

# *Febrile Syndrome in HIV positive patients*

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## ***Abstract***

*Fever is one of the accompanying symptoms of HIV, mainly in the advanced stages of the disease, but its occurrence is related to a number of factors such as CD4+ Lymphocyte level, accompanying opportunistic infections; causative microorganism*

*ect*<sup>1</sup>. Fever accompanies HIV from the initial stage of the “acute retroviral syndrome” infection and during the evolution of the pathology towards the AIDS stage, even in IRIS. Fever-related opportunistic infections are divided into two groups by infectious or non-infectious causes<sup>3,4</sup>. In our study, we included 355 HIV-positive cases who had febrile episodes in different stages of immunodeficiency. In the HIV stage (to which we referred lymphocytes CD4+ over 500 cells/mm<sup>3</sup>, and without AIDS-related opportunistic infections) there were 39 cases. In the AIDS stage, there were 143 cases with a CD4 + level of 200-400 cells/mm<sup>3</sup>: pulmonary manifestations 85 cases, gastrointestinal 58 cases. With a level of CD4+ lymphocytes below 200 cells/mm<sup>3</sup> 123 cases; pulmonary involvement 45 cases, intestinal 32 cases, CNS 11cases, hematological.13 cases, disseminated 15 cases, FUO 7 cases. With CD4+ level below 50 cells mm<sup>3</sup>, 50 cases: non-Hodgkin’s lymphoma 9 cases. MAC 3cases, TBC.19 cases, CNS lymphoma. 6 cases, retinal CMV 3 cases, Kaposi’s sarcoma 10 cases.

**Keywords:** FUO; HIV; AIDS

## Introduction

Fever is one of the common symptoms manifested by HIV patients in different stages of the disease<sup>1</sup>. From the primary infection “acute retroviral syndrome” which is manifested by a subfebrile condition, lymphadenopathy, and pharyngitis similar to mononucleosis. In the evolution of the pathology towards the AIDS stage as a result of the progressive decrease in CD4+, fever is related to the appearance of opportunistic infections. In 80% of cases it is identifiable and in 20% of it may remain FUO<sup>2,3</sup>. According to the CDC, patients with HIV infection are classified in 3 stages based on the level of CD4 lymphocytes<sup>4</sup>. Lymphocytes above 500 cells/mm<sup>3</sup>, between 200 – 500cells / mm<sup>3</sup> and below 200 cells / mm 35 cases.

This division provides a useful, though not perfect, framework for evaluating fever in the HIV-infected patient in each of these categories. In HIV + cases with CD4+ Lymphocytes over than 500 cells/mm<sup>3</sup>, they should be evaluated for febrile syndrome like immunocompetent subjects. In the stage of advanced immunosuppression, fever is increasingly common<sup>4</sup>. With the progressive decline of the CD4+ count, the frequency and variety of infectious complications also increases. In this area, in the differential diagnosis of fever, opportunistic infections such as pneumocystosis, CMV, toxoplasmosis, disseminated MAC, histoplasmosis and disseminates coccidiomycosis and cryptococcal meningitis should be considered<sup>6,7,8</sup>.

## AIM

Evidence of febrile syndrome, one of the companions of acquired immunodeficiency in its initial stage and up to progressively severe ones, even in a paradoxical form during immune reconstitution IRIS.

## Method

The study is a retrospective analytical type. 355 HIV-positive cases, registered in the HIV/AIDS outpatient clinic of the Infectious Service from 2013 to 2018, were analyzed, which manifested fever in different stages of immunodeficiency. We analyzed demographic data such as gender and age; Staging according to the level of CD4+ lymphocytes at the time of the febrile syndrome; Sorting by systems affected and type of opportunism associated with fever.

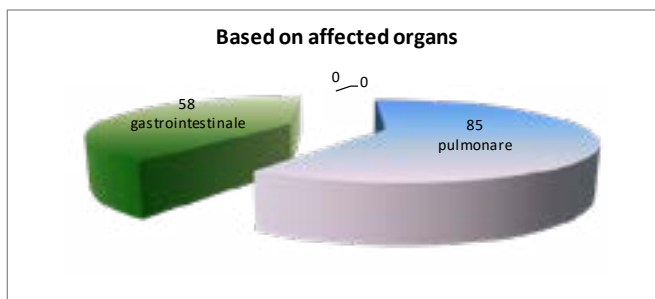
## Results

I Based on gender, 215 were men and 140 were women. Regarding distribution according to age group: 20-30 years old - 56 cases, 31-40 years old - 77 cases, 41-50 years old - 113 cases, 51-60 years old - 65 cases; 61 – 70 years old - 29 cases, over 70 years old - 5 cases.

I.1 In the stage of HIV infection (to which we referred CD4+ lymphocytes over 500 cells/mm<sup>3</sup>, and without AIDS-related opportunistic infections) there were 45 cases.

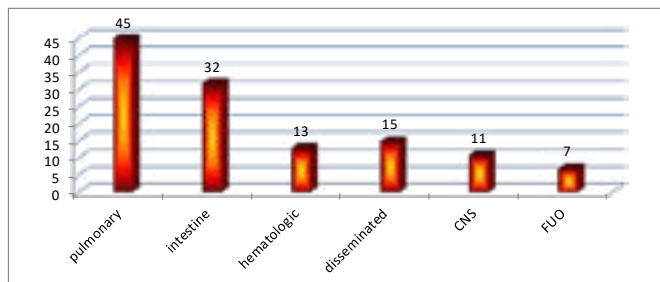
I.2 In the AIDS stage with the level of CD4+ 200-500 cell/mm<sup>3</sup> there were 143 cases; pulmonary manifestations 85 cases, gastrointestinal 58 cases.

**FIG. 1:** Affected systems in the AIDS stage with CD4+ level between 200 – 500 cell/mm<sup>3</sup>



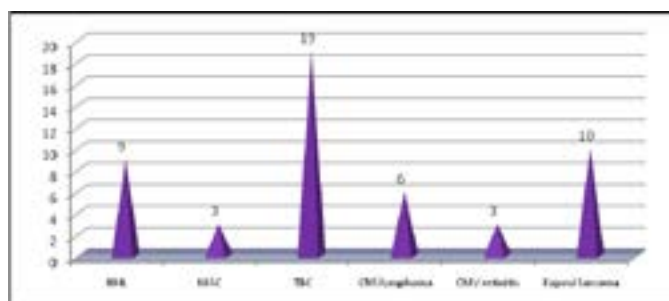
**II.3** The level of CD4+ lymphocytes < 200 cells/mm<sup>3</sup> 123 cases; pulmonary involvement 45 cases, intestinal 32 cases, CNS 11 cases, hematological. 13 cases, disseminated 15 cases, FUO 7 cases.

**FIG. 2:** Affected systems in the AIDS stage with CD4+ below 200 cells/mm<sup>3</sup>



**1.4:** The level of CD4+ < 50 cells mm<sup>3</sup>, 50 cases: non-Hodgkin lymphoma 9 cases. MAC 3 cases, TBC.19cases, CNS lymphoma. 6cases, retinal CMV 3 cases, Kaposi's sarcoma 10cases.

**FIG. 3:** Opportunistic infections with CD4+ below 50 cells/mm<sup>3</sup>



## Discussions

Fever-related opportunistic infections are divided into infectious and non-infectious causes. Infectious agents are: Pulmonary (PCP, TBC, MAC, Aspergillosis, CMV)<sup>6,7,8,9</sup>; Gastrointestinal (Clostridium difficile, Cryptosporidium parvum, microsporidia, Shigella species, Campylobacter jejuni, with Candida, HSV and CMV)<sup>10</sup>; Neurological (Toxoplasma gondii, Cryptococcus neoformans, cryptococcal meningitis, tubercular meningitis)<sup>11,12</sup>; Multisystemic pathology (visceral leishmania, disseminated CMV, disseminated MAC, extrapulmonary TB)<sup>13</sup>.

Fever from non-infectious agents: Drug reactions - Possible explanations for the mechanism of drug hypersensitivity reactions in HIV-positive subjects

include an increase in the use of provocative drugs, an increase in the incidence of viral infections and immune disorders<sup>17</sup>. Rheumatological pathology associated with HIV-1 infection, especially Reiter's syndrome, psoriatic arthritis, Sjogren's syndrome, polymyositis, rheumatoid arthritis, Morbus Still and vasculitis<sup>20,21</sup>. This association is not yet known. Malignancies - non-Hodgkin's lymphoma, primary CNS lymphomas, and rarely Kaposi's Sarcoma. Thrombophlebitis is found in HIV-infected individuals, which is thought to be due to hypercoagulant states and predisposing factors such as immobility<sup>15,16</sup>. Fever can manifest as IRIS - systemic inflammatory response against infection, which is triggered during immune restoration, the clinical syndrome is characterized by lymphadenopathy, fever, leukocytosis and pathology that occur soon after the start of HAART and mainly in patients with CD4 < 100 cells/mm<sup>3</sup>. This immunological phenomenon is associated with infections MAC and M. tuberculosis manifesting as localized lymphadenitis<sup>20,21</sup>. CMV manifesting as acute intraocular infection, hepatitis B and C manifesting as an outbreak of acute hepatitis, herpes simplex manifesting as extreme herpetic lesions that may be hemorrhagic<sup>22,23,24</sup>.

## Conclusions

Fever continues to be a common symptom among HIV+ patients at all stages of disease progression. While antiretroviral regimens and IO prophylaxis have a significant impact on overall survival, they have also added a layer of complexity to the approach to fever in this category through IRIS. The level of T-CD4 + cells can be used as a rough, although not perfect, guide to the assessment of fever. Patients with CD4 + T-cell counts greater than 500 / mm<sup>3</sup> and between 200 & 500 / mm<sup>3</sup> are more prone to M. tuberculosis and pulmonary bacterial infections. Evaluation of fever in patients with CD4 + T-cell counts less than 200/mm<sup>3</sup> is more challenging because the differential diagnosis is greater and the specificity of many presentations is lost. (Atypical mycobacteria, M. tuberculosis, Pneumocystis carini, lymphoma, in areas of endemicity, leishmaniasis) Despite the polymorphism of possible etiologies, the source of fever can be identified in most patients. A thorough diagnostic evaluation should be followed in all cases.

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