IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 20, Issue 8 Ser.13 (August. 2021), PP 27-31
www.iosrjournals.org

The clinical, bacteriological and therapeutic characteristics of tuberculosis in patients infected with HIV (about 42 cases)

Pneumo-phthisiology
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Abstract:
Introduction : *Tuberculosis still remains a public health priority, especially with the emergence of HIV. It is more and more revealing of the HIV infection. The objective of this study is to analyze the clinical, epidemiological, and therapeutic aspect of tuberculosis in patients infected with HIV.*
Material *: This is a descriptive retrospective study of 42 patients co-infected with susceptible tuberculosis and HIV diagnosed and treated in the pneumo-phthisiology department of the Moulay Youssef hospital in Rabat , over a period of 7 years between 2014 and 2020.*
Methods *:4403 patients were hospitalized in our phthisiology department for treatment of tuberculous disease, and among them there are 42 cases of co-infections. The age group between 21 and 59 years old. The average age is 38.23 years old and the male / female sex ratio is 0.82. The pulmonary form is the most common (52.38%). Tuberculosis is the revealing mode of HIV infection in 29 patients. The outcome was favorable in 33 patients (92.86%).*
Conclusion*: HIV infection is frequent in tuberculosis patients, particularly in smear-negative pulmonary tuberculosis. It is associated with excess mortality, especially in cases of severe immune deficiency, despite antiretroviral treatment and co-trimoxazole prophylaxis.*
Keywords*: Tuberculosis -HIV-coinfection*

Date of Submission: 20-08-2021 Date of Acceptance: 05-09-2021

I. Introduction:

People infected with tuberculosis and HIV are 20 to 30 times more likely to develop active tuberculosis than others. Tuberculosis forms a deadly association with HIV, each accelerating the progression of the other [1]. interactions between TB and HIV are multiple and modify the epidemiology, clinical presentation and management of these two diseases. Indeed, the management of this co-infection poses several problems, among which, the increased toxicity of anti-tuberculosis drugs, the possible occurrence of interactions between anti-tuberculosis and antiretroviral treatments, the risk of resistant tuberculosis and the risk of immune reconstitution inflammatory syndrome (IRIS) [2].

It is for the sake of a better knowledge of tuberculosis and HIV co-infection in Morocco that we are carrying out this work, the objective of which is to analyze the epidemiological, clinical, therapeutic and evolutionary aspects of tuberculosis in patients with HIV infection.

II. Material And Methods :

This is a descriptive retrospective study of 42 patients co-infected with susceptible tuberculosis and HIV diagnosed and treated in the pneumo-phthisiology department of the Moulay Youssef hospital in Rabat, from January 1, 2014 to December 31, 2020.

The patients included in this work presented a confirmed HIV / AIDS infection associated with bacteriologically confirmed tuberculosis (BC): when there is positivity of the biological sample (Genexpert, smear or culture) or clinically diagnosed (CD) on epidemiological, clinical, radiological, histological arguments.

The collected information mainly included the epidemiological and clinical characteristics, the category of tuberculosis, its site and the outcome of treatment. For the latter, the definitions standardized by the World Health Organization (WHO) were used: The site of tuberculosis makes it possible to distinguish two forms:

- Pulmonary tuberculosis (PTB): BC or CD tuberculosis in which the lung parenchyma or the tracheobronchial tree is affected.
- Extra-pulmonary tuberculosis (EPTB): cases of BC or CD TB in which organs other than the lungs are affected. Examples: Pleura, lymph nodes, abdomen, genitourinary system, skin, joints, bones, meninges ...

The therapeutic success or favorable outcome included patients declared cured or having completed their treatment; adverse treatment outcome included death, treatment interruption, and treatment failure.
The diagnosis of HIV infection was made when the ELISA serology was positive and the confirmation by the Western blot test was obtained.

III. Results:

During these seven years, 4403 patients were hospitalized in our phthisiology department for management of a tuberculosis disease, and among them there are 42 cases of co-infection, i.e. around 1% of patients with tuberculosis are infected with HIV.

The average age of the patients was 38.23 years, with age extremes between 21 and 59 years. The sex ratio M / F is 0.82. For their family status, there is a predominance of single subjects (38.1%), followed by married subjects (23.81%), then divorced subjects (19.05%).

Of all the cases, 37 patients were of urban origin, while only three were of rural origin and two were homeless.

Chronic smoking was found in 33.3% of patients with an average of 20.44 pack year (61.5% of them were men and 11.7% were women).

Tuberculosis was the revealing mode of HIV infection in 29 patients (69.04%), 22 patients (52.38%) had an isolated pulmonary localization, while 7.14% had an exclusive extrapulmonary localization and 40.48% had a mixed localization. The lymph node location was the most frequent of the extrapulmonary involvements (60%). (Table 1)

Table 1: Extrapulmonary locations of tuberculosis

Location	Number	Percentage
Ganglionic	12	60%
Pleural	6	30%
Bone marrow	2	10%
Hepatic	2	10%
Cerebral	1	5%
Pericardial	2	10%
Intestinal	1	5%

Clinically, the cough-fever-weight loss triad was the most common. The chest x-ray was abnormal in 92.86% of cases, revealing an alveolar syndrome in half of the cases of pulmonary tuberculosis, and a miliary in 38.10% of cases.

Biologically, anemia was the most common abnormality, it was observed in 93.3% of cases, and the C reactive protein (CRP) was always high with an average of 136 mg / l, with an interval between 369 mg and 11 mg / l.

Direct examination of sputum for KB was positive in 47.6% of cases. The genexpert was performed in 52.38% of cases, making it possible to detect Mycobacterium tuberculosis and confirm sensitivity to rifampicin. In 25% of cases, the Genexpert confirmed negative pulmonary tuberculosis on direct examination.

Tuberculosis was the revealing mode of HIV infection in 29 patients, while only 13 cases were known to be HIV positive.

The treatment included quadruple therapy (RHZE) according to the schedules recommended by the national tuberculosis control program, with an overall duration of 6 to 9 months. Antiretroviral therapy combined two nucleoside analogs and one non-nuleoside analog. Furthermore, all patients received co-trimoxazole and vitamin B6 concomitantly with antibacillary drugs.

Immune reconstitution inflammatory syndrome was found in two patients. Drug toxicity was noted in 40.48% of cases, mainly dominated by hepatotoxicity (76.47%) secondary to antibacillary treatment. The outcome was favorable in 33 patients (78.57%), death was reported in 7 patients (16.67%) and 2 cases of relapse were noted.

IV. Discussion:

Tuberculosis / HIV co-infection is a very documented entity in the world and in particular in sub-Saharan Africa where it varies from 16 to 80% [3]. The prevalence of TB / HIV co-infection in our department was around 1%, a lower rate than that recorded globally (8.2%) given the low incidence of HIV in our country.

The most common form of drug-susceptible tuberculosis in HIV-infected patients is exclusive pulmonary tuberculosis in 55% to 60% of cases. However, extra-pulmonary tuberculosis isolated or associated

with pulmonary tuberculosis and multifocal or disseminated tuberculosis are more frequently observed in HIV-positive patients [1]. In our study, exclusive pulmonary involvement was found in 52.38% of cases.

Tuberculosis and HIV infection affect a young population, which has been reported in several studies [4]. In our series, the average age was 38.23 years, with a female predominance at 54.76%.

Recent studies on patients infected with HIV indicate that active and passive smoking represent a risk factor for latent tuberculosis infection, progression to active disease, severe pulmonary or extra-pulmonary tuberculosis, treatment success rate lower and higher tuberculosis-related deaths [5-6].

Reactivation of tuberculosis can occur either very early at the onset of immune depression with a CD4 count (differentiation clusters) between 200 and 400 cells / mm3 at the stage of asymptomatic HIV infection, or a little later with a CD4 count less than or equal to 200 / mm3 at the AIDS-disease stage, rarely the subject is infected with KB at the onset of infection with HIV. In addition, patients with the terminal stage of AIDS and having a lower CD4 count at 100 / mm3, may develop a primary tuberculous infection in the event of massive infestation by KB (kokh bacillus); in these patients, the risk of immediate passage to the tuberculosis disease stage is close to 100% and not 10% as in HIV negative subjects [7]. Unfortunately, in our study, we did not have data on the viral load and CD4 count of all patients.

All of our patients had general signs. In fact, the symptoms of tuberculosis can be more marked in hospitalized patients, which has been shown in studies of subjects hospitalized in specialized services in whom cough, weight loss and asthenia are present in half. in two thirds of patients [8-9]. The clinical examination is poor in pulmonary tuberculosis, contrasting with the importance of functional and radiological signs.

Extrarespiratory clinical signs may be associated with it and depend on the location of the disease [10]. In our study, extrarespiratory signs are dominated by cutaneous and digestive signs.

To confirm the diagnosis of pulmonary tuberculosis, it is now suggested to systematically combine it with a molecular gene amplification test such as Xpert MTB / RIF (rifampycin) and of course to perform cultures in solid and liquid medium [11]. In HIV-infected patients with pulmonary involvement, we most often note a negativity of the search for tubercle bacilli in spontaneous sputum [12], which is consistent with the data of our study where the search for AFB in sputum was positive in 20 cases, ie in 47.6% of the co-infected subjects. This negativity could be explained by the most frequent presence of non-cavitary pulmonary lesions in tuberculosis patients infected with HIV [13]. This is why the recommendations for screening for pulmonary tuberculosis in all subjects consist of performing the Genexpert examination without going through the direct examination, the specificity of Genexpert being very high (97% to 100%) [5 -14]. But culture remains the reference method or the gold standard in the diagnosis of pulmonary and extra-pulmonary tuberculosis [15]. Due to the poor performance of current diagnostic methods, such as smear microscopy, and the urgency of early detection of tuberculosis in HIV-infected patients, a promising recent Chinese study has resulted in a new model diagnostic based on the discovery of potential plasma biomarkers of tuberculosis in HIV-infected patients by quantitative proteomics [16].

Biologically, in our study, there is an inflammatory syndrome in 88.10% of our patients and an elevated CRP. A study by SKogrmar et al. concluded that CRP levels were higher in patients with tuberculosis than in controls, but no significant difference was observed when comparing CRP levels in HIV positive and HIV negative patients [17].

The treatment of tuberculosis in a patient infected with HIV is not a priori different from the treatment of an HIV-negative person and is based on combined treatment (two months of "intensive" quadruple therapy combining rifampicin (RIF), isoniazid (INH), ethambutol (ETB) and pyrazinamide (PZD), and four months of dual "consolidation" therapy combining rifampicin and isoniazid) for a total duration of six months. In the event of localization in the central nervous system, as in the immunocompetent, prolongation of treatment is recommended [2]. In our study, the patients were treated with the combination of the four antibacillaries with a total duration of treatment of between 6 and 9 months depending on the location and extent of the lesions.

Side effects of anti-tuberculosis drugs are frequent and severe in patients infected with HIV and treated for tuberculosis disease [18]. Hepatitis and neuropathies are the most frequent; drug eruptions such as Lyell's syndrome have been described [19]. In our study, the main side effects were hepatic cytolysis in 5 patients, hepatic cholestasis in 4 cases, then digestive intolerance in 4 cases. The management of these effects generally consisted of stopping the treatment and then gradually reintroducing it after correction of anomalies. It is important to know how to detect these effects in time and distinguish those which are serious, requiring the discontinuation or possible replacement of the offending drug, from those which only require symptomatic treatment.

Tuberculosis treatment should be prescribed 2 to 8 weeks before starting antiretroviral therapy. In patients whose immunosuppression is profound (CD4 <50 / mm^3) and whose tuberculosis is pulmonary, the initiation of antiretroviral treatment must be very early (within 15 days of antituberculosis treatment). When this is not limited to a pulmonary form, and in particular in cases of meningeal involvement; it seems desirable to delay the start of ART around the 8th week [1]. In order to obtain optimal suppression of viral multiplication, it is recommended to prescribe at least a triple therapy combining three antiretroviral molecules preferably from at

least two different therapeutic classes with biological monitoring of the tolerance of the treatment and its effectiveness [20]. In our study, all patients received antiretroviral therapy. The Tenofovir, Emtricitabine and Efaviranz protocol was prescribed in 22 patients, while the other patients were put on the Zidovudine, Lamivudine and Efaviranz protocols.

Systematic preventive treatment with cotrimoxasole should be given to all patients with tuberculosis and HIV infection regardless of their CD4 count. This treatment will be administered throughout the duration of the anti-tuberculosis treatment and until the patient's immunity improves with a satisfactory CD4 count which remains stable for at least 6 months (CD4 greater than 200 / mm3 or 15% [21] In our study, all the patients were put on bactrim 800 mg / day once the antibacillary treatment was started.

Immune reconstitution inflammatory syndrome (IRIS) is sometimes described as an undesirable effect of antiretroviral therapy in the presence of antimycobacterial therapy with worsening of a clinical or radiological manifestation of tuberculosis, once antiretroviral therapy has started. Its prevalence is estimated at 4 to 10% of cases [22-23], which is also reported by our study where IRIS occurred in 4.76% of cases.

Preventive treatment is recommended in people infected with HIV after ruling out the diagnosis of active tuberculosis. The reference medicine is INH in a daily self-administered dose at a rate of 5 mg / kg / day for 9 months in adults. Rifampicin monotherapy or the Rif -INH combination for 3 months are also effective. Preventive treatment reduces the risk of developing active tuberculosis in the short term by 40% compared to what it would have been without treatment [1]. In a recent study in South Africa, preventive treatment with isoniazid before starting antiretroviral therapy considerably reduced the risk of developing tuberculosis [24]. Unfortunately, none of our patients whose diagnosis of HIV infection preceded that of tuberculosis had received preventive treatment.

Adherence to treatment is essential to prevent the emergence of resistant strains. Any measure (education, financial support for the cost of treatment, short treatment regimen, combinations of fixed doses of anti-tuberculosis drugs, treatment under direct supervision) that may increase treatment compliance is indicated. In fact, the majority of treatment failures observed in tuberculosis disease are linked to an interruption of medication due to poor therapy [25].

In our study, the outcome was favorable in 33 patients, ie 78.57%. Two cases of relapse were recorded, which is consistent with the data in the literature. Death occurred in 7 cases, ie 16.67% of patients. The causes of death were diffuse and multifocal tuberculosis, pulmonary and cerebral tuberculosis, febrile respiratory distress syndrome and severe sepsis. Recent data in the literature indicate a significant reduction in the mortality rate in tuberculosis patients co-infected and concomitantly treated with antituberculosis drugs and antiretrovirals [3-26]. From the point of view of therapeutic success, there would be no significant difference between seronegative and seropositive tuberculosis subjects [27].

V. Conclusion:

TB-HIV co-infection is a fatal association, hence the importance of strengthening joint TB control activities and prophylactic treatment of suspected latent TB infection in patients with HIV. In this study, tuberculosis is often indicative of HIV infection, hence the interest in carrying out systematic HIV screening in all tuberculosis patients. It is therefore recommended to systematically perform a chest x-ray associated with a Genexpert test in any positive patient in a context suggestive of tuberculosis. We insist on the interest of Genexpert which makes it possible to increase the detection rate of Mycobacterium tuberculosis and the early detection of resistance to rifampicin, and on the interest of monitoring during the continuation of the treatment in order to avoid interruption of treatment.

Abbreviations:

- AFB: Acid-fast bacillus
- KB: Koch's bacillus
- CRP: C-reactive protein
- INH: isoniazid
- PCR: polymerase chain reaction
- Rif: rifampicin
- TB: Tuberculosis
- HIV: human immunodeficiency virus
- CD4: Cluster of differentiation 4

Declaration of interests:

The authors declare that they have no conflicts of interest relating to the article

References:

[1]. Professor Pierre Aubry, Dr Bernard-Alex Gaüzère. Updated on 18/01/2020 www.medecinetropicale.com
[2]. Janssens, F.C.-A.C-J.-P., Tuberculosis and HIV co-infection : therapeutic issues. Swiss Medical Review 2011. www.revmed.ch/RMS/2011/RMS-318/Co-infection.
[3]. Yone é, Kuaban WP, Kengne CAP. Impact of HIV infection on the course of adult tuberculosis in Yaoundé, Cameroun. Rev Pneumol Clin2012 ;68 :338-44, http://dx.doi.org/10.1016/j.pneumo.2012.10.001.
[4]. Dao S., Oumar A.A., Bayogo A., Coulibaly S., Diallo S., Koumare B Y. Kinetics of TCD4 lymohocytes in patients mono infected with HIV and co-infected with HIV and the Bacillus Acido Alcohol Resistant (BAAR) in Bamako, Mali. Med Mal infect 2009 : p.39(01) :21-23. https://doi.org/10.1016/S0399-077X(09)74317-3
[5]. Duarte, R., Lönnroth K, Carvalho C, Lima F, et al. Tuberculosis, social detreminants and comorbidities (including HIV). Pulmonology, 2018.24(2) :p.115-19. https://doi.org/10.1016/j.rppnen.2017.11.003
[6]. Perriot J., M. Underner, and G. Peiffer. Smoking and helping to quit smoking in patients with tuberculosis. Journal of Clinical Pulmonology,2018.74(6) :p.391399.https://doi.org/10.1016/j.pneumo. 2018.09.002
[7]. SWAMINATHAN S., Padmapriyadarsini C, Narendran G. HIV-Associated Tuberculosis : Clinical Update. Clin Infect Dis 2010 :p.50 :1377-86, http://dx.doi.org/10.1086/652147.
[8]. MacGregor RR. A year's experience with tuberculosis in a private urban teaching hospital in the postsanatorium era. Am J Med 1975 ; 58 :221. PubMed CrossRef Google Scholar
[9]. Barnes PF, Verdergem.T., Vachon LA, Leedom JM, Overturf GD., Chest roentgenogram in pulmonary tuberculosis. New data on an old test. Chest 1888 :p.94 :316–20. https://doi.org/10.1378/chest.94.2.316
[10]. Henry et al. Clinical and bacteriological diagnosis of tuberculosis :Prevention and management of tuberculosis in France. Rev Mal Respiratory Medicine ,2003 :p.20 :7S34–40.
[11]. Blanc F.X. Pulmonary tuberculosis and mycobacteriosis : new developments for the year. Respiratory Disease Review News, 2016.8(4) :p.258–262.
[12]. Horo, K., et al., Comparative diagnosis of bacterial pneumonitis and pulmonary tuberculosis in HIV+ patients. Respiratory Disease Reviews, 2016.33(1) :p.47–55.
[13]. Aderaye G, Bruchfeld J, Assefa G, Feleke D, Källenius G, Baat M, et al. The relationship between disease pattern and disease burden by chest radiography. M. tuberculosis load, and HIV status in patients with pulmonary tuberculosis in Addis Ababa. Infection 2004 ; 32 :333–8.
[14]. Jabri, H.,et al . Diagnostic methods of tuberculosis. Journal of Clinical Pulmonology ,2016.72(5) : p.320-325.
[15]. Bicart -See A, Marchou B., Bauriaud R, Louis D, Obadia M Et Auvergnat, Special features of tuberculosis during HIV infection. Med Mal Infect 1995 :p.25 :991-7.
[16]. Shen Y , Xun J, Song W, Wang Z, Wang J, Liu L, Zhang R, Qi T, Tang Y, Chen J, Sun J, Lu H. Discovery of potential plasma biomarkers for tuberculosis in HIV–infected patients by quantitative proteomics based on independent data acquisition. Infect Drug Resist . 2020; 13: 1185-1196. https://doi.org/10.2147/IDR.S245460
[17]. Skogmar S, S.T. , Balcha TT, Sturegard E, Jansson M, Björrkman P,Plasma Levels of Neopterin and C-Reactive Protein (CRP) in Tuberculosis (TB) with and without HIV Coinfction in Relation to CD4 Cell Count. PloS ONE 2015 :p.10(12) :e0144292.
[18]. Lanternier F., Dalban.C. Perez L., et al. Tolerability of antituberculosis treatement and HIV serostatus Int J.Tuberculosis and Lung Dissease, 2007 :p.11 :1203-1209.
[19]. Kouassi B., Horo K., Vilasco B., Koffi N., Kouame Y., Ahui B., Gode C., N'Gom A., Aka-Danguy E., Tchramran M., Kamagate. , Lyell syndrome in three HIV (+) patients on anti-tuberculosis treatment.Rev Mal respir, 2010 : p.27 :247-250.
[20]. AF Luetkemeye., Curent issues in the diagnosis and management of tuberculosis and HIV coinfection in the United States. Topics in HIV Medicine, 2010(18) :p.143-148.
[21]. Who, guidance on couples HIV testing and counselling-including antiretroviral therapy for treatment and prevention in serodiscordant couples recommandations for a public health approach april 2012. www.who.int/publications/guidelines/hiv_aids/en
[22]. Bonnet M, Bhatt N, Baudin E, et al, editor. Results of the CARINEMO-ANRS 12146 randomized trial comparing the efficacy and safety of nevirapine versus efavirenz for treatment of HIV-TB co-infected patients in Mozambique. 6th IAS Conference on HIV pathogenesis, treatment and prevention ; 2011 ; Rome, Italy.
[23]. Karmakar S, Sharma SK, Vashishtha R, et al. Clinical characteristics of tuberculosis-associated immune reconstitution inflammatory syndrome in North Indian population of HIV/AIDS patients receiving HAART. Clin Dev Immunol 2011;2011:239021. [Medline].
[24]. Golub JE, Pronyk P, Mohapi L, Thsabangu N, Moshabela M, Struthers H, Gray GE, McIntyre JA, Chaisson RE, Martinson NA. Isoniazid preventive therapy, HAART and tuberculosis risk in HIV-infected adults in South Africa: a prospective cohort. AIDS. 2009;23(5):631–6. PubMed PubMed Central Google Scholar
[25]. Huchon G., Tuberculosis : infection and disease. EMC-Pneumology, 2012 ; 9(4) :p.1-22.
[26]. Abdool Karim SS. Naidoo K, Grobler A, Padayatchi N, Baxter C, Gray A, et al. Timing of initiation of antiretroviral drugrs during tuberculosis therapy. N Engl J Med 2010 ; 362 :697-706. [PMC free article] [PubMed] [Google Scholar]
[27]. Wa Ilunga, E.N., et al. Prevalence of HIV-tuberculosis co-infection and impact of HIV on tuberculosis patients in the Lubumbashi health zone from 2014 to 2015. Journal of Clinical Pulmonology, 2018.74(1) :p.9-15.

Pneumo-phthisiology, et. al. "The clinical, bacteriological and therapeutic characteristics of tuberculosis in patients infected with HIV (about 42 cases)." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 20(08), 2021, pp. 27-31.