Study of the Epidemiological Profile of Tuberculosis and Coinfection of HIV-Seropositive Patients in a Reference Hospital in the State of Alagoas

Estudo do Perfil Epidemiológico da Tuberculose e Coinfecção de Pacientes Soropositivos para HIV em Hospital de Referência no Estado de Alagoas

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Abstract

Tuberculosis is a disease that has affected the population for more than centuries, it is caused by Mycobacterium tuberculosis with high incidence and prevalence in the population. In Brazil, active tuberculosis is the condition with the greatest impact on mortality in people living with the human immunodeficiency virus, since this part of the population is more likely to develop the disease. In this sense, in order to elucidate the epidemiological profile of patients coinfected with Tuberculosis/HIV, a retrospective study was carried out with a quantitative approach in a referral hospital in the care of these patients in the State of Alagoas. 956 cases of tuberculosis and HIV co-infection were reported, with a higher incidence in males (63.49%), in mixed race (82.42%) and in the age group corresponding to the economically active population, between 21 and 50 years (84,.08%). In addition, the pulmonary clinical form (73.95%) is predominant among the cases, with the peripheral lymph node (32.12%) being the most frequent among the extrapulmonary forms (19.87%). Regarding the clinical outcome of these patients, it was observed that there was a higher rate of treatment drop-out in patients reported with alcoholism, consequently reducing the cure rate of these patients. Therefore, it is evident that socioeconomic variables directly influence the incidence and outcome of patients co-infected with Tuberculosis/HIV and that despite the therapeutic advances and the existing support network, it is still a disease that generates negative impacts on the social development of the country.

Keywords: Epidemiology. HIV. Health Profile. Tuberculosis.

Resumo

A tuberculose é uma enfermidade que afeta a população há mais de séculos, é causada pelo Mycobacterium tuberculosis apresentando elevada incidência e prevalência na população. No Brasil, a tuberculose ativa é a condição de maior impacto na mortalidade em pessoas que vivem com o vírus da imunodeficiência humana, já que essa parcela da população apresenta uma maior probabilidade de desenvolver a doença. Nesse sentido, a fim de elucidar o perfil epidemiológico dos pacientes coinfectados com Tuberculose/HIV, realizou-se um estudo retrospectivo com abordagem quantitativa em um hospital de referência no atendimento destes pacientes no Estado de Alagoas. Foram notificados 956 casos de coinfecção tuberculose e HIV, apresentando maior incidência no sexo masculino (63,49%), na cor parda (82,42%) e na faixa etária correspondente a população economicamente ativa, entre 21 e 50 anos (84,08%). Além disso, a forma clínica pulmonar (73,95%) é predominante dentre os casos, sendo a ganglionar periférica (32,12%) a mais incidente entre as formas extrapulmonares (19,87%). Em relação ao desfecho clínico desses pacientes, observou-se que houve uma maior taxa de abandono do tratamento em pacientes notificados com agravo por alcoolismo, reduzindo consequentemente a taxa de cura destes pacientes. Portanto, fica evidente que variáveis socioeconômicas influenciam diretamente na incidência e no desfecho de pacientes coinfectados com Tuberculose/HIV e que apesar dos avanços terapêuticos e da rede de suporte já existente, ainda é uma doença que gera impactos negativos para o desenvolvimento social do país.

Palavras-chave: *Epidemiologia. HIV. Perfil de Saúde. Tuberculose.*

1 Introduction

Tuberculosis (TB) is the oldest of the current epidemic diseases, also known in the 19th century as gray plague, is among the top ten causes of global health problems, accounting for about 8.9 million new cases and 1.7 million deaths annually[1,2]. It is a disease that can be caused by any of the seven species that make up the *Mycobacterium tuberculosis* complex, presenting high transmissibility and affecting the lungs as a priority, although it may affect other organs and systems, having as main manifestations persistent dry or persistent cough, afternoon fever, nocturnal sweating and weight loss[3,4]. It is estimated that about 25% of the world population is infected with *M. tuberculosis* and presents a potential risk of developing the disease throughout life[1].

According to the World Health Organization - WHO[5], Brazil is among the countries with a high occurrence of tuberculosis, being among the 30 that make up the global ranking of disease incidence[5,6], being considered a priority nation for disease control[7-9]. In line with the general statistics of the country, the State of Alagoas also has an expressive notification rate, totaling 715 cases reported in 2020, 355 of which are only in the capital Maceió. The incidence rate of the disease for the state was 21.3 affected people to every 100.000 inhabitants[10].

After contamination by *M. tuberculosis,* the risk of

illness, that is, the probability of an individual developing active disease depends on factors related to the bacillus, the environment and the immune competence of the host itself[4,11]. The occurrence of associated infectious diseases also has an important aspect in the epidemiology of tuberculosis and, in this context, HIV-related immunodeficiency plays a prominent role, since in some countries the emergence of AIDS has contributed to the increase of new cases of tuberculosis[12].

In the Brazilian territory, active TB is the condition of the greatest impact on mortality among people living with HIV/AIDS (PVHA)[13]. This correlation can be established mainly by the destruction of cellular immunity, which makes the host susceptible to opportunistic diseases, since this is an essential mechanism in the defense of the organism[14]. The TB-HIV association increases the probability of death, since in the co-infection situation, there are mutual changes in the evolution of each infection and, consequently, complications of the clinical signs can be triggered, differentiated responses to drug therapies and uncertain or unfavorable prognoses[12].

Thus, individuals with latent tuberculosis infection and HIV-infected individuals are more likely to develop the active form of the disease, since the immune impairment caused by HIV favors the multiplication of *M. tuberculosis* and TB disease[2,11].

In view of the above, the present study aimed to analyze the epidemiological profile of patients diagnosed with tuberculosis and coinfected with HIV registered at a referral hospital in the State of Alagoas, in order to establish goals and identify the specific needs of the population studied, thus directing, health actions for the identified obstacles.

2 Material and Methods

This is a retrospective cohort study with a quantitative approach, consisting of the analysis of the epidemiological profile of tuberculosis in HIV-positive patients treated at Hospital Escola Dr. Hélvio Auto (HEHA), since this is a reference in the State of Alagoas for the treatment of contagious infectious diseases.

The data were collected at the Hospital Center for Epidemiology of HEHA and the TabWin DATASUS platform, notified by the Notification Records Information System (SINAN), for the period between 2011 and 2020. All confirmed cases of pulmonary and/or extrapulmonary TB that had a positive diagnostic test for HIV were considered as TB/HIV co-infection.

Data were tabulated according to some variables in the SINAN - TB notification form, with gender, age group, ethnicity, level of education, disease worsened by associated alcoholism, clinical form of tuberculosis and situation of termination. These variables were selected in order to outline the patient's profile who is most affected by TB/HIV coinfection and to identify possible correlations with the severity of the situation of termination.

The analysis was carried out using the Microsoft Excel version 2016 program, using simple linear regression to analyze the correlation among age, gender, clinical form and alcohol-related harm with the situation of termination, a term that refers to the clinical outcome presented by the patients. For the other data, such as year of notification, age, gender, ethnicity and level of schooling, descriptive measures were used, such as mean, median, standard deviation and standard error.

In this sense, in order to evaluate the correlation of the variables mentioned with the situation of termination, the following model was estimated:

$$Situence = \beta_0 + \beta_1 gender + \beta_2 worsening + \beta_3 form + \beta_4 age + \varepsilon$$

Where situation measures the patient's situation of termination; however, the variable gender is a categorical variable that explains whether the patient is female (applying the value of 0 for the variable) or male (applying the value of 1); For the worsening, the worsening due to alcoholism was measured, since there are already other studies that elucidate this correlation; the form variable is also a categorical variable, but this one explains the clinical form of TB, whether pulmonary, extrapulmonary or mixed; age measures the correlation between older age groups and worse clinical outcomes, such as death; and ε is the term of regression error.

The data were discussed on the basis of epidemiological bulletins made available by the Ministry of Health on the subject and according to recent studies published on scientific platforms.

The research project of the present study was submitted to and approved by the Ethics and Research Committee of Centro Universitário Tiradentes (UNIT), under the opinion of n° 4.950.324. In addition, the study is in accordance with the Helsinki Declaration of 1964, revised in 1975,1983,1989,1996 and 2000[15] and with the guidelines of Resolution 466/2012 of the National Health Council[16]. In addition, the Free and informed consent term (WCT) was exempted, since there was no contact with the research participants and with information that allowed their identification, and the number of notification was used to individualize the patients.

3 Results and Discussion

Between the years 2011 and 2020, 956 cases of TB/HIV co-infection were reported in HHEHA, including all new cases, recurrence, re-entry after drop-out, transfers, post-death and other unreported cases, as described in Table 1.

Table 1 - Type of entry of TB/HIV co-infection cases

Type of Entry	N (%)
New case	588 (61.50%)
Re-entry after drop-out	226 (23.64%)
Transfer	72 (7.53%)
Recurrence	49 (5.12%)
Post-death	20 (2.09%)
Does not know	1 (0.10%)

Source: Research data

The distribution of cases over the years did not meet a pattern of progression, and an increase in the final number was observed, presenting the following numbers of notifications and their respective annual percentages: 74 notifications in 2011 (7.74%), 83 in 2012 (8.68%), 77 in 2013 (8.05%), 76 in 2014 (7.94%), 62 in 2015 (6.48%), 112 in 2016 (11.71%), 117 in 2017 (12.23%), 111 in 2018 (11;61%), 134 in 2019 (14.01%) and 110 in 2020 (11.50%).

As shown in Table 2, which elucidates the sociodemographic profile of these notifications, the mean age of the patients reported was 36.58 years, with a median of 37 years. A higher incidence of cases between 31 and 40 years was found, totaling 345 (36.08%) notifications for the described range. Furthermore, the age extremes observed in the study were 2 months and 81 years, with 1 case each.

Table 2 - Sociodemographic data in cases of TB/HIV coinfection cases

Data	n(%)
Gender	
Male	607 (63.49%)
Female	349 (36.51%)
Age range	
0-10	6 (0.62%)
11-20	32 (3.34%)
21-30	212 (22.17%)
31-40	345 (36.08%)
41-50	251 (26.25%)
51-60	78 (8.15%)
61-70	27 (2.82%)
71-80	5 (0.52%)
Schooling	
No schooling	88 (9.20%)
Elementary School Incomplete	317 (33.15%)
Elementary School Complete	46 (4.81%)
High School Incomplete	23 (2.40%)
High School Complete	64 (6.69%)
Upper Education Incomplete	4 (0.41%)
Upper Education Complete	24 (2.51%)
Ignored/Not filled	390 (40.79%)

Source: Research data

In addition, the field in the SINAN-TB notification form that highlighted the level of schooling was ignored/not filled in about 390 (40.79%) notifications. However, among the reported data, 317 (33.15%) notifications corresponded to patients with incomplete elementary education, calling special attention as it composes 71.42% of cases with declared schooling.

Regarding the ethnic group of the notified patients, 788 (82.42%) corresponded to brown color, followed by white color with 49 (5.12%) and black color with 36 (3.76%), the remainder was reported as ignored/unfilled, totaling 83 (8.68%) cases.

As for the clinical form of the disease, the exclusively pulmonary type is undeniably the most frequent, representing 73.95% of the cases, followed by the extrapulmonary form and, finally, by the mixed form of tuberculosis, with peripheral ganglion and meningoencephalic being the ones with the highest incidence among the non-pulmonary.

The less frequent extrapulmonary forms were ocular, cutaneous and laryngeal, with a total of 5 cases in the 10-year period. In Table 3, the incidence of clinical forms of TB presentation is described in greater detail.

Table 3 - Clinical form of TB/HIV co-infection cases

Type	n(%)
Pulmonary	707 (73.95%)
Extrapulmonary	190 (19.87%)
Pulmonary+ extrapulmonary	59 (6.17%)
Extrapulmonary Forms	
Peripheral ganglion	80 (32.12%)
Meningoencephalic	68 (27.30%)
Pleural	47 (18.87%)
Miliary	38 (15.26%)
Bone	3 (1.20%)
Laryngeal	3 (1.20%)
Ocular	1 (0.40%)
Skin	1 (0.40%)
Other	8 (3.21%)

Source: Research data

Sputum basciloscopy was positive in 146 (15.22%) cases, negative in 270 (28.24%), not performed in 516 (53.97%), not applied in 22 (2.3%) and was ignored in 2 cases (0.20%).

The analysis of the situation of termination, as detailed in Table IV, shows the outcome of the notifications in the period from 2011 to 2020. In this sense, it was observed that the absolute number of deaths due to TB (140) was higher than those due to other causes (71) and that the percentage of drop-out (23.45%) was almost equivalent to the percentage of cure (24.90%). Furthermore, most of the cases reported in the HEHA were opposed to references to their home municipalities, totaling 242 transfers in this period, and it was not possible to establish the actual outcome of these notifications. In addition, four diagnostic changes were declared, but it was not possible to have access to the new diagnosis and clinical outcome of the patients.

Furthermore, the analysis of the conditions of TB/HIV-infected patients revealed 956 notifications in the period mentioned above, 344 (35.98%) of them being alcohol-related, 573 (59.93%) did not have this condition, and 39 (4.07%) had the item worsened by alcoholism ignored in the notification form. Among these patients with alcoholism as an associated aggravating factor, excluding the transferred patients, it was verified that the percentage of noncompliance was 22.95% and that of death due to TB and other causes was 20.05%. In addition, the proportional percentage of cure of these notifications with worsening due to alcoholism was lower than the general percentage, with a cure rate of 19.47%.

According to the present study, as described in Table 4, it is observed that most TB/HIV coinfection notifications refer

to male patients (63.9%), which corroborates with national and local studies from other regions, which evidenced greater involvement of this portion of the population[17-19]. The justification for this heterogeneity of distribution between the genders is not well explained, but it is suggested that this occurs due to biological and social factors, with lifestyle, socioeconomic conditions, delay in the search for medical support and underdiagnosis in women relevant to this disproportion[20].

Table 4 - Situation of termination of TB/HIV co-infection cases

General situation	n(%)
Transfer	242 (25.31%)
Cure	238 (24.90%)
Drop out	191 (19.97%)
Death from tuberculosis	140 (14.64%)
Death due to other causes	71 (7.42%)
Under treatment	35 (3.66%)
Primary drop-out	33 (3.45%)
Diagnostic change	4 (0.41 %)
Drug-resistant tuberculosis	2 (0.23%)
Situation of Termination- Worsening by Alcoholism n (%)	
Transfer	90 (26.16%)
Drop out	68 (19.76%)
Cure	67 (19.47%)
Death from tuberculosis	45 (13.08%)
Death due to other causes	24 (6.97%)
Under treatment	23 (6.68%)
Primary drop-out	11 (3.19%)

Source: Research data

The highest rate of cases occurred in the age group between 31 and 40 years (36.08%), showing an incidence rate of 84.50% when considering the age range between 21 and 50 years. Considering the socioeconomic profile, it is valid to point out that most of the economically active population is included in this range, generating an impact on the labor and income activities of these patients[17,18].

Another relevant point that may explain the higher incidence in this age group is due to the behaviors and social interactions of individuals in this period of life, since, at this stage, it is inferred that there is a greater exposure of activities that could mean risk of contamination of the disease, such as unprotected sexual relations, contamination with perforating materials and use of injectable drugs, HIV infection being a major risk factor for the development of tuberculosis[1,5,21].

Table 5 - Statistical analysis of the situation of termination and TB/HIV co-infection cases

Dependent Variable: Situation of Termination	
Independent variables	P value
Gender	<0.257
Age	<0.001
Worsening by alcoholism	<0.031
Clinical form	<0.501

Source: Research data

Moreover, as shown in Table 5, the P-value for each term

tests the null hypothesis that the coefficient is equal to zero (no effect). A low P- value (<0.05) indicates that changes in the predictive value are related to changes in the response variable. Thus , when applying the statistical analysis through simple linear regression to correlate the closure situation with age, a P-value[22,23]<0.001, indicating that the patients' prognosis is likely to be worse as the age ranges increases, corroborating with studies that report to exist an association between the advanced age and the unfavorable outcomes of TB in PVHIV[22,23].

In addition, the level of schooling elucidated in this study does not accurately reflect the reality of patients treated at HEHA, since the item of schooling was ignored/not filled in 40.79% of the notifications, and it is not possible to establish a probabilistic relationship with national level data[10]. However, as explained in other literature, the incidence of cases is higher in people with low levels of schooling, as described byKhovat-Isfahani.[24] .In his study, he shows that the best socioeconomic condition is associated with a lower incidence and prevalence of the disease studied, suggesting that public policies for its prevention may be focused not only on the hospital-centric structure but on improvements in social indices that may aggravate the TB state, such as schooling rate and low income.

In addition, in some studies carried out in the USA and the United Kingdom, poverty, income inequality and lack of social capital have proved important to explain the higher incidence of tuberculosis[25,26].

In line with the national epidemiological profile, [10,] table III of this study shows that the pulmonary clinical form was the most common, adding 73.95% of the reported cases, 12.35% less than the Brazilian average that presents TB/HIV coinfection, [10]followed by the peripheral ganglion type, which is more common in the profile of immunocompromised patients, as Nicol[27] had previously reported. In parallel to this, despite the high incidence of the pulmonary clinical form, of the 416 sputum bascilocopy tests performed, the same was only positive in 146 notifications, corroborating data from other studies that have already demonstrated the low sensitivity of the method, between 40 and 60%[3,25]. However, this technique is extremely important from an epidemiological point of view, since the most responsible for maintaining the TB transmission chain are patients with positive sputum baciloscopy[3].

Regarding the general situation of termination, 24.90% of the patients presented cure, slightly higher than the outcome of patients who had alcoholism as reported worsening disease, since they showed 19.47% of cure. This index was slightly lower than the drop-out rate represented in the same population, which was 19.76%. Although in the present study these numbers are not so significant, Andrade has already shown[28] that in chronic alcoholic patients, treatment drop-out and the onset of side effects during treatment are higher when compared to the rest of the individuals.

In addition, as shown in Table V, when analyzing the data by means of simple linear regression, a p<0.031 value was obtained, reaffirming that patients worsened by alcoholism presented a worse outcome when compared to the population without this condition. This information is in line with the study carried out by Barbosa and Levino[29] and with other studies[26,28,30] that described that alcoholism is related to the development of TB-DR, an increase in treatment dropout rate and consequently with worse outcomes of the clinical signs.

4 Conclusion

In summary, this study shows that according to the socioeconomic profile of patients reported with TB/HIV coinfection, there is a predominance of males and mixed color, with a higher incidence in the age group corresponding to the economically active population, between 21 and 50 years of age. According to clinical characteristics, the pulmonary form prevailed, with peripheral ganglion being the most common among extrapulmonary forms. Moreover, regarding the situation of termination, it was evident that patients with advanced age present worse clinical outcomes. Furthermore, the patients who were notified with worsening due to alcoholism presented a higher rate of drop-out and a lower percentage of cure, when compared to the population without this worsening, with alcohol consumption being a determining factor for the patients' worse prognosis.

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