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Original Research Paper Medical Science

Pulmonary complications in HIV/AIDS patients.

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ABSTRACT Introduction: Pulmonary complications are very common during the course of Acquired Immunodeficiency Syndrome. (AIDS). Aim of the study: The main study goal is to assess the patterns of respiratory complications in the HIV/AIDS patients. Materials and methods: In the study are enrolled 77(83.1%male HIV/AIDS)patients with pulmonary complications,with the mean age of the subjects was 46.4±10.2, ,and known as HIV seropositive patients from 5.1 ±2.4. years .Data are elaborated by SPSS17. Results: By occupational,29(37.7%) were unemployed,22(28.6%), employed,5 (6.5%), farmeres,7(9.1%) office-beares,14(18.2%). the others,regard to the count of CD4 cellules, 6(7.8%) from 300-399 cel/ml,15(19.5%) with 200-300 cel/ml,28 (36.4%) patients from 100-199 cel/ml, and 28(36.4%) <100cel/ml. In all of the patients(77) with HIV/AIDS are found 84 pulmonary manifestations, respectively bacterial pneumonia(first episode)in 12 (14.3%) cases,recurent bacterial pneumonia-9(10.6%),pneumocystis carinii pneumonia(PCP) 33(39,3%) cases, tuberculosis 27(32.2%),, divided in 23(27.4%) -cases as pulmonary tuberculosis and 4(4.8%) as generalised tuberculosis. Kaposy Syndrome- 2(2.4%),COPD -1(1.2%).cases. In the end of the study september 2015,13 patients died,12 of them had CD4 count level lower than CD4<199/ml. We found a positive correlations between ages and mortality (p=.003) ,the pattern of pulmonary complications with CD4+ count level.P<0.0001. Conclusions: In our study,the most common respiratory complications and with high mortality rate,are opportunistic infections from pneumocystis carinii pneumonia(PCP) and tuberculosis(TB).The level of CD4+ count is a useful indicator for developing respiratory infections and complications in HIV/AIDS patients.

KEYWORDS : HIV/AIDS,TB,PCP,COPD, CD4+

Introduction

Pulmonary complications are one of the most common causes of illness and mortality in the Acquired Immune Deficiency Syndrome (AIDS). Seropositive patients are exposed to infective and non-infective diseases. However, the type of pulmonary complications depends on the degree of immune deficiency.

In HIV-infected patients are common the pulmonary complications. When the immune reaction is preserved relatively well in early periods of HIV infection, the model of respiratory infections is similar to the one found in the general population, but to a higher frequency. The risk of opportunistic infections and tumours is increased with the progression of the HIV-induced immunosuppression. During the last years, there have been some changes in the pattern of lung diseases, which occur in HIV-infected patients. These changes can be attributed to the high availability and prophylactic treatment against Pneumocystis carinii pneumonia and combined antiretroviral therapy (also known as Highly Active AntiRetroviral Therapy or HAART). (1)

From the first descriptions of HIV/AIDS, the respiratory tract has been the most commonly affected localization from the disease. According to the findings of the autopsy, the lungs were affected with an incidence that varies from 100% in the early period of epidemics to 70% in the HAART period. Up to 70% of HIV patients have experienced pulmonary complications during the evolution of the disease, mainly from infective aetiology. The infections of the lower respiratory tract are 25 times more common in HIV patients than in the general community, which occur up to 90 cases in 1000 people/year. Currently, pulmonary infections, not only opportunistic AIDS-related infections, remain the main cause of illness and mortality and one of the most common causes of hospitalization of HIV-infected individuals worldwide. There is an incidence of 20-25 episodes per 100 hospitalizations per year. These numbers give an idea of the gravity of the problem of pulmonary infections in HIV patients. Furthermore, it has been suggested that the PCP, tuberculosis (TB) and bacterial pneumonia are related to considerably worse progression of the HIV disease, even to permanent decrease of the lungs' function, even though not all researches agree with these results. (Cited 2)

The evaluation of respiratory symptoms in HIV-infected patients can be difficult for several reasons. Respiratory symptoms are common complaints of HIV-infected individuals and can be caused by a wide range of diseases. The range of lungs diseases in HIV-infected patients not only includes the HIV-related ones, but also the non-HIV-related ones. Pulmonary HIV-related diseases include opportunistic infections and neoplasms. Opportunistic infections include the bacterial, mycobacterial, fungal, viral infections, and infections from parasitic pathogens. Each of these opportunistic diseases and neoplasms has a characteristic clinical and radiographic presentation. However, there can be a considerable change and overlap in these presentations. Therefore, there are no pathognomonic constellations of the symptoms, results of physical examination, laboratorial anomalies and the radiological image of the thorax or specifically for a certain disease. Therefore, when possible, the microbiological definitive diagnosis or the pathological diagnosis towards the empirical medication is preferable. The diagnostic tests include cultures of the sputum and blood and of the respiratory samples extracted through invasive procedures such as bronchoscopy, thoracentesis, transthoracic needle biopsy with CT, thoracoscopy, mediastinoscopy and open biopsy of the lungs.

As a result of better management of HIV+ individuals, the comorbidities of the patient appear and become more important. With the antiretroviral medication, the PCP and TB have become less usual and pulmonary mortality has decreased. HIV causes immune deficiency, which increases the risk of pneumonia. Especially in the patients with respiratory problems and advanced deficiency of immunity, it is essential to consider all differential diagnoses.

Materials and methods

It is a retrospective observational study developed during the years 2004-2015. The study was conducted in the University Hospital Center "Mother Theresa", Tirana, Hospital of Infectious Diseases. 77 patients with HIV/AIDS (64 males and 13 females) were included in the study, out of which 60 (77.9%) were from the cities and 17 (22.1%) were from the villages, who have experienced complications with pulmonary pathology. The patients were aged from 30 to 71 years old (median age 46.4 ± 10.2), which were known to be sick for 1 to 12 years (on the average 5.1 ± 2.4) and had a medication period of 0.2 to 10 years (median period 4.5 ± 2.5 years). Until the end of medication, 13 (16.9%) patients have died. Referring to a protocol, demographic data and clinical-radiological characteristics – CD4 cell counts were extracted.

Statistical processing

All collected data were written in the Microsoft Excel program, from which they were exported to the SPSS (Statistical Package for Social Sciences) 20.0, with which statistical analyses of the data have been performed. The values $p \leq 0.05$ were considered significant.

Results

In 77 HIV/AIDS patients have occurred 84 complications with pulmonary pathologies. According to the pulmonary complication, it results to have been bacterial pneumonia (episode I) in 12 (14.3%) cases, recurrent bacterial pneumonia – 9 (10.6%). The more often pathology has been the PCP – 33 (39.3%), followed by tuberculosis – 27 (32.2%), out of which 23 (27.4%) pulmonary TB and 4 (4.8%) generalized TB. There were noticed 2 (2.4%) cases with Sarcoma Kaposi and 1 (1.2%) case with SPOK.

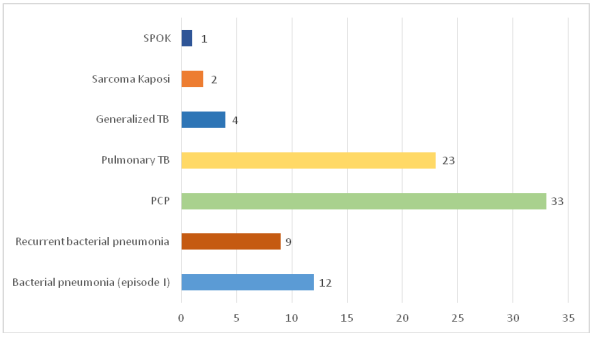

Fig. 1. Pulmonary complications in HIV/AIDS patients

The average age in HIV/AIDS patients, who have experienced pneumonia for the first time was 42.9 ± 5.9 years old (35 to 52 years old); for those with recurrent pneumonia – 44.1 ± 10.9 years old (31 to 64 years old); for those with PCP – 48.2 ± 11.8 years old (30 to 71 years old); for those with pulmonary TB – 48.1 ± 9.8 years old (32 to 67 years old); for patients with generalized Tb – 47.8 ± 10.2 years old (42 to 63 years old).

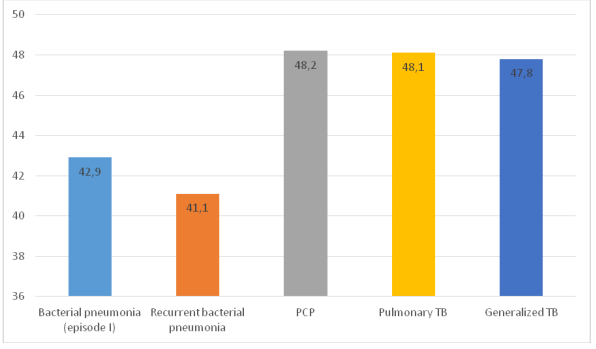

Fig. 2 Average age structure related to the pulmonary complication

The pulmonary complication related to HIV has been the same for both sexes with regards to pneumonia and has predominated in the male sex in cases of recurrent pneumonia, PCP and TB. Pneumonia, PCP and TB have predominated in smoking HIV/AIDS patients.

Patients with higher education have been less frequent, while in the professions structure, TB and PCP have been more frequent in the unemployed people and labourers.

The CD4 cell count related to the pulmonary complication shows that, in the case of pneumonia, for the first time there have been equal cases for CD4 300-399 and 200-299/ml, and no case with a lower CD4 cell count. The recurrent pneumonia is seen in an equal number of cases with 200-299, 100-199 and <100/ml CD4 counts, while in no case has there been a 300-399/ml cell count. The PCP has occurred in 60.6% of the cases, in patients with a CD4 count of 100-199 cells/ml and in 39.4% of the cases in cell counts of <100 cells/ml, while there has been no occurrence in CD4 cell counts >199/ml. The pulmonary TB has been found in patients with a CD4 cell count of 200-299 cells/ml, in 26.1% of the cases, 100-199 cells/ml in 34.8% of the cases and 39.1% in a <100 cells/ml cell count.

Regarding the manner of the disease's onset (%) related to the pulmonary complication, it is noticed that a higher frequency of an acute beginning is present in pneumonias and a subacute beginning in the pulmonary TB. In the tubercular complication, in 7 (30.4%) cases, a hilar and mediastinal adenopathy was noticed in the CT, while in 5 (21.7%) cases in the thoracic radiography. According to the affected pulmonary area (%), regarding the pulmonary complication, an atypical localization of the pulmonary TB in the middle and lower area is noticed (43.2% of the cases).

The time period in which the HIV/AIDS patients are known to be infected, who have experienced pneumonia for the first time, results to be 4.2 ± 1.9 years (2 to 8 years); for those with recurrent pneumonia – 3.9 ± 1.8 years (1 to 6 years); for those with PCP – 5.3 ± 2.6 years (1 to 12 years); for those with pulmonary TB – 6.2±2.2 years (2 to 10 years); for patients with generalized TB – 4 ± 2.2 years (1 to 6 years). According to the period of the recognition of the disease (%) related to the pulmonary complication, it is noticed that there is a longer duration for the TB and PCP cases.

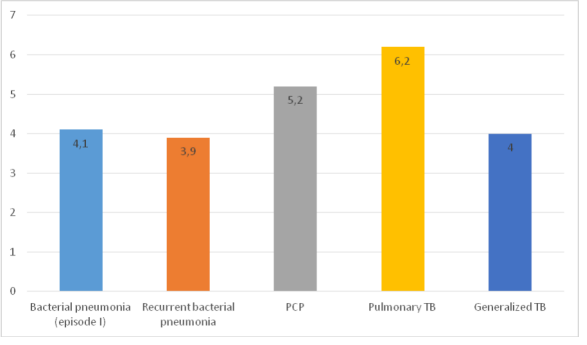

Fig. 3 The average period of disease recognition (%) regarding the pulmonary complication

The time period in which the HIV/AIDS patients have been treated with antiretroviral medicines, who have experienced pneumonia for the first time, results to be 3.4 ± 1.8 years (1 to 8 years); for those with recurrent pneumonia – 3.9 ± 1.8 (1 to 6 years); for those with PCP – 4.9 ± 2.5 years (0.25 to 9 years); for those with pulmonary TB – 5.3 ± 2.8 years (1 to 10 years); for those with generalized TB – 2.9 ± 3 years (0.2 to 6 years).

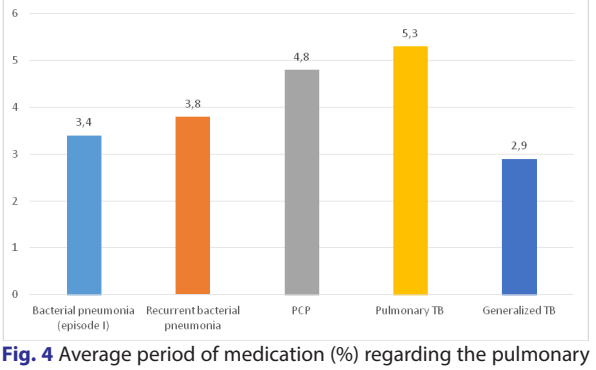

Fig. 4 Average period of medication (%) regarding the pulmonary complication

According to the period of treatment with antiretroviral medicines (%) regarding the pulmonary complication, the majority of cases belong to the 2-4 years period, there is a frequency of cases with recurrent pneumonia, PCP and TB, in the 5-7 years medication period. In patients treated for 8-10 years it is noted a considerable number of cases with TB and PCP.

Except pneumonia, deaths (%), according to the pulmonary complication and the CD4 cell count are grouped in CD4 cell counts < 199 cells/ml.

Discussion

In our study on 77 patients with HIV/AIDS, there have been 84 complications with pulmonary pathology. According to the pulmonary complication, there results to have been bacterial pneumonia (episode I) in 12 (14.3%) cases, recurrent bacterial pneumonia – 9 (10.6%). The most frequent pathology has been the PCP – 33 (39.3%), followed by tuberculosis – 27 (32.2%), out of which 23 (27.4%) – pulmonary TB and 4 (4.8%) generalized TB, which coincides with the literature data. 2 (2.4%) cases were found with Sarcoma Kaposi and 1 (1.2%) case with SPOK.

Important changes have occurred in the epidemiology of pulmonary infections related to HIV. In general, the primary causes are the description of the Pneumocystis jirovecii's prophylaxis and the application of the highly active antiretroviral treatment (HAART). Currently, the most frequent diagnosis in the developed countries is the bacterial pneumonia, especially from pneumococcal pneumonia, the second most frequent cause is pneumonia from pneumocystis and the third is tuberculosis. However, in Africa, tuberculosis can be a more common pulmonary complication of HIV. (2)

Bacterial pneumonia is common in HIV-infected patients and the incidence increases with the progression of the compromised immune system. The Pulmonary Complications of HIV Infection Study Group has monitored a group of 1,130 adult HIV-infected patients and 167 HIV-negative patients for 64 months (3, 4). In that period, HIV-infected patients have had 237 cases of bacterial pneumonia, a frequency of 5.5 episodes per 100 patients/year, compared to 6 episodes for adult HIV-negative people, a frequency of 0.9 for 100 episodes of patients in years. The frequency of pneumonia increases with the decrease of the CD4+ cell count. When patients are stratified in groups according to the CD4+ cell count per cube millimetre, over 500, 200-500 and under 200, the frequency of pneumonia was respectively 2.3, 6.8 and 10.8 episodes per 100 patients/years. Cordero and bshp (5) found a similar trend. In a limited study on 26 HIV-infected patients, hospitalized with pneumonia from H. influenzae, the majority of patients (73%) had a CD4+ cell count under 100 / mm3. Despite the CD4+ cell count, the incidence of pneumonia was higher in injection drug users than in the other HIV-infected patients.

The reaction of the individual to the TB is almost completely controlled by the cellular immunity, firstly from the macrophages and CD4+ cells. The incidence of the TB clinical disease can be expected to increase in patients with damaged cellular immunity after the infection, with the increase of the number of cases with the primary and disseminated disease. Before the HIV epidemics, only 10% of cases with TB were primary diseases. Except a higher incidence of the primary disease, HIV-infected patients have also a higher incidence of disseminated diseases. The extrapulmonary disease is common in HIV-infected patients. There is no organ that can be ignored. The swelling of extrathoracic lymph nodes is present in 20% of HIV-infected patients with TB and 77% are direct BK positive in aspiration. (6) The risk of progression to clinical TB after the MTB infection is higher in HIV-infected patients; the clinical disease is developed in approximately 10% of cases each year, while this disease is developed in 10% of the immuno competent individuals during their whole life. In many clinics of tuberculosis, approximately 10% of the diseased people are with HIV+. In most cases, the progressive form of tuberculosis is developed in the HIV-positives, especially in the AIDS phase. The CD4 count in tuberculosis in these cases is 200-300 cells/mm3 earlier than in other opportunistic infections. In the AIDS-infected people, in 70% of cases, extrapulmonary forms of tuberculosis are seen, but miliary TB and lungs affected by non-cavitary tuberculosis can be seen as well (7). Often, in the AIDS-infected people, the TB diagnosis is made late because of the atypical manifestation of the disease's progress. In the HIV+ diseased people, in 32-76% of cases, extrapulmonary forms of tuberculosis develop, while in 60-70% of cases, lung TB develops. (cited 8)

P. carinii causes life-threatening pneumonia in individuals with compromised immune system. With the beginning of the AIDS epidemics in the beginning of the 1980s, the number of cases has risen exponentially. With improvements in the diagnosis, treatment and prophylaxis, the number of PCP cases has now decreased dramatically. (9) When the AIDS epidemics started, the PCP developed on 75% of the AIDS-patients during their disease. With the use of PCP prophylaxis and HAART, the incidence of PCP has dramatically decreased. HIV-infected patients have the tendency to present a more hidden progress than the non-HIV-infected patients. In the HIV-infected patients, the CD4+ cell count is the most important indicator of the PCP risk, but this, in itself, is not diagnostic of the PCP. When the CD4+ cell count decreases under 200/mm3, the PCP risk increases. In some patients, the PCP can progress in higher levels, but the risk is low.

The category of the patient's HIV transmission and habits (e.g. smoking) provides information on the relative frequency of different infections and neoplasia related to HIV and non-HIV-related states. Bacterial pneumonia is more common in HIV-infected patients, who are injection drug users, than in patients with no IDV anamnesis. (3) Similarly, TB is more common in HIV-infected patients who use injection drugs than in patients with no anamnesis of intravenous drug use. On the other hand, Sarcoma Kaposi is seen in the USA almost exclusively in men who have sex with men (MSM). The use of injection drug or other illicit drugs may cause a variety of pulmonary diseases unrelated to HIV (e.g. septic embolism related to endocarditis or pneumonia, respiratory depression, pulmonary oedema). "The Pulmonary Complications of HIV Infection Study" showed that upper respiratory tract infections, such as sinusitis, pharyngitis and acute bronchitis were more commonly the cause of respiratory symptoms than Pneumocystis Jiroveci Pneumonia (PCP), bacterial pneumonia, tuberculosis or Pulmonary Sarcoma Kaposi. (10) This range of pulmonary diseases dominated by the upper respiratory tract infections and acute bronchitis in an ambulatory clinic clearly shifts towards opportunistic pneumonia in an intrahospital environment and more often towards PCP in a clinical environment of intensive care. (11) Not only that, but demographic and regional changes influence the range of pulmonary diseases. Therefore, the diagnostic approach for the evaluation of respiratory symptoms in an HIV-infected patient should take all these factors into consideration.

The average age in HIV/AIDS patients who have had pneumonia for the first time has been 42.9±5.9 years old (35 to 52 years old); for those with recurrent pneumonia – 44.1±10.9 years old (31 to 64 years old); for those with PCP – 48.2±11.8 years old (30 to 71 years old); for those with pulmonary TB – 48.1±9.8 years old (32 to 67 years); for patients with generalized TB – 47.8±10.2 years old (42 to 63 years). Thus, a shift towards older age is noticed for the PCP and TB, which is related to the increase of immune deficiency as well, with the decrease of the CD4 cell count and the progression of HIV/AIDS over the time.

The pulmonary complication related to HIV has been the same for both sexes with regards to pneumonia and has predominated in the male sex in the cases of recurrent pneumonia, PCP and TB.

Complications in pneumonia, the PCP and TB have predominated in smoking HIV/AIDS patients, which is also related to the described negative influence of tobacco related to the progression of HIV infection. In patients with higher education, the pulmonary complication has been less frequent, which is related to social-cultural and medical factors.

Furthermore, in the origin structure, city inhabitants are more frequent, which might be influenced by sub-diagnosis factors. Regarding the professions structure for TB and PCP, there have been

more unemployed people and workers, which is related to social-economic factors and medical care.

In the study's data, the CD4 cell count related to pulmonary complication, regarding the pneumonia for the first time, results to have an equal number of cases for CD4 300-399 and 200-299/ml, and no case of lower CD4 cell count. The recurrent pneumonia is seen in an equal number of cases for CD4 cell counts of 200-299, 100-199 and <100/ml, and no case of 300-399/ml. The PCP has occurred in 60.6% of cases, in patients with a CD4 cell count of 100-199 cells/ml and, in 39.4% of cases, in a cell count of <100 cells/ml, while in no case cell count CD4>199/ml. Pulmonary TB is found in patients with a CD4 cell count of 200-199 cells/ml in 26.1%, 100-199 cells/ml in 34.8% and 39.1% in the cell count < 100 cells/ml. These results indicate and coincide with the literature data, where the level of immune deficiency, CD4 cells number decrease defines considerably the type of pulmonary complication.

Specific infections of the lower respiratory tract present special patterns according to the number of CD cells in the beginning of the study and the transmission category. Acute bronchitis was the predominant infection in the lower respiratory tract for individuals with a CD4 cell count > or = 200 cells/mm3. In individuals with a CD4 cell count of 200 to 499 cells/mm3, the incidence from bacterial pneumonia and Pneumocystis carinii for each increases with an average of 40% per year. In individuals with a CD4 cell count <200 cells/mm3, acute bronchitis, bacterial pneumonia and pneumonia P. carinii occur in a higher frequency, despite the chemoprophylaxis in more than 80% of them after the first year, and the frequency of other opportunistic lung infections increases over the time. Each year, injection drug users had a higher incidence of bacterial pneumonia than homosexual males. The yearly frequency of tuberculosis was <3 episodes/100 persons/year in each CD4 cell count and HIV transmission group. (10)

According to the study, the manner of the disease's onset (%) regarding the pulmonary complication has more often been an acute beginning for pneumonias and subacute pulmonary TB. This, except the role of the infectious cause, coincides also with the reacting power of the organism regarding the immune state, with the difference the pneumonia occurs in a higher CD4 count than TB. In our study in patients with HIV/AIDS and pulmonary complications, no significant changes have been found in the clinical symptoms and complication type. It results that, in the tubercular complication and recurrent pneumonia, hilar and mediastinal adenopathy was found, which indicates a more advanced stage of immune deficiency and type of pulmonary complication.

According to the affected lung (%) regarding the pulmonary complication, it is noticed that the pulmonary TB and PCP have had more often a bilateral localization, while according to the affected pulmonary area (%) regarding the pulmonary complication, an atypical localization of pulmonary TB is noticed in the middle and lower area of lung (43.2% of cases). TB can have a variety of radiographic images. (12) The characteristic image depends partially on the degree of immunosuppression. In early phases of HIV infection (when the patient has a relatively high count of CD4 cells), TB usually shows an image of reactivation, i.e. infiltrators in the upper lung areas (apical and posterior segments of upper lobes and apical-posterior segment of the inferior lobe), often with cavitary destruction.

On the other hand, caverns are a less common presentation of tuberculosis in HIV-infected patients with a low CD4 cell count. These patients are more likely to either present disease diffusion, which can be miliary, or with infiltrators mainly in the middle and inferior area of the lungs, which may be negatively assessed as bacterial pneumonia. For the differential diagnosis, the "key" is recognition of the patient's CD4 cell count and the fact that this radiographic presentation of TB can occur in a lower CD4 cell count. (12)

The time period in which HIV/AIDS patients are known, who have suffered pneumonia for the first time, has resulted to be 4.2±1.9 years (2 to 8 years); for those with recurrent pneumonia – 3.9±1.8 years (1 to 6 years); for those with PCP – 5.3±2.6 years (1 to 12 years); for those with pulmonary TB – 6.2±2.2 years (2 to 10 years); for patients with generalized TB - 4±2.2 years (1 to 6 years). These data confirm the fact that the progression of HIV/AIDS disease is accompanied with characteristic complications for each type. According to the period of the recognition of the disease (%) regarding the pulmonary complication, it is noticed that a higher frequency of cases with TB and PCP have a higher duration.

The time period in which HIV/AIDS patients have undergone antiretroviral treatment, who have suffered pneumonia for the first time results to be 3.4±1.8 years (1 to 8 years); for those with recurrent pneumonia – 3.9±1.8 (1 to 6 years); for those with PCP -4.9±2.5 years (0.25 to 9 years); for those with pulmonary TB - 5.3±2.8 years (1 to 10 years); for patients with generalized TB – 2.9±3 years (0.2 to 6 years). According to our study, the period of antiretroviral treatment related to the pulmonary complication, where the majority of cases with complications are in the 2-4 years period of treatment, in the 5-7 years treatment duration, there is a frequency of cases with recurrent pneumonia, PCP and TB. In patients treated for 8-10 years, a considerable number of cases with TB and PCP is noticed.

Pulmonary infections remain among the most important causes of illness and mortality in these patients, and the first reason of hospitalization for the HAART stage. Making the etiological diagnosis of the lung infection in these patients is important because of its prognostic reasons. (2)

Except pneumonia, deaths (%) according to the pulmonary complication and CD4 cell count are grouped in counts of CD4 < 199 cells/ml. The number of CD4 cells is a strong indicator of death risk and AIDS (13), Robert et al. (14) evaluated the CD4 count and death risk in HIV-infected patients in HAART and it resulted that almost all deaths have occurred in patients with less than 50 CD4 cells/mm3.

Conclusions

The most frequent pathology was PCP, followed by tuberculosis and shifting towards with older age, which is related to the decrease of CD4 cell count and progression of HIV/AIDS over the time. According to the affected lung (%) regarding the pulmonary complication, it is noticed that the pulmonary TB and PCP have had bilateral localization more frequently, while according to the affected pulmonary area (%), regarding the pulmonary complication, it is often noticed an atypical localization of pulmonary TB in the middle and lower pulmonary area. The CD4 cell count is a strong indicator of death risk.

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