Journal Homepage: - www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/13948
DOI URL: http://dx.doi.org/10.21474/IJAR01/13948

*RESEARCH ARTICLE*

# PNEUMOCYSTIS IN PATIENTS LIVING WITH HIV: EXPERIENCE OF THE INFECTIOUS DISEASES DEPARTMENT OF CHU MOHAMED VI-MARRAKECH

**F. Etoughe N.[1], F. Ihbibane[1], M.El Annaoui[1], M.El Mezouari[2], R. Moutaj[2] and N. Tassi[1]**

1. Infectious Diseases Service CHU Mohamed VI Marrakech- Cadi Ayaad University.
2. Parasitology Mycology Department Avicenne Military Hospital Marrakech.

## *Manuscript Info*

***Manuscript History***
Received: 20 October 2021
Final Accepted: 24 November 2021
Published: December 2021

***Key words:-***
Pneumocystis Jirovecii- HIV- Cotrimoxazole

## *Abstract*

Pneumocystis is the most serious and common respiratory opportunistic infection after tuberculosis during HIV infection. To describe the epidemiological, clinical, therapeutic and evolutionary aspects of HIV-infected patients who presented with pneumocystis. Retrospective study of the records of 45 HIV-infected patients followed at the Department of Infectious Diseases of the CHU Mohamed VI and hospitalized for Pneumocystis jirovecii infection between January 2007 and March 2021. Out of 1286 HIV-infected patients followed at the department during the study period, 45 patients (3.5%) had pneumocystis. Pneumocystis was inaugural to HIV infection in 36 cases (80%). The predominance was male in 63% of cases (28 males to 17 females), with an average age of 35.5 years [16-64 years]. The mean TCD4 cell count was 74 cells/mm$^3$ [0- 656 cells/mm$^3$]. The mean LDH level was 874.89 IU/L. The clinical picture was marked by cough in 84% of cases and dyspnea in 64% of cases. The most frequent radiological signs were a diffuse interstitial syndrome in 84.4% of cases on chest X-ray and ground glass appearance in 63% of cases on chest CT. The diagnosis of pneumocystis was confirmed in 16 patients by the detection of Pneumocystis jIrovecii in sputum and BAL. All our patients were treated with Trimethoprim-Sulfamethoxazole combination. Antiretroviral treatment was started in 32 patients, i.e. 71% of the patients, with a favorable evolution in 24 patients, i.e. 53%. Pneumocystis is a serious infection in immunocompromised patients especially PLHIV. In Morocco, it is still frequent during HIV infection and is one of the main causes of death.



## Introduction:-

Pneumocystis is an opportunistic mycosis caused by a cosmopolitan fungus, Pneumocystis jirovecii, which causes febrile pneumonitis in subjects with severe cellular immunity deficiency, particularly HIV-infected patients.

Despite the decrease in its incidence since the introduction of antiretroviral therapy and cotrimoxazole prophylaxis, pneumocystis remains the most frequent opportunistic infection of HIV infection and one of the main causes of mortality in HIV-infected patients.

**Corresponding Author:- F. Etoughe N.**
Address:- Infectious Diseases Service CHU Mohamed VI Marrakech- Cadi Ayaad University.

The aim of this work is to describe the epidemiological, clinical, therapeutic and evolutionary aspects of pulmonary pneumocystis (PCP) during HIV infection in 45 patients hospitalized in the Department of Infectious Diseases of the Mohamed VI University Hospital -Marrakech between 2007 and 2021.

## Patients And Methods:-

Our work is a retrospective study of 45 cases of pulmonary pneumocystis treated in the department of infectious diseases of the Mohamed VI University Hospital -Marrakech over a period of 14 years from January 2007 to March 2021.

We included all patients followed for HIV infection confirmed by Western Blot and confirmed and/or probable pulmonary pneumocystis in this study.

In the absence of confirmation, the diagnosis was made on the basis of clinical, biological, radiological and evolutionary parameters in relation to a good response to a specific treatment for pneumocystis.

Patients whose files were not usable were excluded from this study.

To carry out this work, we used the medical records of all the patients identified were reviewed and analyzed. This allowed us to bring out the epidemiological, clinical, para-clinical, therapeutic and evolutionary data.

## Results:-

During the period of our study (2007-2021), 1286 patients were followed at the Department of Infectious Diseases of the CHU Mohamed VI- Marrakech.

Pneumocystis was diagnosed in 45 patients, a prevalence rate of 3.5%.

In our study the mean age was 35.5 years [16-64 years].

Of the 45 patients, 28 were male (63%) and 17 female (37%), giving a sex ratio of 1.65.

Of the 45 patients, 43 were already in the AIDS stage at the time of diagnosis of pneumocystis.

The mean CD4 T cell count was 74 cells/mm3 with extremes of 0-656 cells/mm3.

The mean viral load in the patients was: 802,722 copies/ml (5.9Log10) with extremes: 2000 copies/ml -100000 copies/ml].

The history was marked by pulmonary tuberculosis in 32% of cases.

PCP was indicative of HIV infection in 36 patients (80%).

The onset of symptoms was progressive in 86.6% of cases and abrupt in 13.4%.

Weight loss, fever and asthenia were the most frequent symptoms.

The different general signs are reported in Table I.

**Table I:-** General signs in patients living with HIV with pulmonary pneumocystis.

| General signs | **Number** | **Percentage (%)** |
|---|---|---|
| Asthenia | 27 | 60 |
| Weight loss | 33 | 73,3 |
| Fever | 19 | 42,2 |
| Anorexia | 25 | 55,5 |
| Sweating | 17 | 37,7 |
| Chills | 14 | 31,1 |

Cough and dyspnea were the main functional signs.
Stage 3 dyspnea was noted in 19 patients and stage 4 dyspnea in 10 patients.
Productive cough was present in 23 patients (60.6%).
The different functional signs reported in the following table:

| Functional signs | Number | Percentage (%) |
|---|---|---|
| Cough | 38 | 84,4 |
| Dyspnea | 29 | 64,4 |
| Chest pain | 07 | 15,5 |
| Hemoptysis | 05 | 11,1 |

**Table II:-** Functional signs in pneumocystis.

The clinical examination revealed : polypnoea in 21 patients (48%), respiratory distress in 7 patients (15%), crepitus in 11 patients (24%), bronchial rales in 3 patients (7%), condensation syndrome in 3 patients (6%)

All patients had a chest X-ray, i.e. 100%.
The table below summarizes the different radiological aspects found

| Chest X-ray | Number | % |
|---|---|---|
| - Diffuse interstitial syndrome | 38 | 84,4 |
| - infiltrate | 9 | 20 |
| - Normal | 5 | 11,1 |
| - Pleural effusion | 3 | 6,6 |
| - other signs | 1 | 2.2 |

**Table II:-** The different radiological aspects on standard radiography.

Chest CT scans were performed in 13 patients or 28.8% of cases.

The ground glass appearance and the interstitial syndrome were the two most frequent radiological aspects. The results are detailed in figure 11

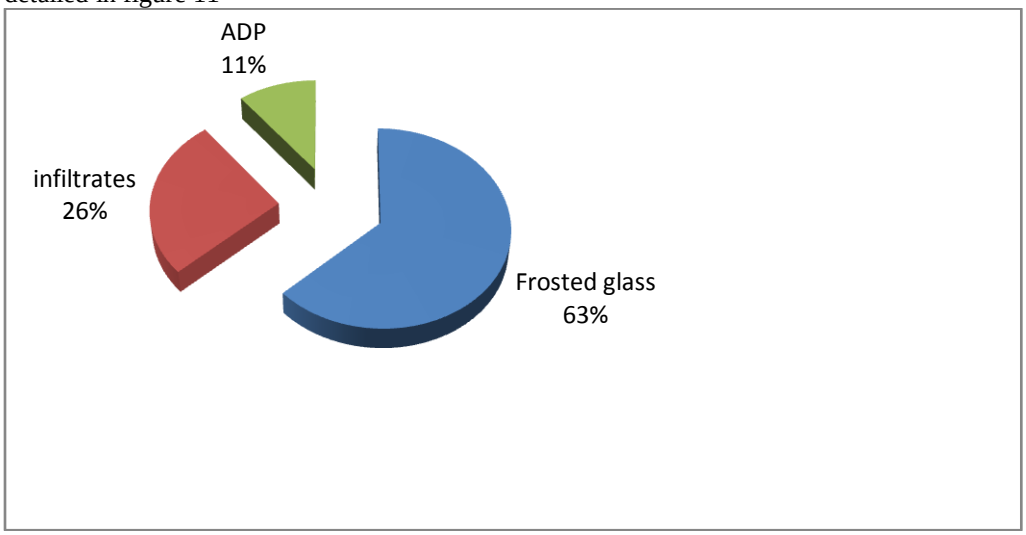


**Figure 2:-** Radiological aspects of the thoracic scanner.

**Regarding the biological workup:**
The mean lactate dehydrogenase (LDH) level was 874.89 IU/L [182 to 4520 IU/L.]
All patients had had sputum mycology examination.
The diagnosis of pneumocystis was confirmed in 16 patients by sputum (13 cases) and BAL (3 cases) with evidence of pneumocystis.
In 29 patients, the diagnosis of CP was presumptive, based on clinical, radiological and biological and therapeutic arguments related to a good response to specific treatments for pneumocystis.

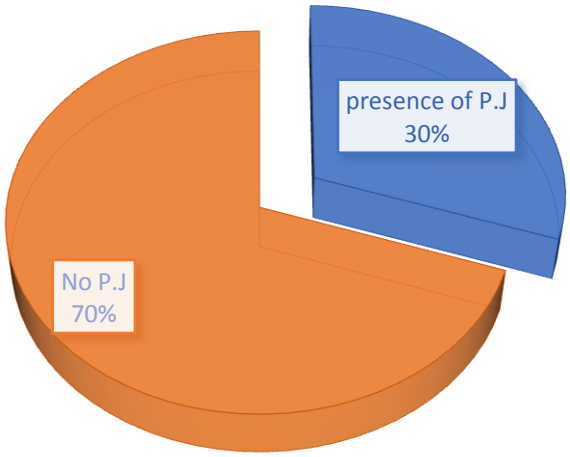


**Figure 3:-** Results of the mycological study of sputum.

Associated opportunistic infections were marked by digestive candidiasis (Table VI):

| **Opportunistic infections** | **Number and % of deaths** | **Number and % of surviving patients** |
|---|---|---|
| - Pulmonary tuberculosis | 7 cas (39%) | 4 cas (16,6%) |
| - Digestive candidiasis | 10 cas (55%) | 20 cas (83%) |
| - CMV Retinitis | 3 cas (16%) | 5 cas (20,8%) |
| - Cerebral toxoplasmosis | 2 cas (11,1%) | 1 cas (4,1%) |
| - Cryptococcosis | 2 cas (11,1%) | 0 cas |
| - BGN sepsis | 2 cas (11,1%) | 0 cas |

**Table IV:-** Opportunistic infections in HIV patients with pulmonary pneumocystis.

All patients received the combination of Trimethoprim and Sulfamethoxazole (TMP/SMX) (Cotrimoxazole). The dosage was 15-20 mg/kg/d of TMP and 75 mg/kg/d of SMX in the initial treatment. The duration of treatment was 21 days.

The oral route was used in all treated patients.

Eleven patients (24%) received symptomatic treatment with intravenous Solu-Medrol 240 mg/day from day 1 to day 3, 120 mg/day from day 4 to day 6 and 60 mg/day from day 7 to day 9.

Nine patients with CD4 counts below 200/mm3 received primary prophylaxis with Cotrimoxazole 1 tablet daily.

After 3 weeks of well-conducted initial treatment, secondary prophylaxis with cotrimoxazole (1 tablet/day per os) was initiated in 26 patients. Five patients died during the initial treatment.

Thirty-two patients received antiretroviral therapy (ARV):

The different treatment regimens are shown in the following figure

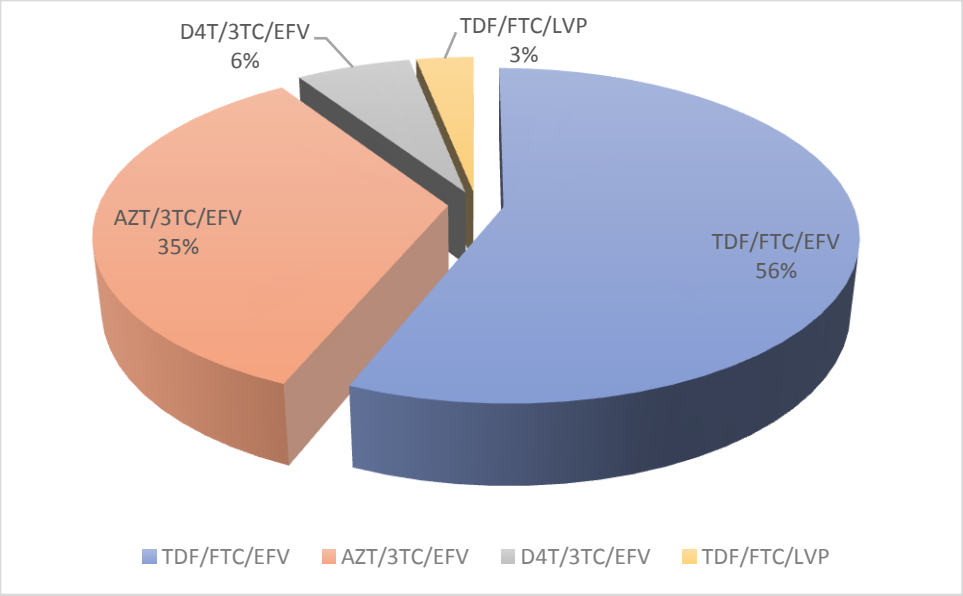


**Figure 4:-** Different antiretroviral regimens used in patients.
3TC: lamivudine. TDF: tenofovir. AZT: zidovudine. D4T: stavudine.
EFV: efavirenz. FTC: Emtricitabine. LPV/r:lopinavir/ritonavir( it must be corrected on the figure! it is not LVP)

The delay in starting ARV treatment in relation to pneumocystis was :
- 15 to 20 days in 19 patients, i.e. 42
-21 to 30 days in 10 patients, or 22%.
-Beyond 30 days in 3 patients, i.e. 6.67%.

The evolution was favorable in 24 patients, or 53.3%. Eighteen patients died, or 40%. Death was early, occurring during the attack treatment in 13 patients, and during the maintenance treatment in 5 patients. The evolution was unknown in three patients who were lost to follow-up (6.6%).

The causes of these deaths were multifactorial: 9 were due to respiratory distress syndrome secondary to pneumocystis, 4 by septic shock, 3 by immune restoration syndrome, one by hepatocellular failure secondary to liver cirrhosis in the context of hepatitis B-HIV co-infection, and the last by pulmonary embolism.

## Discussion:-

Nearly 40 years after the introduction of antiretrovirals (ARVs), PCP remains the main opportunistic infection inaugurating AIDS [1, 2, 3]. In our study, PCP was indicative of HIV infection in 36 patients (80%).

Of the 1286 patients followed, we recorded 45 cases of PJ, i.e. a prevalence of 3.45%. This is consistent with the literature which reports prevalence between 0 and 75% in Africa [1].

Male predominance was found in our study with a M/F sex ratio: 1.65 as described in the study of Harison et al [4] with a sex ratio of 2.9.

Also, the progressive aspect of the installation of pneumocystis in HIV positive patients, while it is brutal in HIV negative patients, is underlined in several studies of the literature [5, 6, 7].The result of our study agrees with that found in the literature since the progressive installation of this infection was noted in 86.6% of the patients.

In our study, the average age was close to that of other studies [8, 9, 10, 11, 12].

Male predominance was noted in our study with a sex ratio M/F: 1.65 as described in the study of Harison et al [4] with a sex ratio of 2.9.

In our study, dyspnea, cough, alteration of the general condition (asthenia, weight loss) and fever were the most frequent symptoms. In contrast, chest pain and hemoptysis were infrequent. These results are consistent with the literature. The productive aspect of cough has been encountered more frequently in the literature [13, 14, 15], this can be explained by the superinfection and the much more advanced stage of the disease in the patients of our study: 60.6% presented a productive cough compared to 39.4% who presented a dry cough.

Thus, we noticed that the results of the study of Harison.met al [4] and the study of Mouttarazouk [8] are comparable with those of our study (See table five)

**Table V**:- Functional signs reported in the different studies.

| | Moutarazouk ; Casablanca [8] | Harison.met al Antananarivo Madagascar [4] | Soweto, Afrique Du sud [16] | Antoin.r et al France [18] | Sheikholeslami FM et al En Iran [11] | Lopez-Sanchez et al en Espagne [10] | our study |
|---|---|---|---|---|---|---|---|
| | | | | | | | |
| Fever | 102 | 30 | 110 | 165 | 105 | 117 | 19 |
| | 67.1% | 88.2% | 91.6% | 74% | 83% | 86% | 42.2% |
| AEG | 107 | 24 | - | - | - | - | 33 |
| | 70.6% | 70.6% | | | | | 73.3% |
| Cough | 125 | 21 | 118 | 170 | 86 | 111 | 38 |
| | 82.2% | 61.7% | 98.3% | 76.2% | 68.2% | 81% | 84.4% |
| Dyspnea | 134 | 12 | 79 | 176 | 92 73% | 114 | 29 |
| | 91.6% | 35.3% | 65.8% | 79% | | 83.8% | 64.4% |
| Pain | 37 | - | 44 | | - | | 07 |
| Chest | 24.3% | | 36.7% | | | | 15.5% |
| Hemoptysis | 4 | - | 8 | | - | | 05 |
| | 2.6% | | 6.7% | | | | 11.1% |

Regarding the physical examination, our results agree with those of the study by Moutarazouk and Alejandro Rey [8, 17].

In our study, the chest radiograph shows a predominance of the typical aspect of pneumocystis, notably the diffuse interstitial syndrome present in 84.4% of cases. Our results agree with those of other studies [4, 8, 11, 17].

Chest CT is more sensitive than chest radiography in detecting PCP and may therefore be useful in symptomatic patients with normal or questionable radiographs [19; 20; 21; 22].

In 80% of cases, PCP presents as confluent, bilateral and symmetrical ground-glass patches, predominantly peri hilar, sparing the extreme periphery and pleural pouches [23,24]. More rarely, condensation patches, micronodules, septal thickening or cystic images predominating in the upper lobes may be observed, which may be complicated by pneumothorax. Adenopathies and pleural effusions are rarer [3, 23, 25, 26, 27].

In our study, the thoracic CT scan was performed in 13 patients, i.e. 28.8% of cases.

The ground glass appearance was the most frequent (63%). Our results are consistent with those of the literature, in particular the study by Harison et al [1, 2, 4], in which the ground-glass appearance was predominant with a frequency of 64.71%. However, the frequency of this appearance is much lower than the results found in the study by Alejandro Rey et al (87.5%) [17].

Non-specific biological examinations are of limited interest in the diagnosis of PCP, but some of them have prognostic value. In our study, no patient benefited from arterial gasometry due to the unavailability of this examination in the department.

An elevated level of lactic acid dehydrogenase (LDH) in the blood above 500 mg/dL has a good predictive value for PCP [28, 29], but this level is also elevated in many other fungal infections and in toxoplasmosis [25].

In our study, LDH was measured in 29 patients; it was elevated in 26 patients, i.e. 58%, and normal in 3 patients, i.e. 7%, with a mean level of 874.89 IU/L. Our results are in line with those of other studies and the literature [1, 8] .

The diagnosis of certainty requires the demonstration of PJ by the appropriate respiratory stains.

In our study, the diagnosis of PCP was confirmed in only 16 patients (35.5%) by the demonstration of PJ in sputum (13 cases) and in the lavage fluid Broncho Alveolar (3 cases).

In 29 patients (65.5%), the diagnosis of pneumocystis was presumptive, based on clinical, radiological, biological and therapeutic arguments related to a good response to specific treatments for pneumocystis.

The combination (TMP/SMX) or cotrimoxazole is currently the first-line reference treatment for pneumocystis, regardless of the form or terrain, despite its adverse effects [30]. Cotrimoxazole has excellent tissue penetration and a rapid clinical response with an efficacy of 80-85% [31]. The dose for oral loading therapy is 100 mg/kg SMX + 20 mg/kg TMP per day, in two to four divided doses, for 21 days in HIV-positive patients.

For intravenous infusion in the severely affected subject, the dose is 75 mg/kg SMX+ 15 mg/kg TMP per day, in four 60-minute intravenous infusions in 5% aqueous glucose solution [31,32].

In our study all patients were treated with the TMP/SMX combination.

Four patients received 2 tablets x 2 per day of cotrimoxazole.

One patient received 1 tablet x 3 per day of cotrimoxazole.

The duration of the initial treatment was 21 days.

The oral route was used in all treated patients.

Our results are in line with those of the ghizlane study and those of Harison[8,17] .

In severe forms of pneumocystis, the addition of corticosteroid therapy is indicated when the pO2 is less than 70 mm Hg[33,34].

Corticosteroid therapy has shown significant benefit on mortality rate, prevention of major hypoxia and fibrosis [35].

In our study, 11 patients received intravenous solumedrol corticosteroid therapy at a dose of 240mg/day from D1 to D3, 120mg/day from D4 to D6 and 60mg/day from D7 to D9 and 12 patients received oral prednisolone at a dose of 1mg/kg/D for a duration of 10 to 15 days.

These results are close to the data of other studies [4, 8, 17,18].

In HIV-positive patients, it is recommended to start primary prophylaxis as soon as the CD4 T-cell count is below 200/mm3 [36]. The efficacy of cotrimoxazole and its activity against pneumocystis and bacterial airway infections justify its use as first-line therapy [37].

In our study, 9 patients (20%) with a CD4 T-cell count below 200/mm3 had received primary prophylaxis with cotrimoxazole (one tablet per day). These data are consistent with those of Ghizlane's study, which showed that among 152 patients, 28 had received cotrimoxazole-based primary prophylaxis. These results are explained by the fact that PCP was indicative of HIV infection in the majority of cases.

After three weeks of well-conducted initial treatment, secondary prophylaxis should be initiated, preferably with the combination (TMP-SMX) or one of the other molecules mentioned above if (TMP-SMX) has been responsible for serious adverse events.

This prophylaxis can be interrupted when the CD4 lymphocyte count is higher than 200/mm3 for more than three months, thanks to the immune reconstitution under ARV[39, 40]. It should be reintroduced if the CD4 count falls below 200 cells/mm3 [30].

In our study, secondary prophylaxis with cotrimoxazole was initiated (1 tablet/day per os) in 26 patients (57.7%).

Five patients died during the acute treatment.

In our study, 24 patients responded favorably to treatment (53.3%). Eighteen died, i.e. 40%. Death was early, occurring during the attack treatment in 13 patients and 5 died during the maintenance treatment.

The evolution was unknown in three patients who were lost to follow-up (6.6%).

| | Total number of employees | Patients reported deceased | Patients declared cured | Patients lost to follow-up | Relapsed patients |
|---|---|---|---|---|---|
| mouttarazouk ; Casablanca [8] | 152 | 54 | 74 | 13 | 11 |
| Harison ; Madagscar [4] | 34 | 7 | 25 | 2 | 0 |
| Alejandro Rey et al ; Argentine [17] | 37 | 3 | 34 | 0 | 0 |
| Porto Alegre ; Brazil [9] | 57 | 5 | 52 | 0 | 0 |
| Our study | 45 | 18 | 24 | 03 | 0 |

**Table VI:-** Course of patients with pneumocystis in various studies.

## Conclusion:-

Pneumocystis is a serious infection in immunocompromised patients, especially PLWHA. In Morocco, it is still frequent during HIV infection and is one of the main causes of death. It should be considered in the presence of any febrile or non febrile dyspneic pneumonia, especially in any patient with immunodepression.

**Conflict of interest:**

All authors report no conflicts of interest.

## References:-

1- M. El Fane , M. Sodqi, A. Oulad Lahsen,A. Chakib, L. Marih, K. Marhoum El Filali. Pneumocystis during HIV infection. J.pneumo 2016 ;72(4) :248-254

2- Christine Katlama, Jade Ghosn, Gilles Wandeler. HIV, hepatitis and sexual health. AFRAVIH 2020

3- Adler D, Chenivesse C, Similowski T. Pneumocystis in the non-HIV immunosuppressed patient. Rev Med Suisse2008;4:2525-30.

4- Harisson et al. Case series | Volume 2, Article 9, 14 Jan 2020 | 10.11604/pamj-cm.2020.2.9.20809

5- Viboon Boonsarngsuk, Supinda Sirilak, Sumalee Kiatboonsri. Acute respiratory failure due to Pneumocystis pneumonia: outcome and prognostic factors. International Journal of Infectious Diseases. 2009; 13 (1): 59-66.

6- Su YS, Lu JJ, Perng CL, Chang FY. Pneumocystis jirovecii pneumonia in patients with and without human immunodeficiency virus infection. J Microbiol Immunol Infect. 2008 Dec; 41(6):478-482.

7- Nuesch R, Bellini C, Zimmerli W. Pneumocystis carinii pneumonia in human immunodeficiency virus (HIV)-positive and HIV-negative immunocompromised patients. Clin Infect Dis 1999; 29: 1519-1523

8- Thesis n 261 in 2015: Pulmonary pneumocystis in patients living with HIV. Experience of the service of Infectious Diseases of the CHU of Casablanca and study of Ghizlane Mouttarazouk.

9- Wissmann G, Alvarez-Martinez M J, Meshnick SR, Dihel ARS., Prolla JC. Absence de mutations de Dihydropteroate Synthas chez Pneumocystis jirovecii provenant de patients brésiliens atteints du SIDA. Journal of Eukaryotic Microbiology. 2006 ; 53 (4) : 305-307.

10- Lopez-Sanchez C, Falcó V, Burgos J, Navarro J, Martin MT, Curran A et al. Epidemiology and long-term survival in HIV-infected patients with Pneumocystis Jirovencii pneumonia in the HARRT Era. Revue médicale. 2015 mars;94(12):1-8. PubMed | Google Scholar
11- Sheikhaleslamii FM, Sadraei J, Farnia P, Forozandeh M, Emadi KH. Taux de pneumonie à Pneumocystis chez les Iraniens séropositifs et les patients présentant des infiltrats pulmonaires. Jundishapur J Microbiol. 2013 mars;6(3):295-300. Google Scholar.
12- . Mikaelsson L, Jacobson G, Andersson R. Pneumocystis pneumonia : a retrospective study 1991-2001 in Gothenburg, Sweden. J Infect. 2006 ; 53:260-265.
13- Demonty. Opportunistic infections of advanced immunodeficiency. RevMéd liège 1993; XL VIII: 83-90.
14- Glatt AE., Chirgwin K.: Pneumocystis carinii pneumonia in human immunodeficiency virus infected patients. Arch. Intern. Méd. 1990; 150: 271 – 279.
15-Touze J.E., Hovette Ph., Martet G. H. : Infection à Pneumocystis carinii. E.M.C. 1991; 8100: A10 : 1 – 7
16-46.. Karstaedt A. S., Grannum S. Pneumocystis carinii pneumonia in patients with AIDS in South Africa. Transactions of the Royal Society of Tropical Medicine and Hygiene, 2001; 95 (1): 40-41.
17-53.Revistachilena de infectología. Print version ISSN 0716-1018 Rev. chil. infectol. vol.32 no.2 Santiago Apr. 2015
18-Emerg Infect Dis. 2014 Sep; 20(9): 1490–1497. doi: 10.3201/eid2009.131668. Pneumocystis jirovecii Pneumonia in Patients with or without AIDS, France
19-Boiselle PM. Crans and CA, Kaplan MA. The changing face of Pneumocystis carinii pneumonia in AIDS patients. AJR Am J Roentgenol 1999; 172: 1301-1309.
20-Kuhlman JE. Pneumocystis infections: the radiologist's perspective. Radiology 1996;198:623-635.
21-Franquet T, Gimenez A, Hidalgo A. Imaging of opportunistic fungal infections in immunocompromised patient. Eur J Radiol 2004;51: 130-138.
22-Gruden JF, Huang L, Turner J.High-resolution CT in the evaluation of clinically suspected Pneumocystis carinii pneumonia in AIDS patients with normal, equivocal, or nonspecific radiographic findings. AJR Am J Roentgenol1997; 169: 967-975.
23- Lacombe C, Lewin M, Monnier-Cholley L, et al. Imaging of thoracic pathologies in HIV patients with AIDS. JRadiol2007;88:1145—54.
24-Kennedy CA, Goetz MB. Atypical roentgenographic manifes-tations of Pneumocystis carinii pneumonia. Arch Intern Med1992;152:1390—8.
25- Denis B, Lortholary O. Pulmonary fungal infectionsin HIV-positive patients. Rev Mal Respir2013;30:682-95.
26- De Castro N, Scemla A, Gallien S. Pneumocystisjirovecii pneumonia in HIV-infected patients. Rev Mal Respir2012;29:793-802.
27- Sokulska M, Kicia M, Wesołowska M, Hendrich AB. Pneumocystisjirovecii from a commensal to pathogen: clinical and diagnosticreview. Parasitol Res 2015;114:3577—85.
28-64. Torres J, et al. Diagnosis of Pneumocystis carinii pneumonia in human immunodeficiency virus-infected patients with polymerase chain reaction: a blinded comparison to standard methods. Clin infect Dis 2000;30:141—5.
29- .Demoule A. Severe respiratory infections. Rev Mal Respir2007;24:173-6.
30- Lacombe K., Girard P.-M. Treatment and prevention of opportunistic infections during HIV infection: update in 2004. Part 1: pneumocystis and protozoosis. Medicine and Infectious Diseases. 2004 ; 34 (60) : 239-245.
31- Stern JB, Parrot A, Cadranel J, Mayaud Ch. Pneumocystiscarinii infections: clinical. EncyclMédChir, Maladies infectieuses, 8-591-A-10, 1996.
32- WHO. WHO model information sheets for prescribers: Drugs used in Parasitology. 2nd edition. 1997; 160 pages
http://apps.who.int/medicinedocs/pdf/h2923f/h2923f.pdf, accessed May 6, 2010.
33-Thomas et al. 2004] Thomas CF Jr, Limper AH, M.D. Review article Medical progress Pneumocystis Pneumonia. N Engl J Med (2004) 350, 2487-2498
34-Consensus. (1990). "Consensus statement on the use of corticosteroids as adjunctive therapy for pneumocystis pneumonia in the acquired immunodeficiency syndrome. The National Institutes of Health-University of California Expert Panel for Corticosteroids as Adjunctive Therapy for Pneumocystis Pneumonia." N Engl J Med 323(21): 1500-4.
35-Briel, M., H. C. Bucher, et al. (2006). "Adjunctive corticosteroids for Pneumocystis jiroveci pneumonia in patients with HIV-infection." Cochrane Database Syst Rev 3: CD006150.
36-Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents (2013).

37-Kaplan, J. E., H. Masur, et al. (2002). "Guidelines for preventing opportunistic infections among HIV-infected persons--2002. Recommendations of the U.S. Public Health Service and the Infectious Diseases Society of America." MMWR Recomm Rep 51(RR-8): 1-52.
38- Roux A, Lemiale V, Kouatchet A, Vincent F, Bollee G, Roux P, Azoulay E. Pulmonary pneumocystis outside HIV infection. Réanimation (2010) 19, 327-338
39-De Quiros JCLB, Miro JM, Pena JM, et al. A Randomized Trial of the Discontinuation of Primary and Secondary Prophylaxis against Pneumocystis carinii Pneumonia after Highly Active Antiretroviral Therapy in Patients with HIV Infection. N Engl J Med 2001; 344(3): 159–167.
40-Ledergerber B, Mocroft A, Reiss P, et al. Discontinuation of Secondary Prophylaxis against Pneumocystis carinii Pneumonia in Patients with HIV Infection Who Have a Response to Antiretroviral Therapy.