Research Article ISSN 2639-9458

Microbiology & Infectious Diseases

Immunological Failure at Six Months of Triple Antiretroviral Therapy at Brazzaville University Hospital: Prevalence and Associated Factors

Ossibi Ibara BR[1,2], Okemba Okombi FH[1,3], Bemba ELP[1,2,3], Babanga R[2], Adoua Doukaga T[2], Angonga Pabota Ella[2] and Ellenga Mbolla BF[1,4]

[1]*Faculty of Health Sciences, NGOUABY University Brazzaville-CONGO.*

[2]*Department of Infectious Diseases, University Hospital of Brazzaville-CONGO.*

[3]*Department of Pneumology, University Hospital of Brazzaville-CONGO.*

[4]*Department of Cardiology, University Hospital of Brazzaville-CONG0.*

***Correspondence:**
Ossibi Ibara Bienvenu Roland, Infectious Disease Unit, Brazzaville CHU, B.P: 1846 Brazzaville, Congo, Tel: 00242 06979 36 94/ 055224226, E-mail: bienvenu_07@yahoo.fr.

Received: 29 September 2018; **Accepted:** 23 October 2018

Citation: Ossibi Ibara BR, Okemba Okombi FH, Bemba ELP, et al. Immunological Failure at Six Months of Triple Antiretroviral Therapy at Brazzaville University Hospital: Prevalence and Associated Factors. Microbiol Infect Dis. 2018; 2(4): 1-4.

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 / mm^3 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 (e-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 / mm^3 (extreme: 1-995 cells / mm^3); 88 patients (27.1%) had CD4< 100 / mm^3 number at initiation of ART and 65 patients (20%) had CD4 between 100 and 200 cells / mm^3. 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 / mm^3. There was a correlation between basic CD4 and six months of triple antiretroviral therapy (Figure 1).

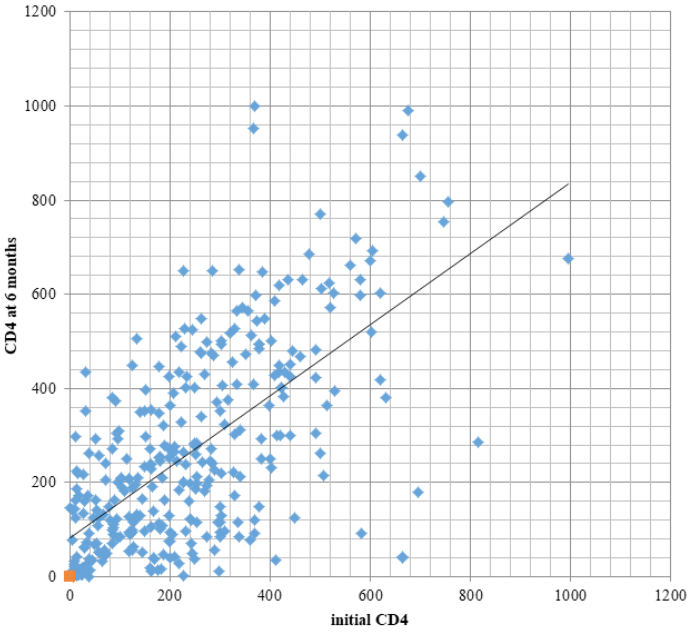

Table 1: Predictive factors immunologic failure.

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).

Risk factors		ß	OR	IC 95%		P
Profession	Retired	6,579	719,659	14,81	- 34970,95	0,001
Marital status	Widower	2,807	16,559	1,07	-256,95	0,045
Opportunistic infections	None	-6,581	0,001	0,00	-0,12	0,004
	pulmonary and ganglionic tuberculosis	-5,437	0,004	0,00	-0,10	0,001
Serological status duration	6months – 12 months	-4,348	0,013	0,00	-0,25	0,004
CD4initial	<100	4,099	60,294	2,10	-1734,81	0,017
	100-200	6,007	406,362	11,85	-13930,81	0,001
	300-400	5,694	297,111	9,21	-9579,68	0,001
	≥400	2,694	14,792	1,51	-144,55	0,021

Table 1: Predictive factors immunologic failure.

		Failure				OR	IC95%	P
		Yes		No				
		n	%	n	%			
Opportunistic infections	Pulmonary and ganglionic tuberculosis	11	4,8	0	0	0,701	0,652-0,753	0,031
	IO Prophylaxis	225	97,4	84	89,4	4,464	1,574-12,664	0,002
	WHO level III	109	47,2	27	28,7	2,217	1,325-3,715	0,002
	Married	33	14,3	22	23,4	0,545	0,298-0,997	0,047
	Singles	85	36,8	25	26,6	1,607	0,946-2,730	0,078
	Chronic diarrhoea	23	10	4	4,3	2,488	0,836-7,401	0,091
	Intercostal shingles	20	8,7	7	7,4	1,178	0,481-2,887	0,72
	Prurigo	21	9,1	12	12,8	0,683	0,322-1,452	0,32
	Nome	25	10,8	35	37,2	0,205	0,113-0,369	<0,001
Serological status duration	6 months	47	20,30	41	43,60	0,33	0,197-0,555	<0,001
	12 months	120	51,90	43	45,70	1,282	0,793-2,074	0,311
	24 months	64	27,70	10	10,60	3,219	1,573-6,88	0,001

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].

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

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

1. Lodwick RK, Sabin CA, Porter K, et al. Death rates in HIV-positive antiretroviral-naive patients with CD4 count greater than 350 cells per micro-L in Europe and North America: a pooled cohort observational study. Lancet. 2010; 376: 340-345.
2. May M, Sterne JA, Sabin C, et al. prognosis of HIV-1-infected patients up to years after initiation of HAART: collaborative analysis of prospective studies. AIDS. 2007; 21: 1185-1197.
3. Lewden C. The Mortality Working Group of COHERE. Time with CD4 cell count above 500 cells/mm3 allows HIV-infected men, but not women, to reach similar mortality rates to those of the general population: a 7 years analysis. CROI. 2010.
4. Borsa LF. Echec de la restauration immunitaire: prise en charge et perspectives. Colloque inter COREVIH Nord/Nord-Ouest, mars. 2009.
5. Tebit DM, Sangaré L, Tiba F. Analysis of the diversity of the HIV-1 pol gene and drug resistance associated changes among drug-naive patients in Burkina Faso. J Med Viral. 2009; 81: 1691-1701.
6. Gazzola L, Tincati C, Bellistri GM, et al. The absence of CD4+T cell count recovery despite receipt of virologically suppressive highly active antiretroviral therapy: clinical risk, immunological gaps, and therapeutic options. Clin infect Dis. 2009; 48: 328-337.
7. Ouedraogo SM, Zoungrana J, Sondo A, et al. Caractéristiques sociodémographiques, cliniques, biologiques, thérapeutiques et determinants de la réponse immunovirologique chez les adultes infectés par le VIH, sous traitement antiretroviral à l'hopital de jour de Bobo-Dioulasso (Burkina-Faso). RAFMI. 2014; 2: 1-44.
8. Anude CJ, Onyegbutulem HC. Immuno-virologic outcomes and immunologic discordance among adults alive and on antiretroviral therapy at 12 months in Nigeria. BMC Infectious Diseases. 2013; 13: 1471-2334.
9. Greder Belan A, Chaplain C, Boussairi A. Suivi Biologique de l'infection à VIH chez l'adulte. Immuno-analyse et biologie spécialisée. 2008; 23: 95-102.
10. Sommet A, Delpierre C, Cuzin L, et al. Etude rétrospective , descriptive évaluant les causes et les conséquences cliniques et immunologiques et virologiques des interruptions de traitement antirétroviral chez les adultes infectées par le VIH-1. La revue de médecine interne. 2003; 24: 350-357.
11. Slama L, Le Camus C, Amiel C, et al. Adherence antiretroviral therapy during HIV infection, a multidisciplinary approach of literature. Medicine et maladies infectieuses. 2006; 36: 16-26.
12. Manga NM, Diop SA, Ndour CT, et al. Dépistage tardif de l'infection à VIH à la clinique des maladies infectieuses de Fann, Dakar : Circonstances de diagnostic, itinéraire thérapeutique des patients et facteurs déterminants. Med mal inf. 2009; 39: 95-100.
13. Deeks ED, Perry CM. Efavirenz/emtricitabine/tenofovir disoproxil fumarate singe-tablet regimen (Atripla) Adis drug Evaluation. Drugs. 2010; 70: 2315-2338.
14. Pierre-marie Girard, Christine Katlama, Gilles Pialoux. VIH, edition. 2011; 432-433.