SOCIOECONOMIC DETERMINATION AND SPATIAL DISTRIBUTION OF TUBERCULOSIS/HIV CO-INFECTION IN A STATE OF BRAZIL

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ABSTRACT
Objective: To investigate the influence of social, economic and housing variables due to Tuberculosis/HIV in the state of Alagoas, Brazil. Methods: This is an ecological and cross-sectional study that evaluates the independent effect of variables from the Brazilian Institute of Geography and Statistics and United Nations Development Programme in the Annual Average Incidence Rate of Tuberculosis/HIV coinfection in the state of Alagoas from 2001 to 2016. We used Generalized Estimating Equation models implemented in SPSS software. Results: Among indicators related to cases of tuberculosis in people living with HIV in the municipalities of Alagoas, such as, the variables of household income per capita and percentage of households without piped water. A significant association in tests and measuring the quantification of important effects in the relationship among the strength association of each risk factors and the development of co-infection. Conclusion: The results can be consistent, allowing the identification of factors associated with the socioeconomic and socio-housing determination of TB/HIV co-infection in the state of Alagoas.

Keywords: Tuberculosis; HIV; Epidemiology; Risk Factors; Socioeconomic Factors.
DETERMINAÇÃO SOCIOECONÔMICA E DISTRIBUIÇÃO ESPACIAL DA COINFECÇÃO TUBERCULOSE/HIV EM UM ESTADO DO BRASIL

RESUMO

Objetivo: Investigar influência de variáveis sociais, econômicas e habitacionais no adoecimento por Tuberculose/HIV no estado de Alagoas, Brasil. Métodos: Trata-se de um estudo ecológico e transversal que avaliou o efeito independente de variáveis de caracterização do Instituto Brasileiro de Geografia e Estatística e do Programa de Desenvolvimento das Nações Unidas na Taxa Anual Média de Incidência Coinfecção Tuberculose/HIV nas unidades territoriais do estado de Alagoas ao longo do período de 2001 a 2016. Análise de regressão linear simples e múltipla foram implementadas no software SPSS através do método de equações de estimação generalizada. Resultados: Dentre os indicadores relacionados à incidência de casos de TB em pessoas vivendo com HIV nos municípios alagoanos, as variáveis renda domiciliar per capita e percentual de residências sem água encanada obtiveram associação significativa nos modelos de regressão e produzir importante medida de efeito na quantificação da relação existente entre a força de associação de cada um dos fatores de risco e o desenvolvimento da coinfeção. Conclusão: Os resultados obtidos mostraram-se consistentes, permitindo a identificação dos fatores associados à determinação socioeconômica e sociohabitacional da coinfeção TB/HIV no estado de Alagoas.

Palavras chave: Tuberculose; HIV; Epidemiologia; Fatores de risco; Fatores Socioeconômicos.

INTRODUÇÃO

With the emergence of the Human Immunodeficiency Virus (HIV), in lately decades, a genuine resurgence of Mycobacterium tuberculosis infection has been observed (WHO, 2018).

In an attempt to understand the context of tuberculosis (TB) and HIV and to try to justify why certain groups become more ill than others, several studies have incorporated in their analysis the framework of the determinants of the health-disease process (MUNAYCO et al., 2015; SANTOS; MARTINS, 2018). At the same time, research that outlines socio-epidemiological profiles related to tuberculosis and HIV/AIDS mention features that are often associated with these diseases, with an emphasis on the conditions and life situations that increase health risks (PARKER; CAMARGO JUNIOR, 2000; ROSSETTO et al., 2018).

Studies had investigated associations of TB/HIV co-infection with environmental, social, behavioral and cultural characteristics, relating these findings as indicators of vulnerability (MAFFACCIOLLI; OLIVEIRA; BRAND, 2017). The set of economic, social, regional, ethnic inequalities and the fragility of public services offer have also been reported as factors influencing the epidemiological situation of these diseases (PEDRO; OLIVEIRA, 2013; CECCON et al., 2017; ROCHA et al., 2018).
Alagoas is one of the Brazilian federative units with the highest incidence of tuberculosis, ranking 4th in relation to the coefficient of new people affected by TB in the country and 5th in relation to the incidence of TB cases in people living with HIV/AIDS (BRASIL, 2017; SANTOS JÚNIOR et al., 2019). The state is still one of the poorest in the country (BRASIL, 2010).

With the intention of deepening the analysis of the scenarios in which people most affected by TB/HIV co-infection are inserted, a survey was carried out in 2018, in the state of Alagoas. This study analyzes indicators and understand its relationship with the occurrence of those affected by TB/HIV co-infection.

This study aimed to investigate the social, economic and housing influences in TB/HIV, in one of the poorest regions of Brazil, with high rates of infection with TB and HIV.

We believed that when we understand the sociodemographic dynamics of the areas in which the greatest records of the occurrence of these co-infection are concentrated we could have a better control and effectiveness of the treatment. Beside it, the association among characteristics of the locations constitute important measures for the health surveillance sector, since they can assist the improvement of public policies favorable.

METHODS

Design of the study

An ecological study was designed with a focus on the possible determinants of socioeconomic and housing components in the Annual Average Incidence Rate (AAIR) of TB/HIV incidence in the municipalities of Alagoas, from January 2001 to December 2016.

Lima-Costa & Barreto (2003) define that ecological studies compare the occurrence of a health-related condition (a disease - for example) and the exposure of interest among households of individuals (populations of countries, regions or municipalities - for example) to verify the possible existence of association among them. In this type of study, there is no information about the disease and exposure of the individual, but it is about the entire population group.
Location of the study

FIGURE 1: MAP OF TERRITORIAL CHARACTERIZATION.

Source: The authors.

The state of Alagoas is located in the East of the Northeast region, Brazil, and comprises a total of 102 municipalities. Alagoas occupies a territorial area of 27,778,506 km² and population of 3,322,820 inhabitants (IBGE, 2010).

Population of the study

New cases of TB / HIV co-infection of residents in the municipalities of the state of Alagoas were selected from January 2001 to December 2016 at the time of TB diagnosis and HIV serology.

Data sources

The selection of socioeconomic and housing variables resulted from documentary consultation, most of which came from the 2010 Demographic Census, conducted by the
Brazilian Institute of Geography and Statistics, and also from other sources such as the United Nations Development Programme (UNDP). Regarding, the databases consulted were obtained at Health Department of the State of Alagoas through National Disease Notification System by Brazilian Minister of Heath. The database of the notified cases of tuberculosis available through protocol 12.251 / 2018 by at Health Department of the State of Alagoas itself. The final variables considered in this study are presented in table 1.

**TABLE 1. AGGREGATED DATA FOR APPLICATION IN THE REGRESSION AND SPACE DISTRIBUTION MODELS.**

| Theme            | Variable                                                                 | Source                                      |
|------------------|--------------------------------------------------------------------------|---------------------------------------------|
| Epidemiologic    | New confirmed cases of tuberculosis with HIV co-infection from 2001 to 2016 | SINAN-MS/SESAU/AL                           |
| Demographic      | Population estimated for Brazilian municipalities from 2001 to 2016 (without sex and age group) | Annual Population Projections IBGE          |
|                  | Municipal Human Development Index                                         | Human Development Atlas UNDP                |
|                  | Theil Index                                                              | Human Development Atlas UNDP                |
|                  | Gini Index                                                               | Human Development Atlas UNDP                |
| Socioeconomic    | Illiteracy Rate                                                          | Census 2010 IBGE                           |
|                  | Household income per capita                                              | Census 2010 IBGE                           |
|                  | % of extremely poor people (up to 1/4 MW)                                | Census 2010 IBGE                           |
|                  | % of poor people (up to ½ MW)                                            | Census 2010 IBGE                           |
|                  | % of people ≥18 years unemployed                                         | Census 2010 IBGE                           |
| Socio-housing    | % of households without piped water                                      | Census 2010 IBGE                           |
|                  | % of households without garbage collection                              | Census 2010 IBGE                           |
|                  | % of households without electricity                                       | Census 2010 IBGE                           |
|                  | % of households where none has elementary studies                        | Census 2010 IBGE                           |
|                  | % of households with inadequate building                                 | Census 2010 IBGE                           |
|                  | % of households with inadequate sewage                                    | Census 2010 IBGE                           |
|                  | % of households with 6 or more people in the residence                   | Census 2010 IBGE                           |
|                  | % of households without bathrooms                                        | Census 2010 IBGE                           |

MW: Minimum wage. UNDP: United Nations Development Program.
Source: IBGE, 2010; UNDP, 2013. Prepared by the authors, 2019.
Data analysis

The data were categorized according to the municipality of origin of the affected people and calculated the Annual Average Incidence Rate (AAIR) of TB/HIV for each of the administrative regions of the territory under analysis. Geographical boundaries of 102 municipality were used. The Annual Incidence Rate by municipality, was calculated as shown below:

\[
\text{AAIR} = \frac{\text{Total new cases of TB-HIV}}{16 \times \text{Population}} \times 100,000 \text{ inhabitants}
\]

To investigate the independent effect of social, economic and housing variables on the occurrence of cases of TB/HIV coinfection in territorial units over the period 2001 to 2016, an association test was carried out among Annual Incidence Rate and the characterization indicators extracted from the Brazilian Institute of Geography and Statistics (IBGE, 2010) and United Nations Development Programme (UNDP) for the municipalities of the state (UN, 2013).

Simple and multiple linear regression analysis were implemented in order to obtain the regression coefficients that relate each variable in the model to AAIR through generalized estimating equation. From the univariate analysis, those indicators for which the AAIR regression had a significance >0.01 were introduced in the multiple regression model. Due to the asymmetric distribution of the data, gamma regression with log connection was used and, as the aggregation of municipalities was not taken into account, the independent correlation structure was chosen.

In order to fulfill the proposed objective, that is, to verify which variables would have the greatest explanatory power on the incidence of TB/HIV, the premise was that all the analyzed information presented homogeneity within the aggregation units studied in this work, such a reasonable consideration, since the municipalities are homogeneous units by IBGE to carry out their census.

The association analysis were estimated by Odds Ratio (OR) and used the SPSS program (Statistical Package for the Social Sciences), version 25.0. Values of \( p <0.05 \) were considered significant.
To investigate the space pattern of the incidence of TB/HIV coinfection and socioeconomic variables in the municipalities, exploratory analysis techniques were used through the production of thematic maps of spatial distribution using the Quantum GIS (QGIS) program, version 2.18.16, with the use of the cartographic base of Brazil by state, in WGS 84 projection, made available by IBGE.

The data were presented using graphs, tables and maps, and the results were discussed in the light of the specialized literature on the subject.

**Ethical aspects**

As this is a study using data from secondary sources, approval by the Research Ethics Committee was not required. The database employed was made available by the Superintendence of Health Surveillance of Alagoas (SVE/SESAU/AL) in September 2018 through protocol 2251/2018.

**RESULTS**

From 2001 to 2016, there was a record of TB / HIV co-infection in 75 municipalities in the state of Alagoas and absence of cases of co-infection in 27 municipalities. The AAIR in the municipalities where occurrence was reported ranged from 0.2 to 4.8 cases per 100 thousand inhabitants. AAIR had an average of 1.05 cases of TB/HIV coinfection in 100 thousand inhabitants (Table 2). In the analysis of the average incidence per municipality, 42%, it means, 43 of the 102 municipalities in the state had AAIR above the state average (Figure 2).

The cities with the largest AAIR were located mostly in the eastern part of the state and distributed unevenly in the space of the Federative Unit. There was no formation of "clusters" and / or spatial clusters of high incidences for AAIR in the period under analysis (Figure 2).
FIGURE 2: SPATIAL DISTRIBUTION OF THE ANNUAL AVERAGE INCIDENCE RATE OF TUBERCULOSIS / HIV COINFECTION PER 100,000 INHABITANTS IN THE STATE OF ALAGOAS, BRAZIL, IN THE PERIOD 2001-2016.

Table 2 presents the results of the descriptive statistics for the AAIR of TB/HIV coinfection incidence and for the socioeconomic and socio-housing variables employed of this study.
TABLE 2. DESCRIPTIVE STATISTICS OF AAIR AND THE SOCIODEMOGRAPHIC VARIABLES APPLIED IN THE REGRESSION MODELS AND IN SPATIAL ANALYSIS.

| Variable                                      | Min.   | Max.   | Avg.   | SD    |
|-----------------------------------------------|--------|--------|--------|-------|
| Annual Average Incidence Rate of TB/HIV       | 0,000  | 4,800  | 1,050  | 1,070 |
| Municipal Human Development Index             | 0,493  | 0,721  | 0,571  | 0,039 |
| Illiteracy Rate                                | 11,860 | 40,350 | 31,257 | 5,781 |
| Theil Index                                   | 0,400  | 0,830  | 0,531  | 0,100 |
| Gini Index                                    | 0,460  | 0,650  | 0,530  | 0,045 |
| Household income per capita                   | 177,550| 792,540| 265,398| 85,345|
| % of extremely poor people (up to ¼ MW)       | 5,290  | 43,440 | 21,726 | 8,312 |
| % of poor people (up to ½ MW)                 | 15,570 | 61,710 | 43,676 | 9,133 |
| % of people ≥18 years unemployed              | 2,100  | 24,420 | 9,874  | 4,387 |
| % of households without piped water           | 2,750  | 71,980 | 24,548 | 15,037|
| % of households without garbage collection    | 0,000  | 33,070 | 5,509  | 6,818 |
| % of households without electricity           | 0,160  | 7,340  | 1,793  | 1,230 |
| % of households where none has elementary studies | 23,790 | 67,390 | 49,032 | 7,998 |
| % of households with inadequate building      | 0,350  | 32,700 | 9,313  | 8,050 |
| % of households with inadequate sewage        | 26,080 | 99,740 | 75,655 | 22,443|
| % of households with 6 or more people in the residence | 5,843  | 24,870 | 13,509 | 3,543 |
| % of households without bathrooms             | 0,690  | 32,070 | 10,642 | 6,963 |

Min.: Minimum value; Max.: Maximum value; Avg.: Average Value; SD: Standard deviation; MW: Minimum wage. Source: IBGE, 2010; UNDP, 2013. Prepared by the authors, 2019.

In the first step, nine variables (illiteracy rate; municipal HDI - Human Development Index; per capita household income; percentage of extremely poor people; percentage of poor people; percentage of people aged ≥18 years unemployed; percentage of households without piped water; percentage of households without garbage collection; percentage of households with more residents in the household) revealed a significant association in the univariate regression analysis with AAIR. The other variables produced a relative measure of effect close to 1.0 (OR), but non-significant p values (Table 3).
### TABLE 3. UNADJUSTED ODDS RATIO OF THE LINEAR REGRESSION WITH LINK TO THE TB/HIV CO-INFECTION RATE FROM THE GENERALIZED ESTIMATING EQUATION (GEE) MODEL.

| Variable                                           | Univariate analysis | Multivariate analysis |
|----------------------------------------------------|---------------------|-----------------------|
|                                                    | OR      | IC 95%       | pvalor | OR      | IC 95%       | pvalor |
| Municipal Human Development Index                  | 47,368  | 1,962-1143,412 | 0,018  | 0,017  | 0,264-225,789 | 0,399  |
| Illiteracy Rate                                    | 0,972   | 0,947-0,998   | 0,034  | 1,014  | 0,948-1,084  | 0,685  |
| Theil Index                                        | 0,710   | 0,106-4,738   | 0,723  | -      | -            | -      |
| Gini Index                                         | 0,653   | 0,009-46,359  | 0,845  | -      | -            | -      |
| Household income per capita                        | 1,002   | 1,001-1,003   | 0,000  | 1,004  | 1,002-1,007  | 0,002* |
| % of extremely poor people (up to ¼ MW)           | 0,975   | 0,955-0,955   | 0,014  | 1,023  | 0,980-1,069  | 0,295  |
| % of poor people (up to ½ MW)                     | 0,982   | 0,966-0,997   | 0,020  | 0,985  | 0,945-1,026  | 0,466  |
| % of people ≥18 years unemployed                   | 1,041   | 1,008-1,074   | 0,014  | 1,027  | 0,982-1,074  | 0,238  |
| % of households without piped water               | 0,984   | 0,974-0,995   | 0,003  | 0,986  | 0,974-0,998  | 0,028* |
| % of households without garbage collection        | 1,015   | 0,999-1,032   | 0,007  | -      | -            | -      |
| % of households without electricity                | 1,017   | 0,882-1,173   | 0,816  | -      | -            | -      |
| % of households where none has elementary studies  | 0,985   | 0,968-1,003   | 0,110  | -      | -            | -      |
| % of households with inadequate building          | 1,014   | 0,995-1,034   | 0,142  | -      | -            | -      |
| % of households with inadequate sewage             | 0,996   | 0,990-1,002   | 0,189  | 1,016  | 1,016-0,997  | 0,095  |
| % of households with 6 or more people in the residence | 0,957   | 0,915-1,001   | 0,050  | 0,995  | 0,995-0,932  | 0,880  |
| % of households without bathrooms                  | 0,995   | 0,977-1,013   | 0,584  | -      | -            | -      |

OR: Odds Ratio; MW: Minimum wage. Source: IBGE, 2010; UNDP, 2013. Prepared by the authors, 2019.
Figure 3 presents the spatial distribution of socioeconomic and socio-housing characterization indicators, respectively, which obtained a measure of statistically significant effect with AAIR in the univariate regression model and/or in the multiple regression model.

FIGURE 3A-3D. SOCIOECONOMIC CHARACTERIZATION INDICATORS IN THE MUNICIPALITIES OF ALAGOAS.

3A: Percentage of people receiving up to 1/4 of the minimum wage; 3B: Percentage of people receiving up to 1/2 of the minimum wage; 3C: Per capita household income; 3D: Percentage of people ≥18 years old unemployed.

Source: IBGE, 2010. Prepared by the authors, 2019.
FIGURE 3E-3H. SOCIO-HOUSING CHARACTERIZATION OF THE MUNICIPALITIES OF ALAGOAS.

3E: Percentage of households without garbage collection; 3F: Percentage of households without piped water; 3G: Percentage of illiterates; 3H: Percentage of households with 6 or more people in the residence. Source: IBGE, 2010. Prepared by the authors, 2019.

DISCUSSION

The results obtained through the method of generalized estimating equation allowed the identification of the factors associated with the socioeconomic and socio-housing determination of TB/HIV co-infection in Alagoas, as well as the exploratory analysis allowed the visualization of the spatial distribution of the related variables in the territory.

The bibliography presents a series of determinants and factors related to the occurrence of tuberculosis and HIV (PEDRO; OLIVEIRA, 2013; PELISSARI et al., 2018). In this study it was found that the population living in areas with the worst vulnerability
indicators get ill more due to TB/HIV coinfection compared to population that reside in the state's territories with the best categorizations in socioeconomic and socio-housing indicators.

Among the indicators associated with tuberculosis cases in people living with HIV in the municipalities of Alagoas, two variables are associated with multivariate analyses. The results of those who lived in regions with higher family income per capita were less likely to have TB/HIV co-infection. This finding is in accordance with publications, which emphasizes the higher TB morbidity in families with the main financial conditions (DYE et al., 2009; XIMENES et al., 2009; PEREIRA et al., 2015; PELISSARI et al., 2018; PEREIRA et al., 2018).

However, an observed odds ratio for those who live in regions with a higher percentage of households without water supply was meaningless contrary to what was expected. This finding contradicts publications, which emphasized greater TB morbidity in houses without water supply (CANTWELL et al., 1998; DYE et al., 2009; PEREIRA et al., 2015; PEDRO et al., 2017; SILVA et al., 2018) and may be linked to Luis David Castiel called an ecological fallacy (cross-level bias), a phenomenon of imbalance where, in an analysis of aggregated data - as adopted in this study, a result is generated that seems paradoxical but, in a more detailed analysis, it appears plausible at the individual level (CASTIEL, 1998).

On a socioeconomic determination of TB/HIV co-infection, Parker and Camargo Jr. to analyze anthropological aspects to HIV related to international documented literature as factors that facilitate the transmission of AIDS viruses and their influence in geographic and population. In their study they conclude that economic underdevelopment and poverty are the main factors related to HIV (PARKER; CAMARGO JUNIOR, 2000). They emphasized that inequalities put women and men in situations of vulnerability and that the process of underdevelopment creates social displacement that produces actions and practices that increase the risk of HIV infection (PARKER; CAMARGO JUNIOR, 2000). Other advanced studies in the African continent and in Brazil have also confirmed this relationship (PARKHURST, 2000; BRUNELLO et al., 2011; FOX, 2012). In the same vein, Pereira et al. (2015) reported a higher occurrence of TB in the neighborhoods of Rio de Janeiro and presented the main socioeconomic conditions. The authors, when carrying out a spatial analysis of TB cases, identified the formation of spatial clusters and major cases of disease in
slum regions - areas that shelter housing in precarious conditions, devoid of regularization by public authorities and, often, services such as treated water, sewage, among others (PEREIRA et al. 2015).

Information on the percentage of illiteracy, poor and/or extremely poor, unemployed, households without garbage collection and the number of residents per household, which revealed significance in the univariate analysis, has also been cited in the specialized literature as conditions associated with infection by TB. Studies (ALBUQUERQUE et al., 2007; XIMENES et al., 2009; BELO et al., 2011; PEREIRA et al. 2015, PEDRO et al., 2017; MAGALHÃES et al., 2017) indicated an association between TB infection and being part of a middle/low social class, mainly in the occurrence of TB infection associated with the HIV virus and resistant forms of the disease (PEREIRA et al. 2018). Others pointed out that low education (ALBUQUERQUE et al. 2007; BELO et al., 2011; PEREIRA et al. 2015; MAGALHÃES et al. 2017; SILVA et al., 2018), absence of sewage (DYE et al., 2009; PEREIRA et al., 2015; PEDRO et al. 2017; MAGALHÃES et al. 2017) and garbage collection service (OLIVEIRA; GONÇALVES, 2013; PEDRO; OLIVEIRA, 2013), as well as job vacancy (PEREIRA et al. 2015; MAGALHÃES et al. 2017) are also associated with a greater presence of TB. Accordingly, Nery et al. (2017) showed that TB incidence rates were significantly reduced in municipalities with high coverage of the Bolsa Família Program in census sectors in the municipality of Olinda (PE). These findings reinforce the evidence that the population most affected by co-infection is composed by individuals who live in worse living conditions and with difficulties in accessing public services.

Baldan et al. (2017) and Pedro (2017) identified in their studies in Mato do Grosso do Sul and Rio de Janeiro, respectively, that areas with expressive population density and with the worst Human Development Index presented the highest rates of co-infection with TB/HIV, data that here were corroborated by the state of Alagoas.

CONCLUSION

The results found concluded that the variables household income and percentage of households without piped water had the greatest explanatory power of correlation among socioeconomic variables and the occurrence of TB/HIV co-infection in the period from 2001 to 2016 in the municipalities of the state of Alagoas. Such findings corroborate by the literature...
consulted to the extent that they express that the existence of inequality increases the risk of occurrence of TB/HIV co-infection.

The relationship among spaces and the influence of socioeconomic and socio-housing determinants with the occurrence of TB/HIV coinfection enabled an expanded understanding of this public health problem. Far from having the homogenization of spaces and their indicators as meaning, this approach allowed the grading of the rates of people affected by TB/HIV and its determining factors. In addition to enabling the association of the occurrence of the disease with local characteristics of the territory. Thus, it allowed the understanding of the disease as a phenomenon that is expressed in the individual who lives in a certain environmental and social context.

Finally, it is worth emphasizing that this study has limitations common to those using secondary databases, in which the accuracy and completeness of the information can limit the findings by not allowing the researcher to control possible errors resulting from typing, registration, omission in the filling in fields and possible underreporting. There may also be a limitation linked to the design adopted, of data analysis at the aggregate level, which may not explain exposure and event at the individual level. However, even with these considerations and respecting the limits of the type of study carried out, there is a possibility that the results obtained can be used to enable a more incisive action by the public authorities in situations associated with a greater risk of the occurrence of TB/HIV coinfection, optimizing the allocation of resources.

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