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Research Article

Impacts of HIV Infection on Pulmonary Tuberculosis in Sub-Saharan Africa

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Abstract

Introduction: Tuberculosis is a major public health problem in developing countries where its incidence is increased by HIV infection. Our main objective was to determine the epidemiological, diagnostic and prognostic impacts of HIV infection on pulmonary tuberculosis. Methods: this was an analytical and descriptive retrospective study, from January 1, 2015 to June 30, 2017, on TB/HIV co-infected patients and cases of pulmonary tuberculosis hospitalized in the infectiology and pneumophtisiology departments of the UTH Point G in Bamako, with a usable radiological image and file. The sampling was exhaustive and the data collected was entered and analyzed using SPSS 21.0 software. The comparison of the proportions was made by the significant Pearson chi-square test of association if $p<0.05$ through a multivariate analysis in which the Fisher test was made in case of confusion between the qualitative variables. Results: the frequency of TB/HIV co-infection was an additional 3.2% of the 42.5% for cases of pulmonary tuberculosis. The diagnosis of TB/HIV co-infection was suggested in the face of deterioration in general condition (81.1%) associated with pulmonary condensation syndrome (73%) or normal pleuropulmonary examination (20.3%). The majority of patients had a CD4<200 cells/µl (88.2%). Bacilloscopic and Gene-Expert were negative in 85.3 and 52.9% of cases respectively and significantly influenced by severe immunosuppression (95%; p=0.000; CI = 0.000 – 0.040 and 95%; p=0.001, CI = 0.000 – 0.040). The chest radiography was mostly pathological (79.7%), made up of diffuse lesions (55.8%), of the military type (21.6%) and caverns (18.9%), respectively linked to severe immunosuppression (95%; p=0.024; CI = 0.000 – 0.064 and 95%; p=0.000; CI = 0.000 – 0.040). Lethality in TB/HIV co-infected was an additional 27% of the 4.2% lethality attributable to isolated pulmonary tuberculosis. Conclusion: the impact of HIV infection on pulmonary tuberculosis is global because it, through the immunosuppression it generates, modifies the clinical, biological and radiological aspects of pulmonary tuberculosis, worsens the vital prognosis of patients and increases the number of tuberculosis cases. A normal pleuropulmonary examination and/or a negative bacilloscopic and Gene-Expert and/or a normal aspect of the chest radiography in the immunocompromised does not exclude progressive pulmonary tuberculosis.

Keywords: immunosuppression; impact; sub-saharan Africa; tb/hiv co-infection

Introduction

Tuberculosis remains today a major public health problem in developing countries where infection with the human immunodeficiency virus (HIV) increases its incidence and reinforces its endemicity. About 15 million people worldwide are co-infected with Mycobacterium tuberculosis complex and HIV, 70% of whom live in sub-Saharan Africa [1–3] where its frequency varies between 50 and 79% [4]. The excess death rate from TB among people living with HIV is 14% globally [5] and 16–50% in sub-Saharan Africa [6–8].

In Mali, tuberculosis is endemic there and the most frequent opportunistic lung disease during HIV infection, with a frequency of 88.3 and 92.1% against 12.4 and 15.1% for TB/HIV co-infection respectively in 2015 and 2016 [9].

The clinical and paraclinical manifestations of progressive pulmonary tuberculosis are varied, ranging from paucity symptomatic forms to severe ones in Person living with HIV (PLHIV), compared to the typical form common in most non-HIV infected subjects [10–13].

The absence of a similar study focusing on the overall impact of HIV infection on pulmonary tuberculosis in Mali motivated this study aimed at describing the epidemiological, diagnostic and prognostic impacts of HIV infection on the pulmonary tuberculosis.

Materials and methods

This was an analytical and descriptive retrospective study, from January 1, 2015 to June 30, 2017, on TB/HIV co-infected patients and cases of isolated pulmonary tuberculosis hospitalized in the Infectiology and Pneumophtisiology departments of the Point G University Hospital of Bamako. Were included included in the study were TB/HIV co-infected patients with a frontal chest radiography and a usable medical file, and cases of isolated pulmonary tuberculosis. We're not included the patients co-infected with TB/HIV who did not have an unusable file were not included in the study.

The TB/HIV co-infected patients were split into two immunological groups: CD4 ≥ 200 cells/mm3 and CD4 < 200 cells/mm3.

The diagnosis of pulmonary tuberculosis was made based on the following arguments:

• Bacteriologically confirmed pulmonary tuberculosis: all cases of pulmonary tuberculosis confirmed by bacilloscopy and/or Gene-Xpert and/or culture [2,14];

• Radiologically confirmed pulmonary tuberculosis: all cases of pulmonary tuberculosis diagnosed on the basis of clinico-therapeutic and radiological arguments suggestive of pulmonary tuberculosis [2,15].

The sampling was exhaustive and involved all patients admitted to the two departments during the study period. Under anonymity, data were obtained from medical records and hospitalization registers. The epidemiological, clinical, paraclinical, therapeutic and evolutionary aspects were studied. Data processing and analysis were done using SPSS 21.0 software. For the comparison of the proportions, we carried out the Pearson chi-square association test with a significance level $p < 0.05$ or the Fisher exact test significant at 0.05 in the event of confusion between the qualitative variables, by an analysis multivariate. The results were presented in the form of frequency tables and figures.

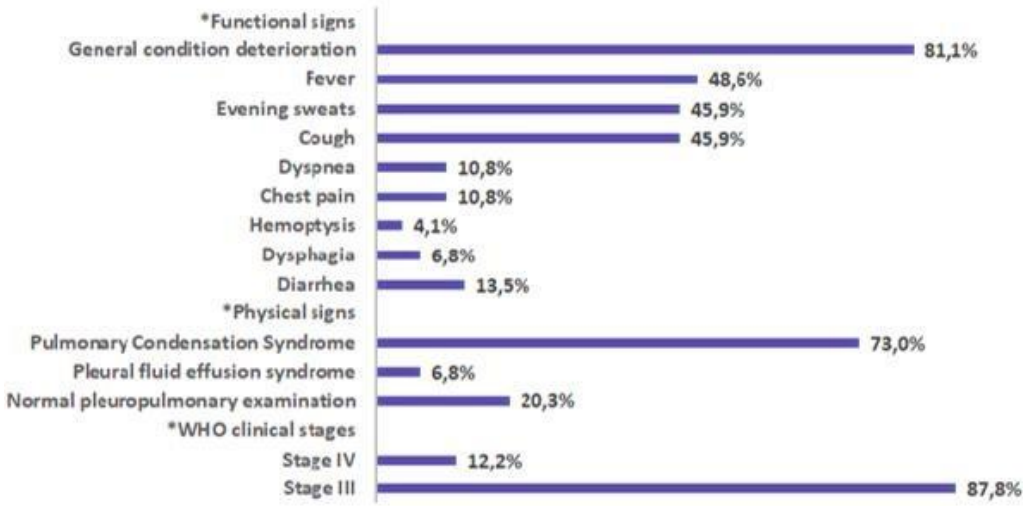
Results

Epidemiological aspect: from January 1, 2015 to June 30, 2017, we collected 970 pulmonary tuberculosis files including 74 cases of TB/HIV co-infection out of 2280 hospitalizations, Either a frequency of pulmonary tuberculosis of 42.5%, that of co-infection -TB/HIV infection at 3.2% (7.2% of all cases of pulmonary tuberculosis) (Table I). Among the TB/HIV co-infected: 44 (59.5%) had an age range of 35 to 54 years (40.5 ± 11.7 years on average) with extremes of 15 to 68 years; 43 (58.1%) were male with a sex ratio of 1.4 M/F; 51 (68.9%) were married; more than 3/4 (81.1%) came from the district of Bamako; 24 (32.4%) were housewives; and 4 (5.4%) had a notion of tuberculosis contagion a history of tuberculosis (table I).

Clinical aspect: among the TB/HIV co-infected: 60 (81.1%), 36 (48.6%), 34 (45.9%) and 34 (45.9%) had as functional signs respectively the deterioration of the general state, the fever, evening sweats and cough; pleuropulmonary examination was marked by pulmonary condensation syndrome in 54 (73%), and normal in 15 (20.3%); 65 (87.8%) patients were classified as WHO stage III (figure 1).

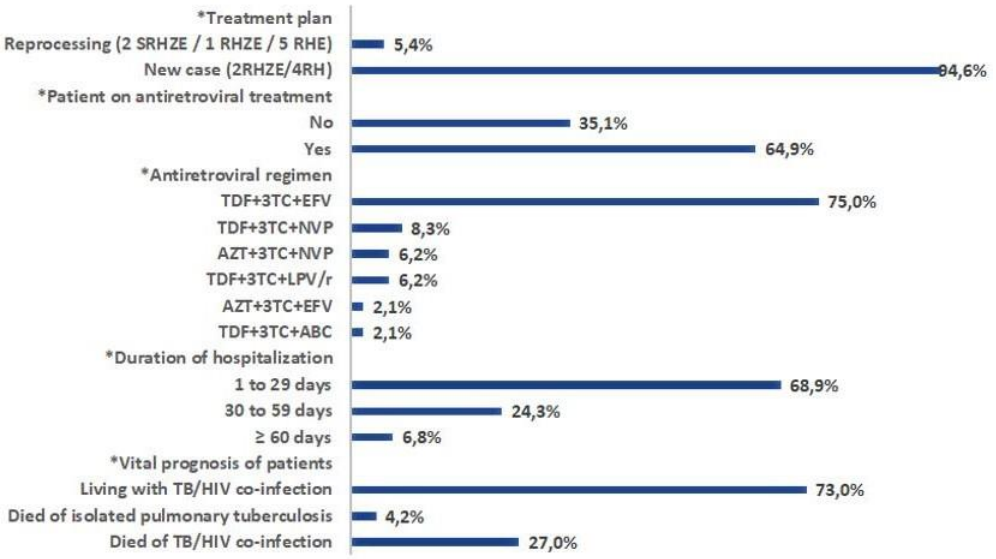
Paraclinical aspect: 72 (97.3%) patients were infected with HIV-1, 30/34 (88.2%) co-infected with TB/HIV had a CD4 count < 200 cells/µl; out of the 74 TB/HIV co-infected 57 (77%) had a positive bacilloscopy, and out of 34 TB/HIV co-infected 26 (74.5%) were Gene-Xpert negative; 16/74 (21.6%) co-infected with TB/HIV had miliary images (table II).

Therapeutic and evolutionary aspects: among the TB/HIV co-infected, there were 70 (94.6%) new cases of pulmonary tuberculosis and 36 (75%) were under the TDF+3TC+EFV regimen; the average duration of hospitalization was 31.7 days and 20 died, either a lethality of 27% against 38 (4.2%) deaths attribuable to isolated pulmonary tuberculosis (figure 2).



(WHO = World Health Organization).

Figure 1: Distribution of patients according to clinical data



(S: streptomycin, R: rifampicin, H: isoniazid, Z: pyrazinamide, E: ethambutol, TDF: tenofovir, 3TC: lamivudine, EFV: efavirenz, NVP: nevirapine, AZT: zidovudine, LPV: lopinavir, r: ritonavir, ABC: abacavir)

Figure 2: Distribution of patients according to therapeutic and evolutionary data

The multivariate statistical analysis in TB/HIV co-infected: bacilloscopy and Gene-Xpert were mostly negative in patients with a CD4 count < 200 cells/mm3 respectively significant (95%; p = 0.000; CI = 0.000 – 0.040 and 95%; p = 0.001; CI = 0.000 – 0.040), the image of miliary predominated in patients with a CD4 count < 200 cells/mm3 (95%; p = 0.024; CI = 0.000 – 0.064), excavations and the fluid pleural effusion syndrome predominated in patients with a CD4 count ≥ 200 cells/mm3 (95%; p = 0.000; IC = 0.000 – 0.040), the other radiological aspects had no relationship with the degree of immunosuppression (p > 0.05); the majority of deaths occurred in patients with a CD4 count < 200 cells/mm3 (95%; p = 0.045; CI = 0.068 – 0.230) (table III).

Discussion

Active pulmonary tuberculosis is a serious pulmonary bacterial infection that can occur at any time, but its occurrence and evolution are favored by immunosuppression, in particular HIV infection, causing a clinical-biological, radiological change and prognosis of pulmonary tuberculosis [10,15–19].

The radiological aspects observed during TB/HIV co-infection are multiple and vary from one patient to another, depending on their immune responses, the associated pneumonitis and the time to diagnosis [3,16,18,20,21].

Epidemiological aspect: in Mali, the frequency of TB/HIV co-infection has decreased in recent years, going from 4.39% in previous years [22] to 4.30% from 2014 to 2016 [23], then 3.2 % from 2015 to mid-2017 (our study), unlike some African countries [1,6,7,24–26], due to early and routine screening for HIV infection and triple antiretroviral therapy in patients, and the inequality of study population sizes.

The predominant age range and average age in our study corroborate those of another study in Mali [23] and other similar African studies [1,18,24,25]. This could be explained by the fact that this age group is made up of subjects who are more sexually active on the one hand, thus exposing them to HIV infection which promotes the onset of tuberculosis, and on the other more dynamic in regular contact with each other, thus exposing them to tuberculosis contagion. Contrary to certain studies on HIV infection [27,28], the predominance of men in our study is explained by the fact that the study focused almost on TB/HIV co-infection and men, the most dynamic in society, are more at risk of tuberculous contagion.

Clinical aspect: the predominant clinical symptomatology (bacillary impregnation syndrome and pulmonary condensation syndrome), as described in certain similar studies and literature [1,25,29], could be explained by the fact that these are two active (chronic) infections affecting the whole system and diagnosis of advanced lung disease. The predominant WHO clinical stage III in our study could be explained by the use of consultation and late diagnosis for some patients and non-compliance with treatment for others.

Paraclinical aspect: the predominance of HIV type 1 infection in our study, also described in certain studies [23,24,28,30], is explained by the fact that this virus is historically the most widespread in Africa according to the literature [31,32]. As in a similar study [18], the CD4 count was mostly below 200 cells/mm3 due to late diagnosis for some and noncompliance with treatment for others, but also tuberculosis itself causes immunosuppression [33]. Of the 74 co-infected with TB/HIV, bacilloscopy was mostly positive, however of the 34 patients who performed their CD4 counts bacilloscopy and Gene-Xpert were mostly negative as in a similar study [1], because the majority of our patient had severe immunosuppression (CD4 count < 200 cells/mm3), this observation was also made in an African study [34]. The radiological images were mostly pathological and predominated by diffuse bilateral lesions of the Miliary type followed by excavations, as described in certain studies [1,15,18], because the cases of Miliary were significantly related to the CD4 count < 200 cells/mm3 (predominant) and the cases of excavations were related to the CD4 rate ≥200 cells/mm3. The more severe the immunosuppression relating to both the quality and the quantity of the immune cells, the more the dissemination of the Mycobacterium occurs just like the other germs [1,17,33], contrary to the caverns which are observed when the immune cells are able to circumscribe the initial focus of inoculation [1,35] which, their occurrence in PLHIV would be explained by the fact that they are « slow progressors » [36,37] and/or under antiretroviral treatment. However, in some literature it is described that caverns are rare in TB/HIV co-infected patients due to immunosuppression [1,3]. The biological and radiological variation of pulmonary tuberculosis is correlated with the degree of immunosuppression of the patients. The presence of a normal radiograph in some of our patients as observed in a similar study [1] is explained by the failure of the immune system becoming unable to trigger the inflammatory reaction generating the granuloma responsible for tissue necrosis.

Therapeutic aspects: the majority of our patients benefited from the TDF+3TC+EFV antiretroviral treatment regimen and the 2RHZE/4RH oral antituberculosis regimen in accordance with the recommendations of the

literature [14,19,38], as in another study [23], because it was the first-line regimen recommended at the time in HIV-1 infected patients who represented the majority of our patients.

Evolutionary aspect: in our study, the death rate recorded among TB/HIV co-infected corroborates those of other similar studies [26,39], but lower than that of another similar study [23] and the death of patients was significantly linked to severe immunosuppression (CD4 count < 200 cells/mm3) which may involve other opportunistic infections and/or a paradoxical immune reconstitution inflammatory syndrome (IRIS) [40] often undiagnosed and contributing to death patients. This increases the overall lethality of pulmonary tuberculosis.

Conclusion

The HIV infection increases the epidemiological data, modifies the diagnosis and increases the lethality of pulmonary tuberculosis, but it is not specific to all these variations due to the existence of other causes of qualitative immunosuppression and /or quantitative. A normal pleuropulmonary examination and/or a normal aspect of the chest radiography in an immunocompromised patient does not exclude active pulmonary tuberculosis. In TB/HIV co-infected, the more severe the immunosuppression, the worse the vital prognosis.

Conflict of interest: The authors declare that they have no conflict of interest related to this article.

Author contributions

→ Design of the study, correction of the manuscript, critical contributions, supervision of the study and approval of the final version for publication: Mariam Soumaré

→ Design of the study, literature review, data analysis, drafting of the manuscript and approval of the final version for publication: Ouo – Ouo Loua

→ Drafting of the study protocol, literature review, data collection and analysis, and approval of the final version for publication: Zuride Ngueta Sabeya

→ Supervision of the study, critical contributions, correction of the manuscript and approval of the final version to be published: Jean Paul Dembélé, Assétou Fofana, Oumar Magassouba, Dramane Sogoba, Yacouba Cissoko, Issa Konaté and Sounkalo Dao

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