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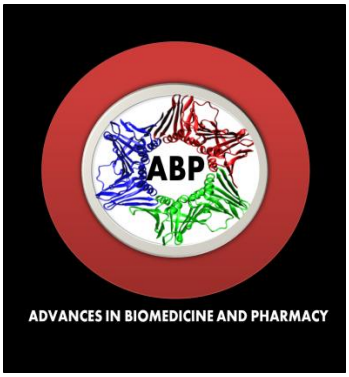


**Original Paper**

# Cause of fevers and diagnostic strategies among the HIV patients hospitalized in the regional hospital of Comè (Southern Benin): A national study.

**Agbodandé KA[1,5], Attinsounon CA[2], Wanvoegbe FA[3], Azon- Kouanou A[1], Kpossou AR[4], Zannou DM[1], Houngbe F[1].**

[1] Department of Internal Medicine, National Teaching Hospital "CNHU-HKM" of Cotonou, Benin, Nigeria.

[2]Department of Internal Medicine, Departmental Hospital of Parakou, Benin, Nigeria.

[3]Department of Internal Medicine, Departmental Hospital of Porto-Novo, Benin, Nigeria.

[4]Department of Hepato-Gastroenterology, National Teaching Hospital "CNHU-HKM" of Cotonou, Benin, Nigeria.

[5]Regional hospital of Comè. Nigeria.

*Corresponding Author: Anthelme Kouessi Agbodande

Assistant Head of Internal Medicine, National Teaching Hospital "CNHU-HKM" of Cotonou, Benin, Nigeria.

E-mail address: agbotem@yahoo.fr

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## Abstract

Over the past decade, considerable progress has been achieved in expanding the access towards antiretroviral therapy (ART) in developing countries against AIDS, however Sub-Saharan Africa continues to record the highest number of deaths related to HIV. A cross-sectional, descriptive and analytical study was conducted in the department of polyvalent medicine of the first referral hospital of Comè over a two-year-period, from 1st January 2012 to 31st December 2013 to determine the cause of fever among the HIV patients. A total of 87 HIV infected patients were hospitalized during the study period. Among them, there were 60 cases of fever (69.0%). The mean age was 39.4 ± 11.3 years old and the sex ratio (M / F) was 0.94. Acute fever was recorded in 41.7% of cases and long term fever in 58.3% of cases. Infectious diseases like diarrhoea, pneumonia, oro-pharyngeal candidiasis, tuberculosis and cerebral toxoplasmosis were the main causes of fever in hospitalized HIV patients (96.3%).

**Keywords:** HIV, fever, AIDS, ART, Immune deficiency diseases, Benin

## Introduction

Over the past decade, considerable progress has been achieved in expanding the access to antiretroviral therapy (ART) in developing countries. The number of people on ART in these countries increased from 300 000 in December 2003 to more than 9.7 million in 2014 [1]. Despite these advances, Sub-Saharan Africa continues to record the highest number of deaths related to HIV. In 2013, there were 1.1 million AIDS-related deaths over 1.5 million worldwide [2]. Immune deficiency caused by HIV increases the risk of developing opportunistic infections, which are the main causes of death in these patients [3-5]. In the context of limited resources, the diagnosis of opportunistic infections in people with HIV is often very difficult [6]. In most cases, caregivers rely on clinical arguments to treat patients and are sometimes, unable to do paraclinical investigations for etiologic diagnosis. Keeping in view the need this study was designed and conducted with a main aim to pinpoint the various opportunistic diseases that are not diagnosed in HIV infected patients, and were the fever was considered as the main reason of hospitalization.

## Patients and Methods

A cross-sectional, descriptive and analytical study was conducted in the department of polyvalent medicine of the first referral hospital of Comè over a two-year-period, from 1st January 2012 to 31st December 2013

Patients with HIV were admitted to the ward for consultation or hospitalization due to the main reason of fever.

The dependent variable was the fever. The associated variables were socio-demographic data, clinical data particularly the characteristics of the fever, the etiologies of fever, treatment data and evolutionary aspects. Fever was defined as any temperature above or equal to 38 ° C. Fever is said to be a long-term if it is evolving for at least 21 days. The etiology of the disease pathology is selected at the end of hospitalization as the most likely to cause fever.

Diagnoses were set on the basis of clinical findings associated with certain para-clinical examinations chosen in terms of the diagnostic orientation and financial possibilities of patients. In some cases, the diagnosis is applied only to satisfactory therapeutic test.

### Statistical analysis

The data collected from medical records of patients were entered and analyzed using SPSS 18.0 software. The qualitative variables were expressed as percentages and the quantitative variables as average combined with a standard deviation. The Chi-square test was used to compare percentages. The differences were considered statistically significant with a $p$ value <0.05.

## Results

### Epidemiological, clinical, immunological and virological data

Among the 652 patients admitted during the study period, 87 patients were HIV positive which indicates a prevalence of 13.3%. Among these, sixty patients (69.0%) had either an acute fever (41.7%) or a long-term fever (58.3%). The sex ratio (M / F) was 0.94. The mean age was 39.4 ± 11.3. Regarding the demographic information majority of patients (89.0%) came from the municipality of Comè and its neighbouring villages.

Clinically, the majority of symptoms associated with fever were general impaired conditions (GIC), asthenia and weight loss (Table 1).

Immunologically, the average of CD4 count made during the hospitalization was 160.17 ± 205.79 cells / L. In 61.1% of cases, the CD4 count was lower than 100 cells / L and 27.8% of patients had a CD4 count between 100 and 350 cells / L.

Virologically, HIV1 was prevalent in 100% of cases and very few cases 1.8% were having HIV 1 + 2 dual profile.

Regarding antiretroviral treatment, 67.2% of patients were on ART and 78.6% on chemo-prophylaxis Cotrimoxazole before admission.

### Main causes of fevers and means of diagnosis

It was observed that infectious diseases are the main causes of fever among the hospitalized HIV patients (95.4%) (Table II). The most frequently diagnosed infectious pathologies were infectious diarrhoea (28.1%), bacterial pneumonia (13.5%), gastrointestinal candidiasis (12.5%), tuberculosis (11.5%) and cerebral toxoplasmosis (7.3%).

Tuberculosis was the most common causes of fever in the long term fevers with a significant statistical difference ($p$ <0.05). In addition four cases of malaria were found in patients with severe fever (Table III).

CD4 count was available in seventy-three pathologies. In most cases (86.3%), the pathologies occurred for CD4 values lower than 200 cells /L (Table IV).

Regarding diagnostics strategies, the diagnostic tests have been done with diagnosis certainty in 14.1% of cases. Diagnosis were mostly made following clinical arguments (syndromic) or conclusive therapeutic test (Table V).

### Evolution during hospitalization

The average stay of hospitalized patients was 11.2 ± 13.4 days. The outcome was unfavourable in twelve cases with a mortality rate of 20.7%. Out of these 20.7% cases the major cause of death was due to following infections, five cases of diarrheal disease, three cases of tuberculosis (two cases of pulmonary tuberculosis and one case of neuro-meningeal tuberculosis), two cases of cerebral toxoplasmosis, one case of pneumocystosis and one of pneumonia.

**Table 1**: Symptoms associated with fever in 60 patients with HIV hospitalized in the polyvalent unit of medicine in the Hospital of Comè from the 1st January, 2012 to 31st December 2013.

| | Acute fever | Long term fever | Total | OR (IC 95%) | p |
|---|---|---|---|---|---|
| **GIC*** | 19 | 32 | 51 | 3,4 (0,8-15,1) | 0,145 |
| **Asthenia** | 22 | 25 | 47 | 0,3 (0,1-1,4) | 0,204 |
| **Weight loss** | 4 | 24 | 28 | 186 (19,5-774) | 0,000 |
| **Anorexia** | 2 | 13 | 15 | 6,8 (1,4-33,6) | 0,015 |
| **Coughing** | 4 | 12 | 16 | 2,7 (0,8 – 9,8) | 0,146 |
| **Diarrhoea** | 6 | 10 | 16 | 1,3 (0,4-4,1) | 0,773 |
| **Vomiting** | 4 | 7 | 10 | 1,3 (0,3-5,1) | 0,748 |
| **Colic** | 2 | 4 | 6 | 1,5 (0,3-8,8) | 0,508 |
| **Dyspnoea** | 2 | 4 | 6 | 1,5 (0,3-8,8) | 0,508 |
| **Dysphagia** | 2 | 3 | 5 | 1,1 (0,2-7,0) | 0,659 |
| **Convulsion** | 1 | 2 | 3 | 1,5 (0,1-17,0) | 0,626 |
| **Headache** | 2 | 1 | 3 | 0,3 (0,0-4,0) | 0,565 |

*GIC: general impaired conditions

**Table 2:** Distribution of cases of fevers as nosological groups of diseases in ICD 10

| Nosological groups * | Acute fever (%) | long term fever (%) | Total (%) | p |
|---|---|---|---|---|
| **infectious and parasitary causes and** | 29 (96,7) | 50 (96,2) | 79 (96,3) | 0,698 |
| **Tumours** | 0 | 1 (1,9) | 1 (1,2) | 0,600 |
| **Morbid and poorly defined states** | 1 (3,3) | 1 (1,9) | 2 (2,5) | 0,634 |
| **Total** | 30 (100,0) | 52 (100,0) | 82 (100,0) | |

* A patient may present several pathologies

**Table 3:** Distribution of infectious etiologies according to the fever duration in HIV infected patients hospitalized for fever in the polyvalent medical unit of the Hospital of Comè from 1st January 2012 to 31 December 2013.

| Disorders* | | Acute Fever | Long term fever | Total (%) | p |
|---|---|---|---|---|---|
| **Diarrhoeal diseases** | | 11 | 16 | 27 (28,1) | 0,586 |
| **Pneumonia** | | 6 | 7 | 13 (13,5) | 0 ,438 |
| **Digestive candidiasis** | | 5 | 7 | 12 (12,5) | 0,694 |
| **Tuberculosis** | | 1 | 10 | 11 (11,5) | 0,038 |
| **Site of tuberculosis** | Pulmonary | 1 | 10 | 11 (11,5) | 0,038 |
| | Pleural | 0 | 2 | 2 (2,1) | 0,530 |
| | Neuro-meningeal | 0 | 2 | 2 (2,1) | 0,530 |
| | Miliary | 0 | 1 | 1 (1,0) | 0,634 |
| | ganglionic | 0 | 1 | 1 (1,0) | 0,634 |
| **Cerebral toxoplasmosis** | | 2 | 5 | 7 (7,3) | 0,493 |
| **Malaria Grave** | hyperparasitemia | 3 | 0 | 3 (3,1) | 0,046 |
| | Anaemia | 1 | 0 | 1 (1,0) | 0,366 |
| **Cryptococcus** | | 0 | 2 | 2 (2,1) | 0,530 |
| **Pneumocystis** | | 0 | 2 | 2 (2,1) | 0,530 |
| **Pyelonephritis** | | 0 | 1 | 1 (1,0) | 0,634 |
| **Total** | | 30 | 66 | 96 (100) | |

* A patient may present several pathologies

**Table 4:** Distribution of etiologies based on the number of CD4 T cells in HIV patients hospitalized for fever in the polyvalent medicine unit the Hospital of Comè from 1st January 2012 to 31st December 2013.

| | CD4 | | | | Total |
|---|---|---|---|---|---|
| | ≤100 | 100-200 | 200-350 | >350 | |
| **Candidiasis** | 9 | 2 | 0 | 0 | 11 |
| **Infectious pneumonitis** | 9 | 0 | 1 | 0 | 10 |
| **Diarrhoeas** | 11 | 7 | 2 | 7 | 27 |
| **TB** | 10 | 1 | 0 | 0 | 11 |
| **Cerebral toxoplasmosis** | 1 | 5 | 0 | 0 | 6 |
| **Malaria** | 2 | 1 | 0 | 0 | 3 |
| **Cryptococcocci** | 2 | 0 | 0 | 0 | 2 |
| **Pneumocystosis** | 2 | 0 | 0 | 0 | 2 |
| **KS** | 1 | 0 | 0 | 0 | 1 |
| **Total** | 47 | 16 | 3 | 7 | 73 |

**Table 5:** Key means diagnosis of etiologies of fever in patients infected with HIV and hospitalized for fever in the polyvalent medicine unit of the Hospital of Comè from 1st January 2012 to 31st December 2013.

| Etiologies of fevers | | Diagnostic means | | | Total |
|---|---|---|---|---|---|
| | | Clinic | Paraclinic | Therapeutic exam | |
| **Diarrhoeas** | | 25 | $2^{\alpha}$ | | **27** |
| **Pneumonia with benign germs** | | | | 13 | **13** |
| **Digestive Candidiasis** | | 12 | | | **12** |
| **TB** | Pulmonary | | $2^{\beta}$ | 9 | **11** |
| | Pleural | | | 2 | **2** |
| | Neuro-meningeal | | | 2 | **2** |
| | Miliary | | | 1 | **1** |
| | Ganglionic | | $1^{\gamma}$ | | **1** |
| **Cerebral toxoplasmosis** | | | | 7 | **7** |
| **Malaria Severe** | hyperparasitemia | | $3^{\delta}$ | | **3** |
| | Anaemia | | $1^{\delta}$ | | **1** |
| **Cryptococcosis** | | | $2^{\varepsilon}$ | | **2** |
| **Pneumocystosis** | | 2 | | | **2** |
| **Pyelonephritis** | | | $1^{\zeta}$ | | **1** |
| **Total (%)** | | **39 (45,9)** | **12 (14,1)** | **34 (40,0)** | **85 (100)** |

α Widal and Felix Serodiagnosis for a typhoid fever
β presence of tubercle bacilli in the sputum
γ Presence of Koch bacillus in the lymph liquid
δ presence of Plasmodium falciparum in the blood smear
ε Review the ink CSF: presence of Cryptococcus neoformans
ζ Review cytobacteriological of identifying Escherichia coli urine

## Discussion

Immune deficiency caused by HIV increases the risk of developing opportunistic infections, which are the main causes of death in these patients [3-5]. The main opportunistic infections diagnosed among the patient in the current study were comparable to those identified in most studies of the sub region [5, 7-9]. In all these studies, a general pattern of similar proportions of infectious diarrhoea, bacterial pneumonia, gastrointestinal candidiasis, tuberculosis, cerebral toxoplasmosis and neuro-meningeal cryptococcosis was found as the main cause of fever among the HIV patients.

We have observed that these conditions are compatible with the immune status of patients. Indeed, in 86.6% of cases, opportunistic infections have occurred in severely immunosuppressed patients (CD4 <200 cells / L) with 64.4% in the group of patients with a CD4 number below 100 cells / L. In the latter group it has appeared that almost all cases are of neuro-meningeal cryptococcosis, pneumocystosis, of tuberculosis (including six cases of extra-pulmonary locations) of oropharyngeal candidiasis and chronic diarrhoea.

So, we notice that despite the WHO recommendations in relation to the early initiation of ART [10] and the implementation effort of these recommendations in our respective countries, the belated recourse to medical care remains the main factor limiting the early initiation of ART, which exposes patients to the most severe opportunistic infections. Studies regardingetiologies of fever have reported the, a predominance of bacteraemia [11], of sepsis, of pneumocystosis [12], Cytomegalovirus

infections [13] and cases of HSV infections [14]. The difference between these studies and ours lies more in the impossibility for us to diagnose these diseases in our context than the actual scarcity of the latter. This is certainly the same for neoplastic conditions under-diagnosed in our study. Indeed, we were only able to diagnose a case of Kaposi's sarcoma. However authors have shown the incidence of cancer in people with HIV as well as their high lethality due to sarcoma disease, Hodgkin's lymphoma and non-Hodgkin's lymphoma, lung cancer and like [13, 15-17].

As far as infectious diarrhoea was concerned studies have shown Cryptosporidium parvum and Isospora belli are among the digestive opportunistic infections [18-20].

Furthermore, it is important to highlight the low prevalence of malaria (4.2%) in the etiology of acute fever. So, the diagnosis of malaria was made only in four patients on the basis of thick blood. The latest WHO recommendations on the management of malaria require test (confirmation of cases) before processing [21]. This strategy would reduce misdiagnosis especially in areas of high endemicity and malaria will undoubtedly improve the quality of care for patients [22].The low prevalence of malaria in people with HIV may also be due to the protective effect of chemoprophylaxis in Cotrimozaxole noted by several authors [23-25].As shown in Table V, diagnostic means are very limited. Most of the diagnosis were based on clinical arguments which guarantee neither a diagnostic certainty nor assurance on the quality of care. The second most used method is the therapeutic test. Often, this practice unnecessarily exposes the patient to heavy therapies for more or less long periods. Indeed, depending on the severity of the clinical picture, it is often worth starting multiple therapies aiming to the most likely opportunistic infections. The difficulty is the impossibility to stop either a treatment or the other one without knowing which led to the favourable evolution of the patient. In this context limited resources, the successful treatment or cure of the patient is much more dependent on the skill and experience of the practitioner than the technical platform. The death rate (20.7%) registered in this study may be encouraging for the clinician because of the working conditions, but still remains high. It is therefore necessary to improve the technical platform and subsidize some further tests to facilitate their access to patients, who mostly live below the poverty line.

## Conclusion

This study shows not only the importance of increasing access to antiretroviral treatment to ensure the immune restoration but also the prominence to keep HIV patients from opportunistic infections. On the other hand it depicts the need to improve the technical platform and to facilitate access to modern means of diagnosis in order to ensure proper management of patients through accurate diagnosis and proper treatment which will reduce mortality rate in these patients considerably.

## Conflict of interest

The authors declare that there is no conflict of interest to reveal.

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