ABSTRACT

Objective: The objective of this study is to determine the prevalence of immunological failure at six months of antiretroviral therapy in people living with HIV and to identify associated factors.

Patient and Method: A descriptive and analytical cross-sectional study covering the period from March to September 2017, including all types of PLWAs who had been under highly active antiretroviral therapy for at least six months and gave their informed consent freely.

Results: A total of 325 female patients (n = 249, 76.6%) with an average age of 42 ± 44 years, unemployed (n = 70, 21.5%), low socio-economic status (n = 261, 80.3%), single in 33.8% (n = 110). Patients were in WHO stage IV in 15.4% of cases (n = 50). The average initial CD4 was 235 ± 178.95 cells / mm3. Chronic diarrhoea was the most common opportunistic infection in 98.15% of cases. The most commonly used protocol was TDF + FTC + EFV with 215 patients (66.2%). This average CD4 at six months was 160.02 ± 121.44 cells / mm3, and immunologic failure was reported in 231 patients (71.1%). The occupation (P = 0.001), basic WHO stage (P < 0.001), the duration of serologic status (P = 0.001), tuberculosis (P = 0.001) were statistically significant with the occurrence of failure and there was a correlation between the initial CD4 rate and that at 6 months.

Conclusion: Our study demonstrates that the prevalence of immunologic failure remains high in relation to low socioeconomic status, screening and late management of HIV infection in addition to opportunistic infection.

Keywords
Prevalence, Immunological failure, Brazzaville, Associated factors.

Introduction
The advent of highly active antiretroviral triple therapy has positively changed the natural history of HIV infection by significantly improving the quality of life and increasing the life expectancy of patients living with HIV (PLWHIV). This has been reported in several series and COHERE cohort data which show that the life expectancy of patients with CD4 < 500 / mm³ lymphocyte number for more than 3 years is similar to that of the general population [1-3]. However, immuno-virological responses may vary from one individual to another. They can result in immuno-virological success or failure or immuno-virological discordance (IVD). In Europe and North America, 10 to 27% of immunological nonresponse and 1 to 25% of poor virological response were reported in 2009 [4]. In Africa, as in Burkina Faso, immunological failure varied between 7 and 27% according to series between 2007 and 2012 [5]. The occurrence of immunologic failure in patients under antiretroviral therapy is due...
to many factors. This case is more likely to occur in patients who initially have low pre-therapy CD4 cell number and at an advanced age. This failure may be accompanied by virological success or failure [6]. In the Congo, few studies provide information on the prevalence of immunological failure in well-treated patients, hence the present work, whose main objective is to determine the prevalence of immunological failure and to investigate the factors involved driving data from patients living with HIV under highly active triple antiretroviral therapy.

Patients and Method

Type, period and setting
This study is a cross-sectional, descriptive, analytical and covers the period from March 1 to September 30, 2017, at the infectious diseases department of the University Hospital Centre of Brazzaville.

Target population
This study targets patients at least 17 years of age, immunocompromised by any type of HIV, pre-hospitalized or in-hospital, in the active service queue, under highly active antiretroviral therapy for at least six months and benefiting from the inclusion of basic TCD4 and then at six months.

Study variables
The study variables were epidemiological (age, sex, occupation, marital status, socio-economic level) clinical (stage of evolution of the disease, the type of opportunistic infection, the time of discovery of HIV infection, and the duration of serologic status), paraclinical (CD4 cell numbering at initiation of treatment and six months after, other co-morbidities) therapeutic (ARV initiation time and antiretroviral molecule type) used) and evolving (the notion of failure, relapse, or death).

Operational definitions [3]
- The immunological failure was defined by the absence of ascension of CD4 lymphocytes despite effective antiretroviral therapy for at least 6 months.
- The socio-economic level was considered low in the presence of one of the following items: foreigner in an irregular situation, no access to water and electricity, monthly income below 300,000 FCFA, no profession.

Statistical Analysis
Data entry was done on CSPRO 6.1 software, tabulation on Excel (Microsoft®), and processing and analysis of results on SPSS 17 software (IBM®). Qualitative variables were expressed in terms of numbers (n) and percentage (%); quantitative variables on average (X) plus or minus (±), standard deviation (s-t) and extremes. We resorted to a bi-varied analysis with calculation of odds ratio (OR) with 95% confidence interval (CI) to determine the factors associated with immunological failure. Similarly, we used a logistic regression analysis to identify the impact of these factors. A CD4 correlation curve at baseline and at 6 months was constructed. We also apply student's t test to compare the initial CD4 number against the 6-month CD4 number. The threshold of significance was set at <0.05.

Results
A total of 325 retained patients with an average age of 42 ± 11 years amongst whom female (n = 249; 76.6%), male (n = 76, 23.4%) with a sex ratio F / H of 3.27. Traders represented 29.5% (n=96) followed by unemployed (n = 70, 21.5%). The socioeconomic level was considered low in 80.3% (n = 261), medium (n = 59, 18.2%), high (n = 5, 1.5%) and 110 patients were singles (33.8%). Married men accounted for 16.9% (n = 55). Patients had a primary level of study in 51 cases (15.7%) and were classified in WHO stage III in 136 cases (41.8%) and stage IV (n = 50, 15.4%). We found undernutrition in 96 patients (29.5%). Tuberculosis was the most common opportunistic infection in 13.54% (n = 44) and chronic diarrhoea probably related to coccidiosis (n = 59, 18.15%). The average duration of serologic status before management was 13.11 ± 6.4 months (range: 6-24 months). The average number of initial CD4 was 235.42 ± 178.95 / mm³ (extreme: 1-995 cells / mm³); 88 patients (27.1%) had CD4< 100 / mm³ number at initiation of ART and 65 patients (20%) had CD4 between 100 and 200 cells / mm³. The protocol combining TDF + FTC + EFV was the most prescribed in 215 patients (66.2%) followed by AZT + 3TC + NVP (n = 62, 19.1%). In 309 patients (95.1%). Chemoprophylaxis with cotrimoxazole was administered. Immunological failure was found in 231 patients (71.1%) with an average CD4 count of 160 ± 121.44 cells / mm³. There was a correlation between basic CD4 and six months of triple antiretroviral therapy (Figure 1).

Table 1: Predictive factors immunologic failure.

Patients' age, occupation, low socio-economic status, duration of HIV status, WHO stage, tuberculosis are amongst factors which had influenced the occurrence of immunologic failure in patients (Table 1). Other factors associated with immunologic failure in patients were the duration of HIV infection before management, marriage and prophylaxis of opportunistic infections (Table 2).
The present study carried out in a resource-limited country with the difficulties of regular supply of antiretroviral molecules, limitations in the planning of regular monitoring of PLWHIV, and the weakness of the technical platform in the early diagnostic of opportunistic infections in patients starting late the management of their disease partly justifies the high rate of immunological failure compared to other African series [5,7,8]. In addition, many patients were under therapeutic regimens with hematotoxic drugs such as Zidovudine (AZT) and almost all patients were under long-term co-trimoxazole prophylaxis, which may contribute to the maintenance of persistence. CD4 lymphopenia observed in most patients [9].

The patients are still young, sexually active and predominantly female patients are mostly affected by this situation of immunological failure as reported elsewhere [7]. The difficulties of sharing the serological status, the fear of being rejected by the other, explain the frequency of the failure observed by the therapeutic nonobservance in the patients living in serodiscordant couple. Some authors, sharing the same observation, point out that these cases of failure are met with both single persons and married couples. The daily occupations of shopkeepers who spend most of their time in gainful activities may justify the reasons for nonobservance or even therapeutic interruption leading to failure in this category of population. These data corroborate those obtained at the subregion level by some African authors [10,11].

Many of our patients with immunologic failure were malnourished at the beginning of antiretroviral therapy and some had already developed pre-therapeutic opportunistic infections such as chronic diarrhoea probably related to coccidiosis and tuberculosis. These pathologies thus influence the absorption of the molecules on the one hand and the immune restoration on the other hand [6].

The delay in the therapeutic management of patients after finding the serological status was long. These long delays in patient care are typical in sub-Saharan Africa, in relation to the denial of the disease, poverty and difficulties in accessing health services [7,12].

The majority of patients were under antiretroviral therapy with the combination of triple TDF / FTC + EFV, which is well-known and now widely used combination in most countries, especially those with limited resources as reviewed and confirmed by some authors [13]. It should also be noted that in the context of advanced immunosuppression before starting antiretroviral treatment, in some patients, the rise of CD4 lymphocytes is slow, particularly in patients who have had a very low CD4 count; which may lead to

### Table 1: Predictive factors immunologic failure.

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>β</th>
<th>OR</th>
<th>IC 95%</th>
<th>P</th>
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<td>6,579</td>
<td>719,659</td>
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<td>0,00</td>
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<tr>
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<td>0,013</td>
<td>0,00</td>
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<tr>
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<td>297,111</td>
<td>9,21</td>
<td>-9579,68</td>
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<tr>
<td>≥400</td>
<td>2,694</td>
<td>14,792</td>
<td>1,51</td>
<td>-144,55</td>
</tr>
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</table>

### Table 2: Immunological failure at 6 months for triple antiretroviral therapy and associated factors.

### Discussion

The present study carried out in a resource-limited country with the difficulties of regular supply of antiretroviral molecules, limitations in the planning of regular monitoring of PLWHIV, and the weakness of the technical platform in the early diagnostic of opportunistic infections in patients starting late the management of their disease partly justifies the high rate of immunological failure compared to other African series [5,7,8]. In addition, many patients were under therapeutic regimens with hematotoxic drugs such as Zidovudine (AZT) and almost all patients were under long-term co-trimoxazole prophylaxis, which may contribute to the maintenance of persistence. CD4 lymphopenia observed in most patients [9].

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The majority of patients were under antiretroviral therapy with the combination of triple TDF / FTC + EFV, which is well-known and now widely used combination in most countries, especially those with limited resources as reviewed and confirmed by some authors [13]. It should also be noted that in the context of advanced immunosuppression before starting antiretroviral treatment, in some patients, the rise of CD4 lymphocytes is slow, particularly in patients who have had a very low CD4 count; which may lead to
mistaken thinking about immunological failure [14].

There is also a correlation between the initial CD4 level and six months of triple antiretroviral therapy. Indeed, the situation of immunological failure is more likely to occur in patients who initially have a lower pre-therapeutic CD4 lymphocyte level, a more advanced age. These results corroborate those found out by several authors [3,7,10]. It should nevertheless be highlighted that in some patients, the rise of CD4 lymphocytes is slow, in a context of advanced pre-therapeutic immunodepression [6]. The low socio-economic level of our patients for whom consultation is only late in a screening and comprehensive management of HIV infection, the management of opportunistic infections is out of reach in a context of hospital stay and profession. The WHO stage and tuberculosis were statistically significant in relation to the occurrence of immunologic failure in patients.

Conclusion
It comes out from discussion and analysis that the prevalence of immunologic failure in our series remains worrying with its corollary, the occurrence of opportunistic events or events directly related to HIV. We come to the conclusion that associated factors identified are similar to those described in the literature. Yet, screening and early treatment of HIV infection would help to prevent from this situation.

References
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