TUBERCULOSIS IN PATIENTS WITH HIV-1 INFECTION IN THE SOUTH-WESTERN REGION OF ROMANIA (2005-2015)

DOCTORAL THESIS ABSTRACT

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2021
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1. INTRODUCTION

TB (tuberculosis) / HIV (human immunodeficiency virus) coinfection is an important public health problem with particularities of diagnosis and treatment, but also significant economic costs. Globally, the increase in the number of people infected with HIV (PIH) also causes changes in the clinical and epidemiological data of tuberculosis. TB and HIV act synergistically, accelerating the decline of immune functions but also the risk of death. HIV infection increases the chance of progression from latent infection with Mycobacterium tuberculosis to active forms of TB by 20 times.

The increased risk of developing the disease is correlated with severe immunosuppression; clinical expression, radiological and bacteriological aspects are often atypical. Early diagnosis of tuberculosis in PIH is imperative to reduce morbidity, mortality, incidence rates of Immune Reconstitution Inflammatory Syndrome (IRIS) and nosocomial transmission of M. tuberculosis.

In this thesis I would like to describe the profile of patients with double HIV / TB infection in the HIV population in southern Romania by analyzing cases registered between 2005-2015 and comparing them with similar groups of patients diagnosed only with TB or only with HIV.

The thesis is structured in a theoretical part and the personal research. The theoretical study is a monographic synthesis of data from the literature on TB infection in HIV-infected patients. The analyzed lots of patients and the evaluation of the items proposed as objectives of the doctoral thesis are presented in the personal research part.

2. CURRENT STATE OF KNOWLEDGE

Tuberculosis is the most common infection found in PIH. Globalization and increasing population mobility have created the HIV/TB syndrome. Agglomeration and poverty in suburban areas will continue to drive HIV-associated TB transmission resulting in increased HIV/TB-associated mortality. (24, 25) Approximately 1.17 million new cases of TB occurred in 2015 among PIH, and 400,000 PIH died of TB in the same year. It is estimated that 25% of the 36.7 million PIHs in 2015 had latent tuberculosis infection (LTBI). (3 - 7)

Romania ranks first as an incidence of TB in the European Union and among the first places in the Europe-WHO region. In Romania, according to the European Tuberculosis Monitoring Report of 2012, morbidity remained above the European average, oscillating around 100%000 inhabitants between 2006-2010. A WHO monitoring in 2016 on TB cases in 2014 in Romania reports a percentage of 69% investigated for HIV status (detecting 3% positive for HIV infection). (14, 15)
Between 2008 and 2017, in Romania, the number of cases with HIV / TB coinfection decreased from 4% 000 in 2008 to 1.5% 000 in 2017, which can be explained by the decrease in the incidence of TB in the same period, from 115% 000 in 2008 to 72 % 000 in 2017. (15)

PIHs with active TB have fewer or no TB-specific symptoms, and screening for cough, fever, and weight loss appears to be effective and practical in excluding active TB in HIV-infected patients. (106)

PIHs with high CD4 counts have clinical manifestations of TB similar to those of TB patients not infected with HIV. In all stages of HIV/AIDS infection, the most common form of TB is pulmonary. (67) PIHs with extrapulmonary TB frequently also have pulmonary TB. (81-89)

Chest X-rays of PIH with pulmonary TB and CD4 count > 350 cells/µl frequently show upper lobe infiltrates, caverns and/or pleural involvement, similar to aspects of reactivated pulmonary TB in non-HIV infected patients. (62, 67, 69, 70)

The diagnosis of active TB, regardless of location, is based on the identification of M. tuberculosis in cultures of various pathological products or on the histopathological evidence of TB granuloma.

Tuberculosis in PIH is curable but HIV increases mortality associated with TB. (12) Antiretroviral therapy (ART) is associated with a decrease in the incidence of TB in PIH. The use of ART, immunological recovery and increased CD4 count significantly decreased the incidence of TB especially in patients with restored CD4 cell count> 500 cells/µl. (96-99) For those, the incidence of TB remained double that of adults without HIV. (100-102)

Treatment of tuberculosis without drug resistance in HIV-infected patients follows the same basic principles as for TB in non-HIV-infected patients: multiple drugs, fixed-dose combinations and a two-phase regimen administered under direct observation (DOT). (146-148) The treatment is instituted in collaboration with the infectious disease doctor who treats HIV patients; patients need psychological and social support for the successful completion of the treatment. (15, 103-105)

PIHs diagnosed with TB will continue the same ART regimen. For patients who are not receiving ART at the time of DOT (but have CD4 <200 cells/µl), ART will be associated after initiating DOT, but not simultaneously. (38)

Paradoxical reactions (inflammatory reconstruction immune syndrome) may occur during antituberculosis treatment due to the restoration of the inflammatory immune response involving a transient secretion of proinflammatory cytokines. There are no serological, radiological, or definitive clinical markers to determine whether or not a patient has developed IRIS. IRIS is a diagnosis of exclusion. (183)
The World Health Organization (WHO) recommends the 3 “I’s” for PIH: Intensified Diagnosis, Isoniazid Chemoprophylaxis (INH), and Control of Associated Infections.

3. PERSONAL CONTRIBUTIONS

3.1. Working hypothesis and general objectives

I consider that the HIV patient has certain peculiarities (epidemiological, clinical, of diagnostic and treatment) that predispose him to the appearance of active tuberculosis, especially in endemic areas for TB such as certain counties in southwestern Romania (e.g., Dolj and Olt counties are constantly among the top 5 counties for the incidence of TB in Romania). By identifying the risk factors that favor HIV/TB coinfection, we will be able to diagnose TB earlier in PIH and we will be able to take appropriate prevention measures.

The proposed objectives are:

1. characterization of the profile of patients with double HIV/TB infection in PIH living in southern Romania for cases registered between 2005 - 2015 compared to similar groups of patients diagnosed only with TB or only with HIV for the same time interval and the same geographical area;

2. identification of risk factors that may influence the occurrence of TB in PIH (epidemiological, clinical, of diagnostic and treatment);

3. estimate the latent TB forms in HIV-infected patients and analysis of the general context of TB occurrence in HIV-infected patients;

4. analysis of the multidisciplinary team working modalities imposed by the complex diagnosis and treatment of patients with HIV/TB coinfection, as well as the success or failure of national prevention programs for TB and HIV control applied in order to increase the early identification and diagnosis of people with HIV, TB or HIV/TB coinfection in the South-West region of Romania.

The place of study is the Infectious Diseases and Pneumoftiziology Hospital "Victor Babeş" Craiova, respectively the Pneumoftiziology Polyclinic (PNF) Craiova and the Regional Center for Monitoring and Evaluation of HIV/AIDS infection Craiova (CRC). We retrospectively collected data from HIV/TB coinfection patients from the Oltenia area registered in the CRC (demographic data, immunological, clinical, radiological and bacteriological evaluation at the time of TB diagnosis, associated infections, TB prophylaxis in HIV-infected patients, treatment performed for both diseases) in order to identify risk factors for active TB.

3.2. Material and method

The study project included next stages: study planning, selection of batches, preparation of the database, processing and statistical analysis of data, presentation of results and conclusions. We used
data collected directly from patients and information from medical documents (observation sheets and patient monitoring sheets) from the records of the 2 specialized centers in southwestern Romania (2005-2015). We included HIV-infected patients (± TB) from the Oltenia region (Dolj, Olt, Mehedinți, Gorj counties) and TB patients only from Dolj county. The documents of patients with TB were analyzed in the PNF Craiova Policlinic and those for HIV patients were analyzed in the CRC located in the same hospital.

We used 3 groups of patients similar as a structure:
- group A of 413 patients diagnosed with tuberculosis (regardless of location),
- group B of 207 patients with TB-HIV coinfection,
- group C of 207 patients with HIV infection.

We created a database with demographic, epidemiological, clinical-biological, radiological, diagnostic, therapeutic and evolutionary variables of the patients from the 3 groups. Patients without demographics, those transferred to other centers or those lost from the records were excluded from the study. The data processing complied with the personal data protection regulation (GDPR) adopted by the European Union in 2016.

We used binary, categorical, continuous data. Statistical data analysis is descriptive and analytical using Microsoft Excel (Microsoft USA) and Matlab (Mathworks, USA).

Secondary data processing - descriptive analysis of the batch on different parameters, calculation of important statistical parameters and graphical representation were performed using Microsoft Excel. The characterization of the numerical data was performed by the following statistical indicators: arithmetic mean, standard deviation (SD), minimum, maximum. The Shapiro-Wilks and Kolmogorov-Smirnov normality tests were used to verify the Gaussian distribution of the recorded values. To compare the average values of the data, we used the t-Student test (for two batches) or the multi-batch variant - the ANOVA test. As the data were distributed normally, no non-parametric tests were required. We tested the dependence between the parameters using Relative Risk (RR) and Odds ratio (OR). The results of the statistical processing are presented in tables and figures for a better understanding of the data obtained.

3.3. Results

Demographic aspects (sex, address, ethnicity, marital status, education, occupation)

The 3 study groups included 413 F and 414 B with a slight predominance of men in the group with TB. 52.4% of patients came from urban areas. Comparing the groups studied for the environment of origin we obtained a statistically significant difference between the groups with HIV and TB (p <0.0001) and between the groups with TB and HIV/TB (p = 0.00018) but we did not obtain a statistically significant difference between the groups with HIV and HIV/TB (p = 0.37127).
Most patients are Romanian. Of Roma ethnicity are 9.66% patients from the TB group, 8.21% patients from the HIV / TB group, 13.52% patients from the HIV group.

Analyzing the marital status, we found statistically significant differences (p <0.0001) between the groups with HIV and TB: 25.7% of patients with TB, 58.5% of those with HIV and 55.1% of those with HIV/TB being unmarried. Patients with TB are better educated compared to the groups of PIH - 80.7% of those with higher education have TB (p <0.0001). There are large differences between the HIV groups and the TB group in terms of patient occupancy. The socially assisted represent 73.4% of the HIV group and 66.2% of the HIV/TB group. TB patients are 60.3% employed. The Chi2 test identified p <0.0001 for all occupancy categories between any 2 of the 3 groups analyzed.

![Figure 1. Annual detection of HIV and TB cases between 1994 -2015](image)

**Age at HIV diagnosis and TB diagnosis**

At the time of HIV diagnosis, the mean age calculated in the HIV group was 16.71 years (SD ± 10.49) and in the HIV/TB group 17.96 years (SD ± 12.39). At the time of diagnosis of TB, the mean age calculated for the TB group was 39.55 years (DS ± 16.03) and for the HIV/TB group it was 22.87 years (DS ± 10.79). The difference is statistically significant: p <0.0001.

Figure 1 shows the cases diagnosed with HIV and TB each year between 1994 and 2015, for the groups analyzed in southwestern Romania. Although they influence each other as endemic diseases, the 2 are not superposable as incidence in southwestern Romania having different evolutions with "peaks" of incidence in the years 2002-2005 and 2012-2015 for HIV and 2001-2004 and 2007-2012 for TB.

**Vicious habits (smoking, alcohol, drugs)**

Of the total number of patients analyzed 28.9% were smokers, 53.6% of whom came from the group with TB. We find a statistically significant difference only between the group with HIV and the
one with TB. Smoking in our study was not considered an important risk factor associated with TB for PIH (RR = 1.19; OR = 1.41, 95% CI: 0.96-2.06).

Alcohol consumers represent 7.1% of the total (88.1% are from the TB group, 8.5% from those with HIV/TB and 3.4% from those with HIV). The statistically significant difference is found between the groups with TB and HIV (p <0.0001), TB and HIV/TB (p <0.0001).

Only 3 drug users (0.72%) were identified in HIV groups.

**HIV infection (staging, immune status, viremia, prophylactic measures)**

The HIV / TB group included more severe patients in terms of CDC classification by HIV / AIDS disease categories (p <0.0001), most patients being in classes B3 and C3.

<table>
<thead>
<tr>
<th>Group</th>
<th>Category A1</th>
<th>Category A2</th>
<th>Category A3</th>
<th>Category B1</th>
<th>Category B2</th>
<th>Category B3</th>
<th>Category C1</th>
<th>Category C2</th>
<th>Category C3</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>1</td>
<td>22</td>
<td>4</td>
<td>3</td>
<td>73</td>
<td>77</td>
<td>0</td>
<td>7</td>
<td>20</td>
</tr>
<tr>
<td>HIV/TB</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>31</td>
<td>59</td>
<td>3</td>
<td>14</td>
<td>99</td>
</tr>
</tbody>
</table>

Table 1. HIV / AIDS status according to CDC classification, in HIV groups

PIH with CD4 > 500 cells/µl represents 49.8% of those with HIV and only 4.8% of those with HIV / TB (p <0.0001). PIH with CD4 <100 cells/µl represents 31.4% of the HIV/TB group and 1% of the HIV group (p <0.0001). Viremia values > 1 mil copies/ml were associated exclusively with the HIV/TB group and values below 0.5 mil copies/ml are found only in the HIV group. Undetectable viremia is found in 50% of HIV patients. Viremia over 0.5 million copies/ml is considered a risk factor for TB.

PCP prophylaxis received 15.94% of the HIV group and 22.7% of the HIV/TB group. TB prophylaxis with INH received 1.93% of the HIV group patients and 4.83% of those with HIV/TB.

**Characteristics of tuberculosis (previous contact, detection, new cases or recurrences)**

Previous TB contact had 5% of those with HIV/TB, 1.9% of those with HIV and 16.22% of those with TB (RR = 2.10; OR = 15.3, 95% CI: 5.41-43.38).

Preventive screening in CRC actively detected TB in 80% of the HIV/TB group. In TB group 78% of patients were detected passively (p <0.0001). New TB cases represent approximately 90% of the TB group and 80% of the HIV/TB group (p <0.05). The percentage of those with a first recurrence of TB (R1) was different in the two groups: 7.7% of those with TB, 16.4% of those with HIV/TB (p <0.0001).

**Differences in tuberculosis symptoms**

Cough was present in 3 out of 4 people with TB and more than 9 out of 10 people with HIV/TB: p <0.0001 (RR = 2.68; OR = 3.71, 95% CI: 2.16-6.4).

Weight loss was identified in 82.1% of HIV/TB patients and 61.3% of those with TB (p <0.0001; OR = 2.91, 95% CI: 1.93-4.47).
Hemoptysis occurred in 5.3% of HIV/TB patients and 12.8% of TB patients (p <0.001). The aspect of their radiological findings was predominantly of ulcerative and cavitary infiltrative type.

At the time of diagnosis, 61.4% of those with HIV/TB had lymphadenopathy with different sizes and locations. On chest X-ray 33.3% of PIH with lymphadenopathy had bilateral lesions, double as percentage comparing to those without lymphadenopathy (p <0.0001).

Radiological changes encountered in groups with TB

A percentage of 50.2% of the patients with HIV/TB and 44.3% of those with TB had bilateral pulmonary radiological changes. Approximately 25% of those with HIV/TB had nodular infiltrative (IN) radiological lesions and 25% of those with TB both IN and infiltrative ulcer (IU) lesions. Miliary lesions had 9.7% of those with HIV/TB and 2.9% of those with TB (p <0.0001).

Diagnostic confirmation of TB and bacteriological evolution under DOT

At the time of diagnosis (T0), a quarter of HIV TB patients had a sputum examination for bK negative on microscopy and culture (M-C-) and 59% of them had a positive microscopy and culture examination (M+C+). M+C+ results had 70.46% of those with TB. The difference is statistically significant: p <0.0035; p <0.05 for microscopy at T0 and p <0.0001 for culture at T0.

After two months of DOT, only 1.45% of HIV/TB patients and 10.41% of those with TB had M+C+. The difference is statistically significant for M (p <0.0001) but statistically insignificant for C (p = 0.798).

MDR-TB was identified in 3.4% of HIV/TB patients and in 1.7% of TB patients (p <0.05). There is also a statistically significant difference in the case of those confirmed histopathologically: 16.22% in the group with TB and 10.14% in the group with HIV/TB (p <0.0001).

Duration of antibacterial treatment in tuberculosis groups

The mean duration of antibacterial therapy in the TB group was 7.14 months (SD ± 3.11) and for the HIV/TB group the mean was 11.41 months (SD ± 2.61). They have statistical significance deducible from the recommended duration of treatment which is different between the two groups: 6 months for those with TB and 12 months for those with HIV/TB.

Distribution of pulmonary and extrapulmonary TB cases

Analyzing Table 2 we notice that in the group with HIV/TB there were more cases of concomitant respiratory and extrarespiratory TB (p <0.05), and extrarespiratory TB was more common in those with TB (p <0.05). Pleural TB was three times more frequently diagnosed in the TB group compared to the HIV/TB group (12.1% compared to 3.9%) (p <0.0001). Compared to the TB group, patients with HIV/TB and malnutrition or hepatitis B virus have more frequent forms of TB with multiple locations suggesting lymphohaematogenic dissemination under conditions of severely compromised immunity.
<table>
<thead>
<tr>
<th>TB location</th>
<th>Number of patients with HIV/TB</th>
<th>Procent of patients with HIV/TB</th>
<th>Number of patients with TB</th>
<th>Procent of patients with TB</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary</td>
<td>124</td>
<td>59.9 %</td>
<td>265</td>
<td>64.2 %</td>
<td>p =0.33</td>
</tr>
<tr>
<td>Extrapulmonary</td>
<td>31</td>
<td>15.9 %</td>
<td>101</td>
<td>24.4 %</td>
<td>p &lt;0.001</td>
</tr>
<tr>
<td>Pulmonary and extrapulmonary concomitent</td>
<td>52</td>
<td>25.1 %</td>
<td>47</td>
<td>11.4 %</td>
<td>p &lt;0.001</td>
</tr>
</tbody>
</table>

Table 2. Comparative analysis of TB location for HIV/TB and TB groups

Concomitant diseases monitored in groups with TB

Positive IGG result for T. gondii had 47.3% of patients with HIV/TB and 32.9% of those with HIV, predominating women in both groups [p = 0.0052 (RR = 1.41; OR = 2.01, 95% CI: 1.36 - 3.0 )].

Cytomegalovirus (CMV) positive IGG results had 13.8% of PIH; more from the group with HIV/TB- 15.9% [p = 0.199 (RR = 1.19, OR = 1.45, 95% CI = 0.82-2.55)] and in rural areas.

Hepatitis B virus had: 1.69% of the TB group, 27.53% of the HIV group, 30.43% of the HIV/TB group. The difference between HIV groups is not statistically significant: p = 0.4224 (RR = 1.07; OR = 1.15 95% CI: 0.75 - 1.76). Only 1% of the group with TB and about 3% of PIH had hepatitis C virus.

Malnutrition was found in 73.9% of the group with HIV/TB and 16.5% in the group with TB (p <0.0001). For malnutrition between the groups with HIV/TB and TB we calculated RR = 5.12 (OR = 15.63, 95% CI: 10.43 - 23.4) and between the groups with HIV/TB and HIV we calculated RR = 1.42 (OR = 1.93, 95% CI : 1.28 - 2.93).

Neurological disorders were common in PIH, more common in those with HIV/TB. In the case of patients with TB, who are older, the common associated diseases were: DM (9.2%), digestive disorders (6.1%), cardiac (6.8%), surgical (4.6%), oncological (3.6%).

TB mortality in the analyzed groups

From the group with HIV/TB 9.17% died from TB in the time frame analyzed in our paper and from the group with TB 9.22% died due to TB in all 10 years. The difference is not statistically significant and can be explained by the early diagnosis of HIV/TB which allowed patients to heal and so, decrease mortality from TB to PIH.

Comparisons of blood tests in TB groups

Table 3 presents the results for comparative analyzes (hemoglobin, white blood cells, ESR, blood glucose) between the TB and HIV/TB groups. There is statistical significance (p <0.05) for all
analyzed parameters. Within the same group there are no statistically significant differences between those with pulmonary TB and those with extrapulmonary TB for the compared blood tests.

<table>
<thead>
<tr>
<th>Analized test</th>
<th>Group</th>
<th>Media</th>
<th>Standard deviation</th>
<th>Min</th>
<th>Max</th>
<th>Mdiana</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>TB</td>
<td>11.69</td>
<td>1.28</td>
<td>7</td>
<td>15</td>
<td>12</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>HIV /TB</td>
<td>10.31</td>
<td>1.77</td>
<td>5</td>
<td>15</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>White blood cells (cel/mmc)</td>
<td>TB</td>
<td>8170.75</td>
<td>3163.65</td>
<td>2600</td>
<td>20490</td>
<td>7800</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>White blood cells (cel/mmc)</td>
<td>HIV /TB</td>
<td>5534.75</td>
<td>2767.22</td>
<td>1400</td>
<td>20190</td>
<td>5200</td>
<td></td>
</tr>
<tr>
<td>ESR – 1 h (mm)</td>
<td>TB</td>
<td>92.25</td>
<td>18.77</td>
<td>40</td>
<td>140</td>
<td>90</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>ESR – 1 h (mm)</td>
<td>HIV/ TB</td>
<td>84.46</td>
<td>32.31</td>
<td>17</td>
<td>140</td>
<td>86</td>
<td></td>
</tr>
<tr>
<td>ESR – 2 h (mm)</td>
<td>TB</td>
<td>111.72</td>
<td>17.20</td>
<td>68</td>
<td>157</td>
<td>108</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>ESR – 2 h (mm)</td>
<td>HIV/ TB</td>
<td>100.13</td>
<td>30.85</td>
<td>5</td>
<td>165</td>
<td>101</td>
<td></td>
</tr>
<tr>
<td>Blood glucose (mg%)</td>
<td>TB</td>
<td>100.05</td>
<td>29.84</td>
<td>56</td>
<td>321</td>
<td>91</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Blood glucose (mg%)</td>
<td>HIV/TB</td>
<td>89.15</td>
<td>15.21</td>
<td>56</td>
<td>145</td>
<td>88</td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Analysis of hemoglobin, white blood cells, ESR, blood glucose values for TB and HIV / TB groups.

4. DISCUSSIONS

The remarkable magnitude of the association of this double infectious pathology led to its inclusion in the concept of emerging syndrome. The patient having the two infections at the same time must be approached through the prism of a complex nosological entity of the “mycoHIV” type. The particularities of the entity (demographic, immunopathogenic, diagnostic, evolutionary, therapeutic, preventive) are more than the sum of the separate aspects of the 2 diseases. (19, 20)

In both groups with TB we found a polymorphism of tuberculosis symptoms, detected during medical consultations but often ignored by patients. Pulmonary TB is still the most common form of TB regardless of the stage of HIV. The risk of developing active TB remains twice as high in PIH, even in those with effective ART; ART treatment and the restoration of cell-mediated immunity lead to a decrease in cases of extrapulmonary TB. (85, 101, 143-145)

Only 20% of TB cases in PIH were detected by symptoms (passive detection), the rest being identified by early screening during CRC visits. For about a third of HIV/TB cases, the diagnosis of the two diseases was made almost simultaneously (+/- 3 months), which is a success of HIV and TB screening and prevention programs in our country. The lower rate of positive sputum for bK on microscopy is partly due to the early diagnosis of TB in PIH in the active record of CRC. HIV/TB patients have benefited from bacteriological confirmations through Xpert MTB/RIF rapid tests only since 2015.
Chest Xray is used for screening and monitoring, but has no specificity, and the final diagnosis of TB disease requires confirmation by culture. In both groups with TB, most patients had specific bilateral pulmonary radiological TB features and associated symptoms such as coughing and weight loss. The lesions in the group with TB are more advanced, because of symptoms disregard with longer evolution towards aggravation of TB until diagnosis.

The high number of extraespiratory TBs in PIH was more often associated with a low number of CD4 lymphocytes and other comorbidities (malnutrition, candidiasis, T. gondii infection and HBV).

HIV infection and malnutrition decrease immunity and increase the risk of reactivation of latent TB. Tuberculosis and/or HIV infection lead to weight loss. Malnutrition significantly increases mortality in both TB and HIV/AIDS patients and should be treated concomitantly with the treatment of infections. Patients with HIV/TB and malnutrition or HBV have more frequent forms of TB disease with multiple locations compared to the TB group, suggesting that tuberculosis can rapidly reach lymphoematological dissemination under severely compromised immunity.

The profile of the HIV/TB patient from southwestern Romania, which is outlined in the data presented, is that of a young patient, probably born between 1988-1990, coming from rural areas, residing in Dolj or Olt counties, with high school education, unmarried, unemployed, beneficiary of the minimum income guaranteed by the state. It is associated with comorbidities such as malnutrition, candidiasis, or infection with T. gondii or HBV. Patient has severe immunodepression with Ly CD4 number <100 cells/µl and high viremia value. In general, the diagnosis of TB is established as a new case (CN), identified by screening for symptoms in CRC. Common symptoms presented at the time of diagnosis of active TB are cough and weight loss. It is frequently discovered with pulmonary TB +/- extrapulmonary TB. TB confirmation is frequently by culture on Lowenstein Jensen solid medium or by HP examination. Antibacterial treatment is well tolerated and healing is done with minimal sequelae. May have anemia, high ESR and blood sugar levels and low white blood cell counts at the time of TB diagnosis. The HIV/TB patient receives prophylaxis for PCP but not for TB.

The HIV patient retains the demographic characteristics of the HIV/TB group. The HIV patient is much less affected by malnutrition and other concomitant infections and has an increased number of Ly CD4> 500 cells/µl and an undetectable viremia. It is periodically evaluated in CRC and follows specific ART treatment. The disease category according to the CDC is less severe than that of the HIV/TB patient. This group of patients also does not receive INH prophylaxis for TB.

The profile of the TB patient is different from that of the HIV/TB patient. The patient with TB is a man, from an urban area, with an average age of approximately 39 years, employee, married, high school or college graduate. The TB patient is often a smoker and alcohol user and may associate diabetes and cardiovascular conditions. It is passively detected with pulmonary TB, and symptoms
include coughing, weight loss and sometimes hemoptysis. Being a more advanced TB at the time of TB diagnosis there are more bacteriological and histopathological confirmations. Radiological aspects in pulmonary TB are more advanced: unilateral or bilateral ulcerative or cavitary aspects. These patients are more contagious and are more difficult to become negative for bK in sputum than patients in the HIV/TB group. Biologically, they have mild or moderate anemia, an increase in ESR and blood glucose at different values, with statistically significant differences from those in the HIV/TB group.

5. CONCLUSIONS

1. In the South West of Romania HIV/TB coinfection is a reality and a challenge for both the medical system, patients and the community.

2. HIV/TB patients are young, with poor socio-economic status, have more comorbidities and are more prone to TB recurrences and drug resistance to antibacterial medication. The most common form of TB in both the HIV/TB group and the TB group was the one with pulmonary localization. Miliary and lymph node TB, but also forms of pulmonary TB concomitant with extrapulmonary TB are more common in PIH and pleural TB is more common in TB group.

3. The general context of TB diagnosis in PIH was characterized by significant immunosuppression and a high level of viral replication. Permanent screening for symptoms suggestive of tuberculosis (cough, weight loss) in severely immunocompromised patients allows early identification of TB. HIV/TB patients have clinical, biological, bacteriological, radiological and treatment particular features.

4. For the period 2005-2015, the evolutionary trends of TB and HIV/TB diagnosis in the general population of Romania and in the analyzed area partially overlapped. Data on the incidence of TB in PIH are similar to those in the literature.

5. The study highlighted the success of HIV and TB screening programs in the early detection of HIV/TB coinfection. The collaboration between the infectious disease physician and the pulmonologist is permanent and is supported by psychological support leading to the cure of TB with minimal sequelae and a significant decrease in TB mortality at PIH.

6. We reconfirmed the need for INH prophylaxis in HIV-infected patients in the analyzed territory, as the counties with the most PIH also have an increased incidence for TB.

7. I consider it useful to create a common database between HIV and TB monitoring programs for HIV / TB patients.
8. Our research will continue through a genetic study in HIV patients called "HIV / Tuberculosis Coinfection - Epidemiological, Clinical, and Genetic Correlations in Investigating Possible Causal Links (HTB)."

**Bibliografie selectivă**


