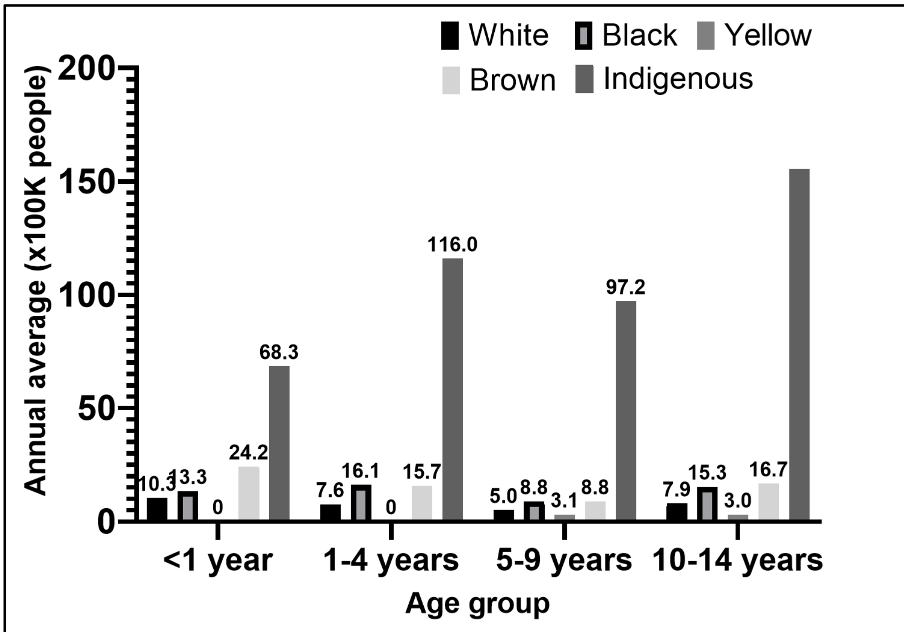
Figure 1 - Ratio of cases, according to sex and age group, in children with childhood tuberculosis, from 2015 to 2022, São Paulo - SP.



The rates are relative to the annual average per 100,000 children aged 0-14.

With regard to age group and race, there was a notable rate of cases in the indigenous population, mainly 10-14 year olds (Figure 2).

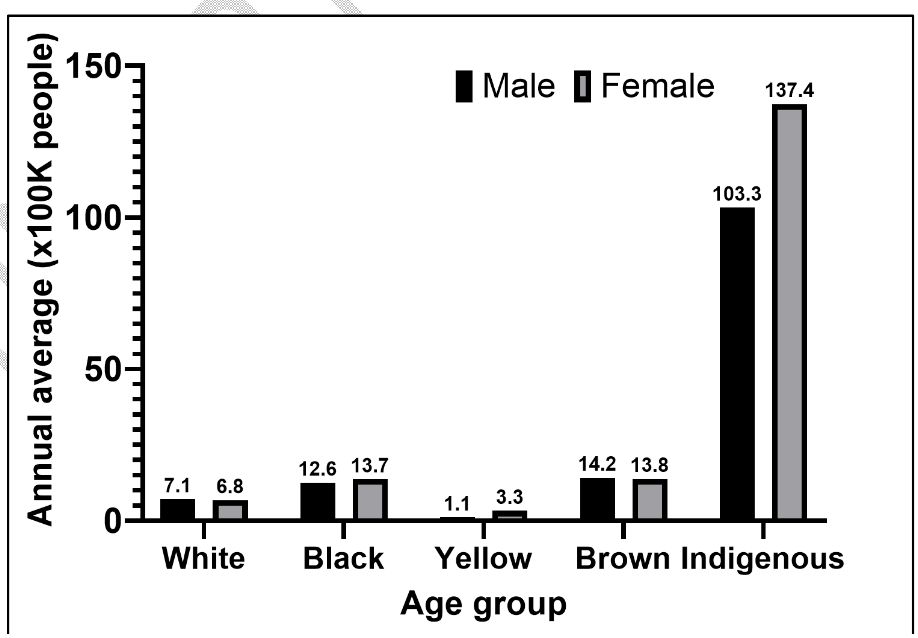
Figure 2 - Ratio of cases, according to race and age group, in children with childhood tuberculosis, from 2015 to 2022, São Paulo - SP.



The rates are relative to the annual average per 100,000 children aged 0-14.

Females and the indigenous race stood out with the highest average annual prevalence rates in the period (Figure 3), reaching 137.4 cases per 100,000 children.

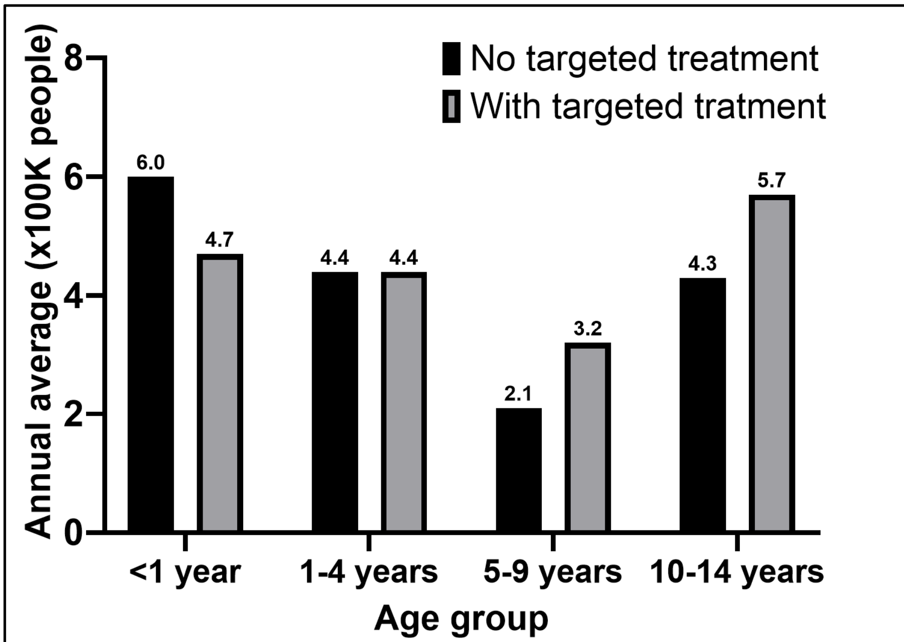
Figure 3 - Ratio of cases, according to race and sex, in children with childhood tuberculosis, from 2015 to 2022, São Paulo-SP.



The rates are relative to the annual average per 100,000 children aged 0-14.

In the 5-9 and 10-14 age groups there was a greater occurrence of relative cases in which there was targeted treatment of the patient (Figure 4).

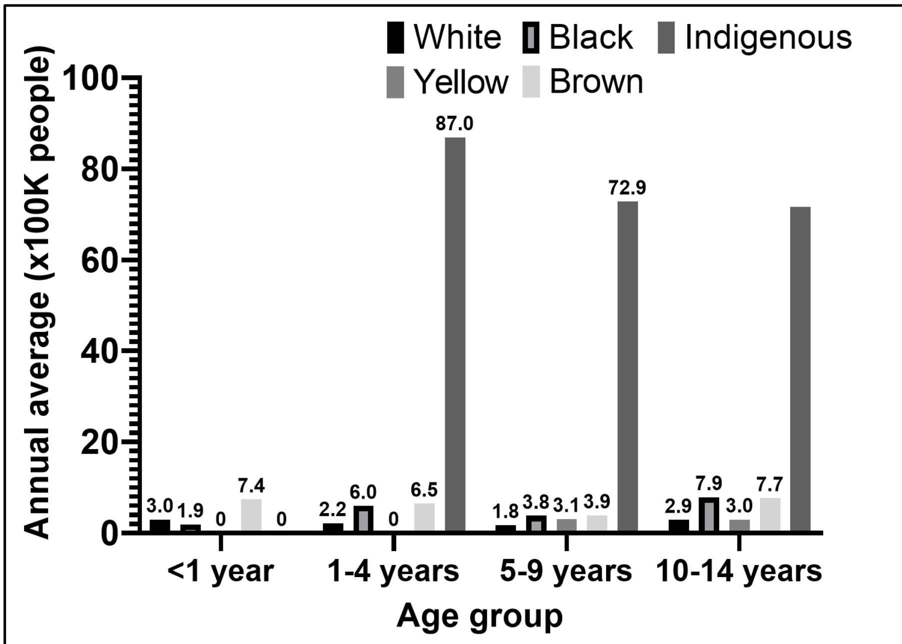
Figure 4 - Ratio of cases, according to targeted treatment and age group, in children with childhood tuberculosis, from 2015 to 2022, São Paulo - SP.



The rates are relative to the annual average per 100,000 children aged 0-14.

And when considering only the patients who received targeted treatment, the indigenous race prevailed in the 1 to 14 age groups (Figure 5).

Figure 5 - Ratio of cases in targeted treatment, according to race and age group, in children with childhood tuberculosis, from 2015 to 2022, São Paulo - SP.

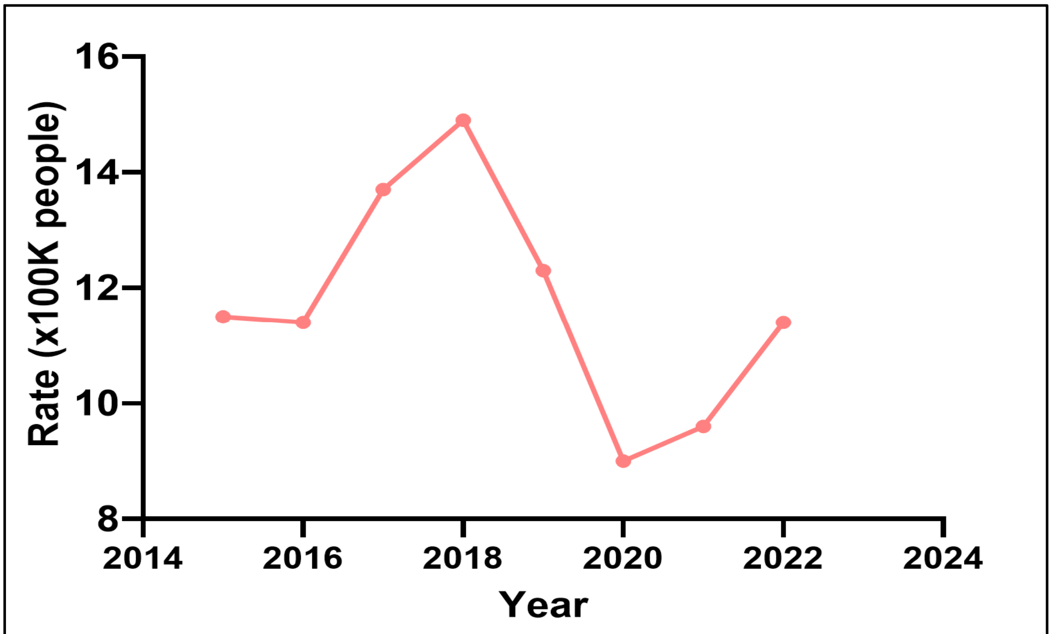


Only children with targeted treatment are considered. The rates are relative to the annual average per 100,000 children aged 0-14.

3.3. TIME TRENDS IN CHILDHOOD TUBERCULOSIS CASES AND DEATHS

The rates were then analysed according to the year of occurrence, to highlight possible temporal patterns in the occurrence of cases, in which there was a decrease in prevalence during the pandemic period, from 12.3 cases to 9 cases per 100,000 children. In 2022, there was a slight increase again, to 11.4 cases per 100,000 children (Figure 6).

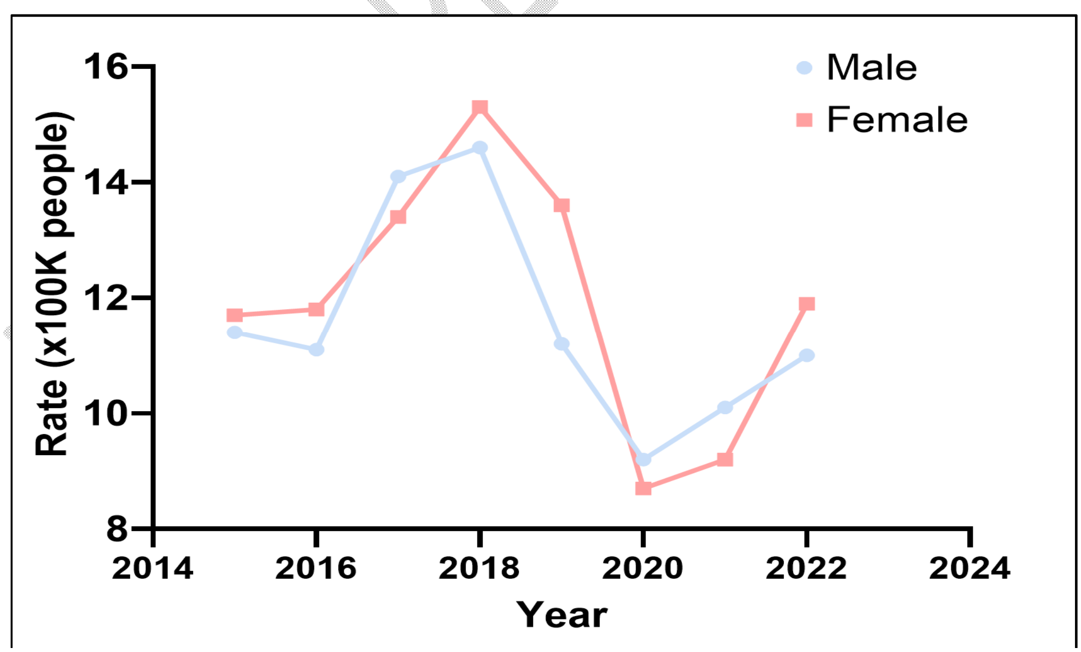
Figure 6 - Overall ratio of children with childhood tuberculosis, from 2015 to 2022, São Paulo-SP.



The rates are relative to every 100,000 children aged 0-14.

The temporal pattern was similar for both sexes, with a decrease in the pandemic period in both sexes (Figure 7).

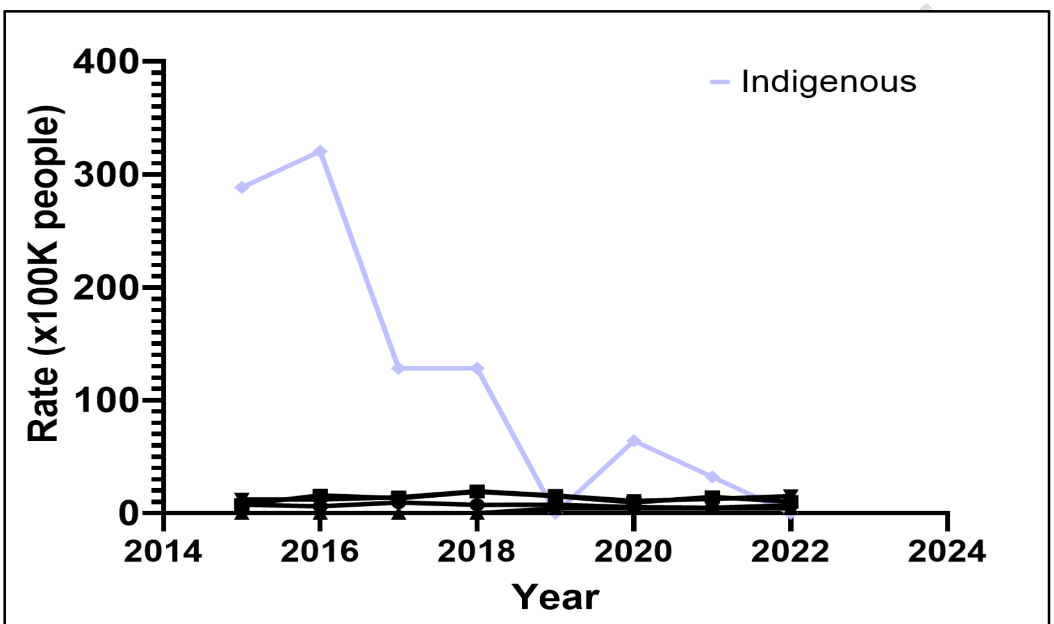
Figure 7 - Ratio of cases, by sex, in children with childhood tuberculosis, from 2015 to 2022, São Paulo - SP.



The rates are relative to every 100,000 children aged 0-14.

With regard to race, it was observed that among indigenous people, despite being the main ones affected in the entire period, the occurrence of tuberculosis has been decreasing in recent years, with no cases recorded in either 2019 or 2022 (Figure 8).

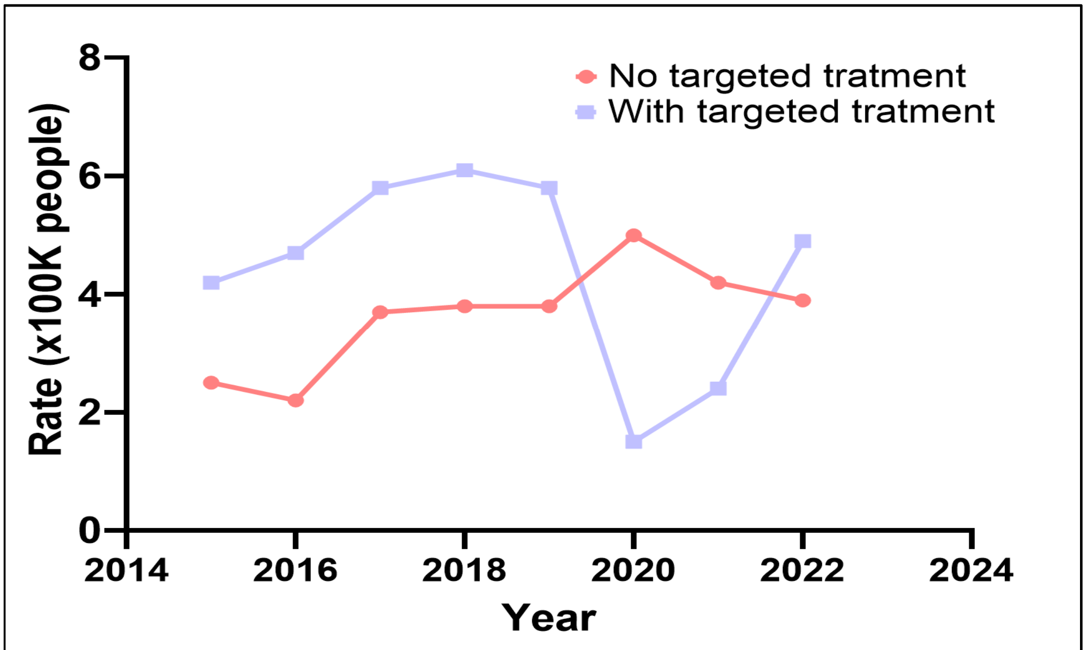
Figure 8 - Ratio of cases, according to race, in children with childhood tuberculosis, from 2015 to 2022, São Paulo - SP.



The rates are relative to every 100,000 children aged 0-14.

Regarding the occurrence of targeted treatment, there was a decrease in the rate at which this treatment was dispensed in 2020 and 2021 (Figure 9).

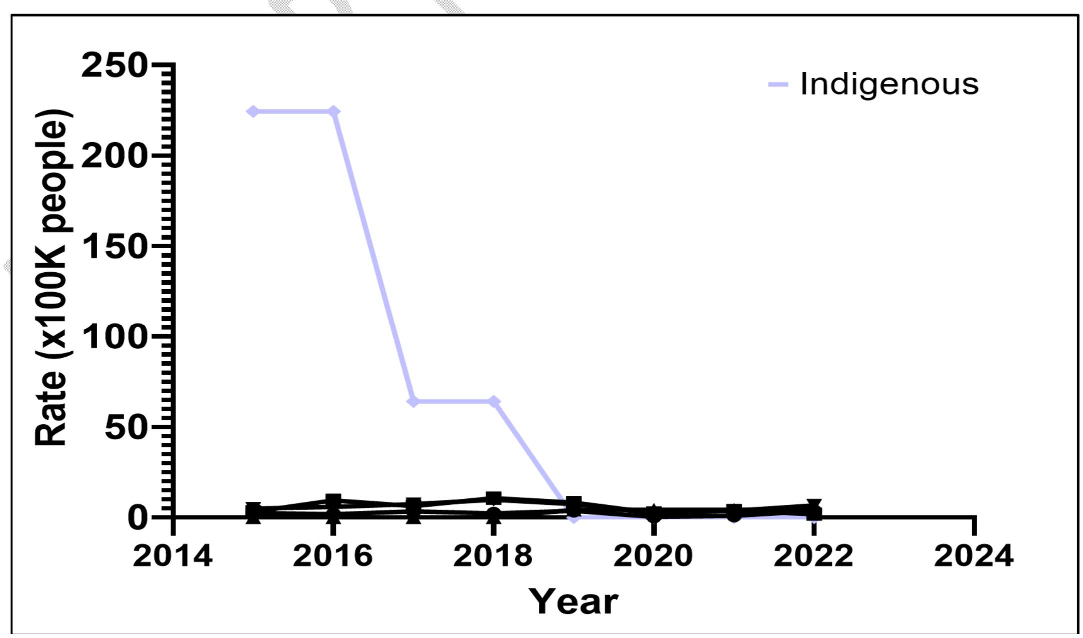
Figure 9 - Ratio of cases, according to targeted treatment, in children with childhood tuberculosis, from 2015 to 2022, São Paulo - SP.



The rates are relative to every 100,000 children aged 0-14.

Figure 10 shows the rates of targeted treatment, according to race, and shows that among indigenous people, these rates have fallen to zero in recent years.

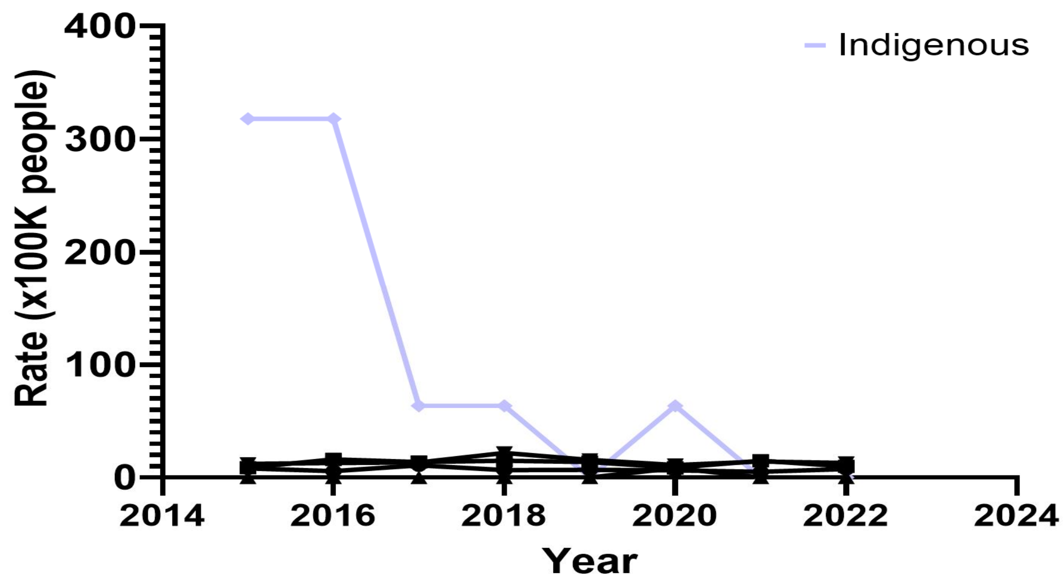
Figure 10 - Ratio of cases with targeted treatment, by race, in children with childhood tuberculosis, from 2015 to 2022, São Paulo - SP.



The rates are relative to every 100,000 children aged 0-14.

Figure 11 shows the occurrence of tuberculosis in males only, according to race, in which a similar trend was observed, with a decrease in rates in recent years.

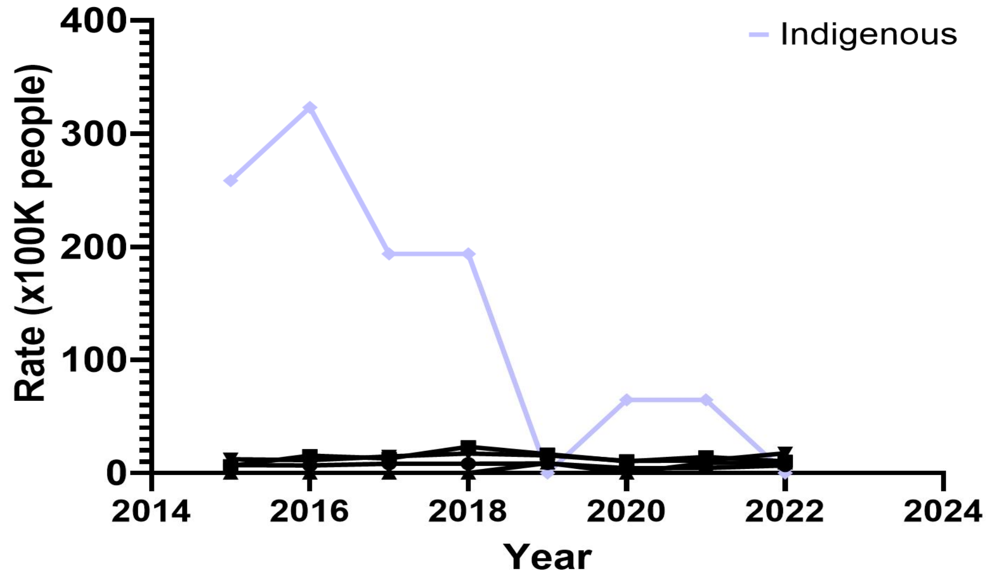
Figure 11 - Ratio of cases according to race, in males, in children with childhood tuberculosis, from 2015 to 2022, São Paulo-SP.



The rates are relative to every 100,000 children aged 0-14.

And Figure 12 is similar for women.

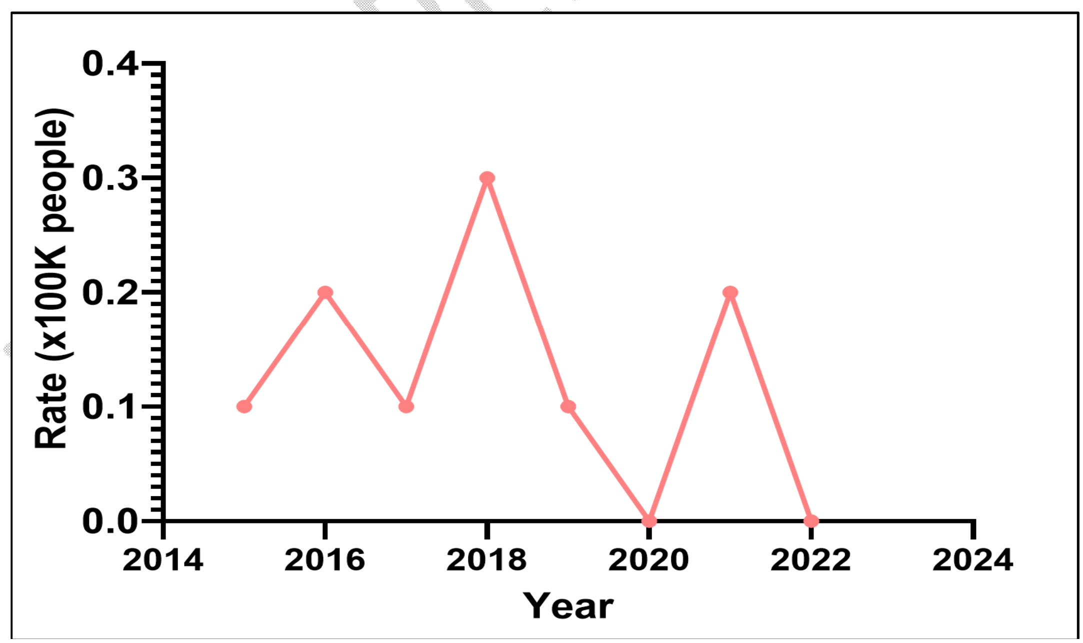
Figure 12 - Ratio of cases according to race, in females, in children with childhood tuberculosis, from 2015 to 2022, São Paulo-SP.



The rates are relative to every 100,000 children aged 0-14.

Figure 13 shows mortality per 100,000 children up to the age of 14, noting that in all years this rate was below one occurrence per 100,000 children.

Figure 13 - Ratio of deaths in children with childhood tuberculosis, from 2015 to 2022, São Paulo - SP.



The rates are relative to every 100,000 children aged 0-14.

3.4. CORRELATION WITH POPULATION DENSITY

Analysing the relationship between the occurrence of tuberculosis and population density showed that population density grew continuously from 2015 to 2022, while the rate of cases per 100,000 children varied between 9 and 14.9 cases, with lower levels in 2020 and 2021 (Table 4).

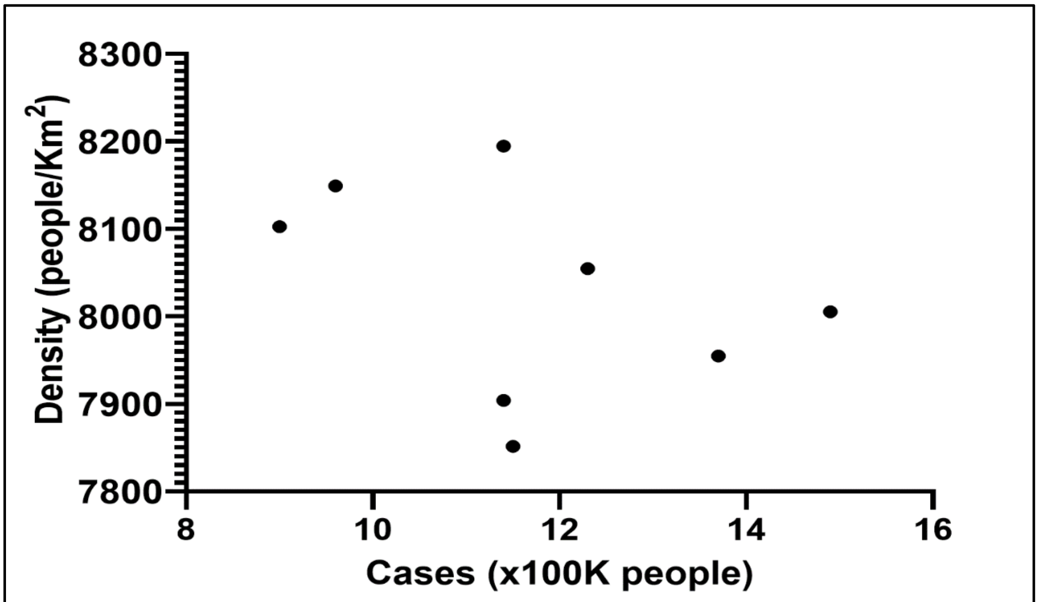
Table 4 - Demographic density and ratio of cases of children with childhood tuberculosis, from 2015 to 2022, São Paulo - SP.

Variable	**Fee**	**Demographic density**
Year		
2015	11,5	7851,4
2016	11,4	7904,0
2017	13,7	7954,6
2018	14,9	8005,3
2019	12,3	8054,6
2020	9,0	8102,6
2021	9,6	8149,2
2022	11,4	8194,6

The rates are relative to every 100,000 children aged 0-14.

Figure 14 graphically displays this relationship between case rate and density.

Figure 14 - Demographic density and ratio of cases in children with childhood tuberculosis, from 2015 to 2022, São Paulo-SP.



The rates are relative to every 100,000 children aged 0-14.

Table 5 shows the correlation between demographic density and tuberculosis occurrence rates in general and according to sex, age group, race and treatment strata. Specifically, the analysis showed the relationship between density, gender, race, treatment carried out and not carried out, in which a strong positive correlation was observed between density and yellow race (r=0.87, p=0.005) and a strong negative correlation between density and indigenous race (r=-0.89, p=0.003). A strong positive correlation was also found between density and targeted treatment (r=0.78, p=0.021). In addition, a positive correlation indicated that the higher the density, the higher the tuberculosis rate in the yellow race and in the targeted treatment. The negative correlation indicated an inverse relationship, i.e. the higher the density, the lower the annual prevalence, and the significant p-values in these cases indicated that the respective correlations were significantly different from zero.

Table 5 - Correlation between demographic density, sociodemographic characteristics and treatment of children with childhood tuberculosis, from 2015 to 2022, São Paulo-SP.

Variable	Mean (SD)	n	r	Method	p-value
General	11,7 (2,0)	8	-0,39	Pearson	0,343
Male	11,6 (1,8)	8	-0,40	Pearson	0,326

Female	11,9 (2,2)	8	-0,35	Pearson	0,391
White	7,0 (1,5)	8	-0,44	Pearson	0,277
Black	13,1 (3,8)	8	-0,01	Pearson	0,973
Yellow	2,2 (2,3)	8	0,87	Spearman	0,005
Brown	14,0 (2,7)	8	0,12	Pearson	0,780
Indigenous	120,2 (124,4)	8	-0,89	Pearson	0,003
Targeted treatment carried out	3,6 (0,9)	8	0,78	Pearson	0,021
Targeted treatment not carried out	4,4 (1,7)	8	-0,34	Pearson	0,405

(r): Correlation Coefficient.

4. DISCUSSION

The results presented below were discussed in the light of comparisons with similar and contrary findings in the literature, as well as comparisons of the theoretical data that elucidate the phenomena found here with other studies. Firstly, they were compared to the findings of other researchers who have exclusively investigated the epidemiological profiles of patients with childhood tuberculosis; secondly, they were also compared to the findings of studies with methodologies and objectives similar to those of this research. In addition, the phenomena found in this research were discussed with studies that elucidated them and/or touched on them, in order to explain the data reported here in this research, but which had not been reported in the articles in this field of study. For this reason, the most accessible and relevant published works were shown below, as well as the most prominent findings in the four categories covered in this research: bibliographical review of tuberculosis in children and adolescents; characterisation of childhood tuberculosis cases and deaths; as well as temporal trends in childhood tuberculosis cases and deaths, and the correlation between the occurrence of tuberculosis and demographic density, as can be seen in the following sections:

4.1 CHARACTERISATION OF CHILDHOOD TUBERCULOSIS CASES AND DEATHS

As the results section above showed, there were a total of 1,835 registered cases, with an equal distribution between the sexes and a notable prevalence in the 10 to 14 age group, in addition to a higher incidence rate among indigenous children, highlighting the vulnerability of this specific population, and the analysis of sociodemographic data revealed that the brown race was the most affected, followed by the white race. These findings were in line with the study by Galesi and Fukasava (2015), who also reported a high incidence of tuberculosis among brown children in São Paulo, however, the high incidence rate in the indigenous population, of 1202 cases per 100,000 children, reflected a particular concern that is not widely addressed in the literature, since according to de Alencar *et al.* (2023), this disparity can be attributed to socioeconomic factors and limited access to health services in indigenous communities. Analysing the treatment data revealed that only 37.7% of children received targeted treatment, while 31.0% did not receive treatment and in 31.3% of cases the information was not specified. This can be compared with the findings of Carvalho *et al*. (2018), who emphasised the importance of adequate treatment to reduce child morbidity and mortality, and the results suggest an urgent need to improve the coverage and quality of treatment for children with tuberculosis in São Paulo. Thus, in relation to deaths from childhood tuberculosis, this study recorded 17 deaths in the period from 2015 to 2022, with a slightly higher distribution among girls, while the under 1 year age group had the highest proportion of deaths, which corroborated data from Starke (2017), who also identified greater vulnerability in this age group, emphasising a need for preventive interventions and early diagnosis to reduce mortality in babies from this cause. And when comparing the data from São Paulo with other studies, it was found that the incidence and mortality rates were similar to those observed in other urban regions of Brazil, according to Barbosa and Cosme's (2013) study on tuberculosis in metropolitan regions, which also found high incidence rates and significant challenges in treatment management. However, according to Miranda and Pereira (2021) on tuberculosis in children in Brazil as a whole, it pointed to a significant variation in incidence rates between different regions, suggesting that specific regional factors, such as living conditions and access to healthcare, play a crucial role in the epidemiology of the disease. Furthermore, a comparison with international studies, such as that by Pequeno *et al*. (2010), which analysed childhood tuberculosis data in countries with robust health systems, revealed that the incidence in São Paulo is significantly higher, a phenomenon that can be attributed to socioeconomic disparities and challenges in the local public health system, since while developed countries have implemented more effective tuberculosis control programmes, São Paulo still faces considerable obstacles, such as a lack of adequate infrastructure and trained human resources. At the same time, the high incidence of tuberculosis among indigenous children highlighted in this study was also observed by Silva *et al*. (2021), who emphasise the need for specific and culturally adapted health policies for these populations. And such findings suggest that targeted interventions, such as health education programmes and improved access to health services, will be essential to reduce the disease burden among vulnerable groups. Similarly, in terms of treatment, the data indicated that the implementation of targeted treatments needs to be strengthened, and the existing literature, such as Lindoso*et al*. (2021), pointed to the effectiveness of well-structured treatments in reducing morbidity and mortality rates, however the challenges in implementing such programmes in São Paulo, as evidenced by the results presented, suggest the need for more effective strategies and the allocation of adequate resources to ensure that all affected children receive the necessary treatment, In addition, the results also suggest the need to improve health records, especially with regard to the treatment of childhood tuberculosis, as the absence of information on treatment in 31.3 per cent of cases highlighted a significant flaw in monitoring and recording systems, as observed by the study by Matos *et al*. (2012), and optimising data collection and quality was essential for developing more effective health policies and implementing tuberculosis control programmes. Thus, this research revealed that although progress has been made in controlling childhood tuberculosis in São Paulo, there are still significant challenges, especially among vulnerable populations such as indigenous children, and the comparison with other studies highlighted both similarities and differences in epidemiological patterns and treatment outcomes. It is therefore essential that public health policies adapt to the specific needs of these populations in order to reduce the incidence and mortality of childhood tuberculosis. Thus, prevention programmes, early diagnosis, appropriate treatment and improvements in health infrastructure are fundamental to achieving these desired improvement goals in the coming years, while also contributing to the understanding of the epidemiology of childhood tuberculosis in São Paulo by providing a basis for future research and policy interventions.

4.2 TIME TRENDS IN CASES AND DEATHS FROM CHILDHOOD TUBERCULOSIS

In this study, the results showed an analysis of the data in relation to deaths from childhood tuberculosis, with 17 deaths in the period from 2015 to 2022, in which the age group of less than 1 year had the highest proportion of deaths, which corroborated the data of Starke (2017), who also reported a high vulnerability and higher risk of deaths in part of the same period, in addition to also exposing the same vulnerability in this age group.

In addition, analysing the time trend of childhood tuberculosis cases and deaths revealed a decrease in prevalence during the pandemic period, with cases falling from 123 to 9 per 100,000 children. However, in 2022, there was a slight increase to 114 cases per 100,000 children and this temporal pattern was similar for both sexes, with a notable decrease in the pandemic period (Figure 6 and Figure 7), which corroborated studies that identified significant impacts of the COVID-19 pandemic on the notification and treatment of other infectious diseases, including tuberculosis (MENDES *et al.*, 2021).

In addition, there has also been a decrease in the occurrence of tuberculosis among indigenous children in recent years, with no cases recorded in 2019 and 2022 (Figure 8), which makes this result encouraging, but it should be interpreted with caution, considering possible underreporting during the pandemic and the persistent vulnerability of this population (MENDES *et al.*, 2021). The rate of targeted treatment also decreased in 2020 and 2021, which can be attributed to the overload of the health system during the pandemic (Figure 9). Thus, child tuberculosis mortality remained below one occurrence per 100,000 children in all the years analysed (Figure 13), which was consistent with ongoing efforts to optimise the early diagnosis and treatment of tuberculosis during the period analysed, as highlighted by Santos *et al*. (2020).

This being said, the discussion of this research prism has highlighted that even with falls in the rates observed during the pandemic period, these findings may be the result of underreporting or greater attention by policies to the treatment of airway infections that occurred in the same period, so by analysing the averages and historical trends, lessons can also be learned about optimising public health policies, as well as preparing professionals and the public and private health system in advance to tackle tuberculosis in the most neglected groups.

4.3. CORRELATION WITH POPULATION DENSITY

Analysing the correlation between population density and the incidence of childhood tuberculosis in São Paulo between 2015 and 2022 revealed important epidemiological information, since during this period population density showed continuous growth, while the rate of tuberculosis cases per 100,000 children varied significantly, with the lowest rates observed in 2020 and 2021.

The results showed that the population density in São Paulo increased progressively, from 78,514 inhabitants per square kilometre in 2015 to 81,946 in 2022, in concomitance with the incidence rate of childhood tuberculosis which varied, peaking at 149 cases per 100,000 children in 2018 and falling to 90 cases in 2020, with a partial recovery to 114 cases in 2022. This variation suggests that factors other than population density, such as changes in health policies and events like the COVID-19 pandemic, have influenced tuberculosis rates (PEREIRA *et al*., 2022). The correlation between demographic density and child tuberculosis rates, according to different sociodemographic and treatment strata, revealed significant correlations, especially with a strong positive correlation between density and the incidence of tuberculosis among children of the yellow race (r=0,87, p=0.005), and a strong negative correlation between density and incidence among indigenous children (r=-0.89, p=0.003), such that these findings were consistent with the observations of Galesi and Fukasava (2015), who also reported racial disparities in the incidence of childhood tuberculosis in urban areas. In addition, a significant positive correlation was also observed between demographic density and the provision of targeted treatment (r=0.78, p=0.021). This suggests that in more densely populated areas, children with tuberculosis were more likely to receive appropriate treatment, possibly due to greater availability and access to health services (CARVALHO *et al*., 2018). However, the negative correlation between density and incidence of tuberculosis among indigenous children highlights the need for more inclusive health policies adapted to the specific needs of these vulnerable populations (OLIVEIRA *et al*., 1996). The results of this study also indicate that although demographic density has a significant influence on the incidence of childhood tuberculosis, other factors, such as socioeconomic conditions and access to health services, play crucial roles. As can be seen in the negative correlation between density and tuberculosis incidence among white and brown children (r=-0.44 and r=-0.12, respectively), suggesting that in more densely populated areas, these populations may have better access to health resources that contribute to lower incidence rates (LINDOSO *et al*., 2021). This may also have been substantially impacted by the COVID-19 pandemic, as tuberculosis notification and treatment rates changed during these periods, and during 2020 and 2021, childhood tuberculosis incidence rates fell significantly, This can be attributed to the restructuring of health systems and the predominant focus on combating the coronavirus, a phenomenon already reported in several studies, which pointed to an underreporting of tuberculosis cases during the pandemic due to the reduction in medical consultations and diagnoses (MENDES *et al*., 2021). Therefore, even though the results of this study highlight the complexity of the relationship between demographic density and the incidence of childhood tuberculosis in São Paulo, it can be seen that population density has also revealed significant correlations with certain subpopulations, and it is clear that a broader set of factors influences the epidemiology of tuberculosis. This is something that public health policies should therefore consider, as these polysemic dimensions could be the key to developing new, more effective strategies for controlling and treating childhood tuberculosis, especially in vulnerable populations. So this study has made a significant contribution to understanding the epidemiological dynamics of childhood tuberculosis, especially by suggesting the need for more targeted and inclusive public health interventions to mitigate the impacts of this disease in São Paulo.

5. CONCLUSION

The outcome of this research was initially based on the findings of the literature review, which showed that tuberculosis continues to be a significant public health concern, especially in vulnerable populations such as children and adolescents, as several studies have highlighted the complexity of controlling tuberculosis in this age group, due to factors such as the difficulty in early diagnosis, the variability in clinical presentation and the need for prolonged therapeutic regimens, and the review also indicated that public health policies need to be continuously updated and adapted to meet the specific challenges of this disease, as suggested by the authors of this research. Furthermore, the analysis of DATASUS data revealed significant variations in the incidence rates of childhood tuberculosis in São Paulo over the last 10 years, and among the most relevant was a peak in incidence in 2018, followed by a significant drop in subsequent years, especially in 2020 and 2021, which coincide with the period of the COVID-19 pandemic. Similarly, when comparing data from São Paulo with other studies, it was found that the city showed variations in the incidence of childhood tuberculosis that are in line with trends observed in other urban regions with high population density, with a correlation between demographic density and tuberculosis incidence, highlighted in the results of this study, and supported by other studies that have also reported a positive relationship between high population density and higher rates of tuberculosis, especially among vulnerable populations. Furthermore, detailed analysis of the data also revealed that demographic density had a significant positive correlation with the incidence of tuberculosis among children of the yellow race and a negative correlation with the incidence among indigenous children, indicating the need for public health interventions that are sensitive to the sociodemographic and cultural particularities of the various populations affected by tuberculosis, as well as the positive correlation between demographic density and targeted treatment carried out, suggesting that more densely populated areas may have better access to health resources, facilitating proper diagnosis and treatment. That said, at the end of this research it can be concluded that although demographic density is an important factor in the epidemiology of childhood tuberculosis, other factors such as socioeconomic conditions, access to health services and effective public policies also play crucial roles. Therefore, the findings of this research also reinforced the importance of comprehensive and inclusive public health strategies that take into account the diversity of urban populations and their specific needs, which can greatly contribute to understanding the epidemiological dynamics of childhood tuberculosis in São Paulo and provide subsidies for the development of policies and interventions that can mitigate the impacts of this disease on vulnerable populations. Based on the findings of this research, recommendations include the need for greater investment in targeted health programmes, strengthening epidemiological surveillance networks and promoting awareness campaigns about the importance of early diagnosis and adequate treatment of childhood tuberculosis.

Disclaimer (Artificial intelligence)

Option 1:

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of manuscripts.

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