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RESEARCH ARTICLE

FACTORS PROMOTING THE EVOLUTION OF CD4 T CELL OF ADULT PATIENTS DURING THE TWELVE MONTHS OF ANTIRETROVIRAL TREATMENT IN GOMA, DR CONGO

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A B S T R A C T

Introduction

Factors favoring the evolution of CD4 T cells of adult patients on the 12th month of antiretroviral therapy (ART) were investigated. This is a retrospective study of 121 cases of PLHIV all followed as outpatients.

Results

The predominant age bracket is that of 30-39 years (32.2%). Women are mostly represented 66.1%. The married were predominant. 52.1% and 32.2% patients are unemployed.

The gain of CD4 to M6 is higher in subjects who started HAART with CD4 ≥ 500 /µL, with a difference is very significant (p = 0.00). Moreover, the comparison of CD4 gains to M6 and M12 also shows a significant difference between the three groups.

The difference is statistically significant for the gain of CD4 between patients observing and those not observing the antiretroviral treatment.

While for patients aged 20-29 years, the gain of CD4 tends to be higher between D0 and M6 (p = 0.174) and between M6 and M12 in patients aged 50-59 years (p = 0.192) but the difference is not significant in 4 age groups studied.

There is no significant difference of CD4 gain depending on the presence or the absence of opportunistic infection at D0, but also between M6 and M12. There is no significant difference in CD4 gain according to whether patients received AZT 3TC NVP or TDF 3TC EFV.

Conclusion

The CD4 count at the start of ART and the treatment adherence arethe factors that are significantly associated with the rising rates of CD4 + infected patients with HIV on antiretroviral treatment in Goma.

INTRODUCTION

Since its identification in the United States of America in 1981, the HIV infection is increasing [1]. It is a pandemic that remains a concern worldwide, especially in developing countries [2]. According to the estimates, in 2012, 35.3 (32.2 to 38.8) million people were living with HIV (PLHIV) in the world. There is an increase in comparison with previous years due to the increase in the number of people on antiretroviral therapy. Globally 2.3 (1.9 to 2.7) million of new HIV infections were reported, a decrease of 33% compared to 3.4 (3.1-3.7) million in 2001. This is the lowest annual figure ever recorded of new infections since the mid-1990s, when about 3.5 million people (3.3 to 4.1 million) contracted HIV infection each year [3]. AIDS deaths associated with AIDS also recorded a decline from 2.3 (2.1-2.6) million in 2005 to 1.6 (1.4-1.9) million in 2012 [3]. Increased political commitments, judicious investments associated with more strategic programs and massive reductions in the cost of treatment led to the historical figure of 9.7 million people with access to antiretroviral treatment in low-income countries. The percentage of intensification has increased exponentially in recent years. In 2012, only 1.6 million of additional people had access to treatment for the first time [4, 5].

If significant progress has been made over the past decade, there remain significant challenges. Still in 2013, about 70% of people living with HIV (PLHIV) live in sub-Saharan Africa, a region that only accounts for 12% of the world

population but cause 72% of new infections and 70% of deaths. There still exists in Sub-Saharan Africa significant variations in HIV prevalence depending on the regions, no country experienced an increase in the incidence of HIV / AIDS in 2014 [5]. However, these advances are not all homogenous and the future of the epidemicremainsun certain, hence the need to intensify the action towards the universal access to prevention, treatment, care and support in HIV concern [6]. Antiretroviral therapy whose aim is to reduce plasma viral load as low as possible, must comprise a powerful association currently made up of three antiretroviral (HAART), the observance of which could ensure its effectiveness in the short-long [7].

In the DemocraticRepublic of Congo (DRC) and more specifically in the city of Goma, itisdifficult to accessto the evaluation of viral load for the proper monitoring of PLWHA patients due to non availability of equipment in sanitary structures of the country.

The onlywaythatisavailableis the counter of the CD4 to accessthe immunological changes in patients, the latter constitutesthe measurement basis of the quality of the response to ART.

No knownstudywhich has been conductedso far in North Kivu province, particularly in the city of Goma to determinewhat are the epidemiological and clinicalfactorsrelated to changes in CD4 count during the first month ofantiretroviraltherapy, whileseveral studies conducted world wide have shownthatduring the youngage, therapeuticadherence and the rate of lymphocytes T CD4 for the initiation for initiation of antiretroviraltherapycouldbe thefactorsinfluencing the evolution of CD4 T lymphocytesin the 12 first months of antiretroviraltreatment [2, 10, 12, 22, 24].

The main question of this study is to find out what factors favoring the evolution of CD4 T lymphocytes in adult patients for 12 months of antiretroviral treatment in Goma. Al though statistics are eloquent, a careful analysis of these data shows that the mastery of the factors related to treatment failure in our study area will allow the clinician to make a more specific follow-up of this category of patients in order to anticipate them, there by avoiding resorting to a second-line treatment, which is very heavy and expensive for patients in the DRC in general and in the city of Goma in particular.

MATERIAL AND METHODS

Framework of the Study

This study was conducted in the HIV Service of the Department of Internal Medicine of the Provincial Hospitalof North Kivu in Goma. This service is responsible for the care of people living with HIV / AIDS. It employs 6 general practitioners, a nurse A1 trained in management stocks of medicines (according to the standards of National Programme for the Fight against HIV-AIDS infection) and acting office pharmacist, two nurses A1 and one nurse A0 in management of ambulatory patients, a data manager also acting receptionist.

Performed diagnostic tests are the numeration of CD4 lymphocytes, biochemical tests for liver and renalfunction tests, electrolytes as well as bacteriological and serologicalanalyzes.

MATERIAL

The study involved 121 patients, including 41 male and 80 female. Their ages ranged from 20-59 years with an average age of 39.5 years.

METHODS

This is a descriptive cross-sectionalstudy. It wasintended to restore the clinical and biologicalhistory of patients followed in the service fromtheirmedical records. It covered a period of one yearfrom 1 January to 31 December 2014: either a period of 12 months per patient.

Wereincluded in ourstudy: patients withagegreaterthan or equal to 15 years, submitted to antiretroviraltherapy for 12 months and adhering to a regularhalf-yearly count of CD4 T cells as prescribed by the doctor. Wereexcludedfrom the studythe patients under 15 years of age or withundetermined HIV status or not subject to antiretroviraltreatment, the unseen patients and the cases of death.

The study variables weredefined as follows: The dependent variable isthe evolution in CD4 count from the patient admission to the Provincial Hospital of North Kivu to 12 months of treatmentwhile the independent variables are socio-demographicfactors (age, sex, marital status and occupation), clinical and biological data (clinical stage, opportunistic infections and CD4 + lymphocytes rate) and therapeutic (molecules of the first line and adherence).

As regards statistical analysis, we made the descriptive calculation of socio-demographic, clinical, biological and therapeutic variables with the variables of the evolution of CD4.

For the comparative analysis, we sought to understand the factors that influence the evolution of the CD4 rate by the analysis of the variance which is a statistical technique for comparing the averages of more than two people. It is also the equivalent, for qualitative variables, of linear regression. We accept the null hypothesis H0 when the calculated rob ability is greater than 0.05 or the value of the calculated file is smaller than the value of the tabulated file. Otherwise, we accept the alternative hypothesis H1. The data obtained were analyzed using SPSS Version 20 software.

RESULTS

Sociodemographiccharacteristics

We present in the following table I sociodemographic characteristics of the patients.

Table I Sociodemographiccharacteristics of the patients.

Characteristics	Number	Percentage
AGE (years)		
20 - 29	22	18,2
30 - 39	39	32,2
40 - 49	34	28,1
50 - 59	26	21,5
SEXE		
Male	41	33,9
Female	80	66,1
CIVIL STATUS		
Single	14	11,6
Married	63	52,1
Divorced	14	11,6
Widowed	30	24,8
PROFESSION OF PATIENTS		
Cultivators	4	3,3
Civil servants	14	11,6
Businessmen	3	2,5
Military	4	3,3
Freelance workers	39	32,2
Unemployed	9	7,4
Nurses	1	0,8
Housewives	35	28,9
Students	12	9,9

This table I shows that the predominantage group wasthat of 30-39 years (32.2%). Women are mostlyrepresented 66.1% as well as married 52.1% and 32.2% unemployed.

Evolution of CD4 T lymphocytes

The gain of CD4 Cells during treatment is presented in Tables II to VI according to the following patient parametersatthe initiation of treatment.

Table II Comparison of gains of CD4 T cells on the 6th and 12th months of antiretroviraltherapybased on CD4 rates oftreatmentstart

Slice of CD4 /µLinitiated ART	Number of patients	Mediangain ofCD4 TL between D0-M6	Median gain of CD4 T cellsbetween M6-M12
< 200	52	129,5385	28,12522
200-499	67	327,27	77,88734
≥ 500	2	570,9375	257,93904
Comparison of distributions of CD4 M6 to gain, according to the CD4 levelat the ARV: p = 0.00			
Comparison of CD4 gain distributions between M6 and M12, according to the CD4 levelat the ARV: p = 0.00			

The analysis of Table II shows that the gain of CD4 TL to M6 is significantly higher in subjects who started HAART with CD4 ≥ 500 / µL (p = 0.00). Moreover, the comparison of gains of CD4 to M6 and M12 also shows a significant difference between the three groups.

Table III Comparison of gains of CD4 T lymphocytes on the 6th and 12th months of antiretroviral treatment according to the patient'sageat the initiation of ART.

Age group (years) on the initiative of ART	Number of patients	Median gain of CD4 TL between D0-M6	Median gain of CD4 T cellsbetween M6-M12
20-29	22	332,8667	499,1364
30-39	39	362,2414	573,0256
40-49	34	282,375	448,4706
50-59	26	284,8696	595,2692
Comparison of CD4 gains between D0 and M6: p = 0.174			
Comparison of CD4 gains between M6 and M12: p = 0.192			

Table III shows that the gain of CD4 tends to be higher among patients aged 20-29 years between D0 and M6 (p = 0.174) and between M6 and M12 in patients aged 50-59 years (p = 0.192) but statistically significant difference in the four studied age groups.

Table IV Comparison of gains of CD4 T cells on the 6th and 12th months of antiretroviraltherapybased on the presence of opportunistic infections in early ARV treatment

Presence of opportunistic infections in early ART	Number of patients	Mediangain of CD4 TL between D0-M6	Median gain of the CD4 T cellsbetween M6-M12
Yes	111	238,46	520,3836
No	10	304,7	543,0417
Comparison of CD4 gain of M6 between 0 and p = 0.088			
Comparison of CD4 gain between M6 and M12: p = 0.64			

In analyzing Table IV, wefind out thatthereis no significantdifference of CD4 gain according to the occurrence of opportunistic infections between D0 and M6 and M12.

Table V Comparison of gains of CD4 T lymphocytes on the 6th and 12th months of ART basedon the molecules of the initial line therapy

Molecules of the initial line	Number of patients	Mediangain of CD4 TL between D0-M6	Median gain of CD4 T cellsbetween M6-M12
AZT 3TC NVP	83	324,9063	514,1084
TDF 3TC EFV	38	294,0571	562,71
Comparison of CD4 gain of M6 between 0 and p = 0.356			
Comparison of CD4 gain between M6 and M12: p = 0.412			

Table V shows thattherewas no significantdifference in CD4 gain according to whether patients received AZT 3TC NVP or TDF 3TC EFV.

Table VI Comparison of lymphocyte gain medians of T CD4on the 6th and 12th months of antiretroviraltreatmentbased on therapeuticadherence

Therapeutic Observance	Number of patients	Median gain of CD4 T cellsbetween D0-M6	Median gain of CD4 T cellsbetween M6-M12
Observance	118	571,8375	357,839
Noncompliance	3	127,17	78,18734
Comparison of CD4 gain between 0 and M6: p = 0.00			
Comparison of CD4 gain between M6 and M12: p = 0.00			

On the analysis of table VI, wefindout that the differenceisstatisticallysignificant for the gain of CD4 betweenpatients observing and thosenot observing ARV treatment.

DISCUSSION

Sociodemographic profile of patients

AGE

The study population is predominated by the age group 30-39 years with 32.2%. DIARRA MS as well as YOUMMA T found a predominance of respectively 36% and 45.2% in the same age group [12].

These results are consistent with several literatures which state that Sub-Saharan Africa, because of spread before all heterosexual infection, HIV prevalence increases from adolescence, becomes maximum in women around 25 years of age and in male around 30 to 40 years [13, 14].

SEX

Female subjects are most affected in a proportion of 66.1%. This outcome is comparable to that of KONE MC who got a female rate of 70% [15] and LAPOINTE N et al. who reported that 67% of patients were female [9]. This proves that women are the most exposed groups to HIV infection.
The analysis of trends at the provincial level in North Kivu shows that there is a feminization regarding the distribution of this pandemic with a sex ratio M / F 1 / 1.3. This situation may well be explained by the socio-political environment dominated by armed conflicts and an increase in cases of sexual violence that make women more vulnerable to STIs and especially to HIV / AIDS [16, 17].

Civil Status

We find that the married are more affected 52.1%. These results confirm those of a previous study conducted at the Hospital by SENGOMA Rwengeri P. who reported that 58.2% of married were infected with HIV [18].

This predominance of married could be explained partly by the fact that this category is part of sexually active people who are more exposed to HIV and, on the other part, by sexual habits (non-condom use between spouses) which are increasingly found among the married than the single [10, 13, 16, 18].

Profession

It turns out from our study that the unemployed patients are the most affected by AIDS in a proportion of 32.2% and the housewives come in the second position with 28.9% of cases.
The unemployment rate was estimated at 60% in 2013, but the situation in the eastern DRC and could especially be more alarming because of the presence of armed groups whothreaterthe villages with as consequence, the massive rural exodus, the impoverishment of populations without employments in the city of Goma. According to the 2002 UNFPA report, HIV and goes with poverty and is spread by the latter and in turn generates poverty [4].

Changes in cd4 t cell.

This is the comparison of the gains of CD4 T cells on the 6th and 12th months of antiretroviral treatment.

Analysis of the gain of cd4 and cd4 lymphocytes rate on the initiation of art

We found out that it was during the first quarter that the gain of CD4 is higher in subjects who initiated the ART with CD4 ≥ 500 / µL. This difference is highly significant (p = 0.00). Also, the comparison of CD4 gains on the 6th and 12th months shows a statistically significant difference among the three groups.

Several studies conducted in the countries with limited resources, have shown that the patients who start the treatment earlier clinically evolve more towards the discontinuation of treatment, especially if they do not receive a good treatment education [17, 18, 19, 21]. In this category of patients we find many who sometimes end up questioning their HIV status because they have never experienced the clinical reality of the disease (the occurrence of opportunistic infections).

The same observation was made by MEWENENESSI T, of which it was found that 52% of cases of non-adherence of patients were formed before the Antiretroviral Treatment began during the preclinical phase of the disease [19].

While for DIARRA MS, the CD4 gain on the 6th month of ARV treatment tends to be higher among patients who initiated ART with a CD4 count> 200 /µL, but this difference was not significant (p = 0,21) [12].

Gain Analysis of CD4 and patient ageon the initiation of ART

The gain of CD4 tends to behigheramong patients aged 20-29 yearsbetween D0 and M6 (p = 0.174) and between M6 and M12 in patients aged 50-59 years(p = 0.192) but the differenceis not significant in the 4 slices of agesstudied.
Admittedly, severalliteratures showthe place of age in the reconstitution of CD4 heritage, thisis due mostoften in childrenfrom 0 to 14 years (20, 21,22), but oursampleconsists of patients aged 20-50 years,whichcanexplainthatthereis no statisticaldifference inimmunologicalresultscompared to antiretroviraltherapyaccording to age groups.
For SADOU O. K, the lymphocytes T CD4 gain between the start of ART and the 12th month of ARV treatment tends to beslightlyhigher (p = 0.09) in patients aged 30-39 years. [11]

Analysis of the CD4 gain and existing opportunistic infections and the inclusion of ART

The comparisons of CD4 gain between 0 and M6: p = 0.088 between M6 and M12: p = 0.64 show that there is no significant difference in CD4 gain depending on the presence or absence of opportunistic infection to D0, but also between M6 and M12. We must show that in the literature it is said that the most frequent occurrence of opportunistic infections has an impact on the evolution of CD4.

In literature, the appearance of opportunistic infections depends on the degree of immunodeficiency (CD4 T cell counts).

The occurrence of certain opportunistic infections can affect the immunological profile of patients therefore a fall in CD4 lymphocytes.

This situation is directly related to certain diseases such as tuberculosis, chronic enteritis affecting the impaired digestive function and a syndrome of poor absorption that limits the quality of ART and even those of other opportunistic infections of HIV [23, 24, 25].

But it must be noted that in this study it is difficult to conclude very quickly, because the frequency and even the type of opportunistic infections of HIV in patients were not clear,hence it will be difficult to directly link the presence or absence of opportunistic infections in relation to their impact with the development of CD4. Thus, DELFRAISSY J found more cases of immunological failure in patients who presented opportunistic infections in the pre-treatment phase as well as under the ARV treatment, 81% of patients had a CD4 rate <200 /µL and observed in these patients: an impaired general condition, an underweight [16].

Analysis of the gain of CD4 lymphocytes and molecules of the initial therapeutic line

After comparing the CD4 gain between 0 and M6: p = 0.356 and M6 and M12: p = 0.412, there is no significant difference in CD4 gain according to whether patients received AZT 3TC NVP or TDF 3TC EFV.

Several studies have demonstrated that patients submitted to second-line treatment made from a combination of nucleoside inhibitors with protease inhibitors experience faster immune restoration than those submitted to the first-line treatment because of nucleoside inhibitors with inhibitors either nucleotides or nucleotides [20, 21, 22].

SISSOKO K. conducted a comparative study of the immunological changes in patients undergoing a combination made of Zidovudine (AZT) and those of Tenofovir (TDF). Il was observed a greater adherence to treatment in patients for TDF than those subjected to AZT over the five years of treatment [27].This observation was made by AI and SIADOU MAIGA KO, but for them, there was no statistically significant difference compared to the evolution of CD4 in both groups of populations [1].

Gain Analysis of CD4 lymphocytes and adherence with respect to changes in CD4 of patients

The gain comparisons of CD4 between 0 and M6 (p = 0.00) and M6 and M12 (P = 0.00) show a statistically significant difference in gain of CD4 between the patients observing and those not observing the treatment. These results confirm the literature data whichstipulate that adherence to ARV treatment constitutes the key to its therapeutic success [7, 8, 12, 21, 23].

Many studies measured the adherence of an active host of patients transversely, that is at a given moment of time. Observational studies of APRACO cohort of patients who initiated a treatment comprising a protease inhibitor showed that adherence significantly changes according to the time. According to this study, at every monitoring, we find between 50 and 60% highly observing subjects, only a third of the cohort maintains this behavior over a 20 months period and only a quarter over a period of 3 years [6].

In the context of the eastern Democratic Republic of the Congo, the demographic instability of the population due to the armed conflicts may constitute a limit for good adherence to antiretroviral treatment. This may also explain the early poor progress of CD4 count in patients already in the first two months of treatment.

CONCLUSION

It appears from this study that treatment adherence and the CD4 count at the start of antiretroviral therapy are the factors that significantly promote the development of the rate of CD4 T lymphocytes of the patients infected with HIV on antiretroviral treatment in Goma. On the other hand, age, existing opportunistic infections to the inclusion of ARVs and the molecules of the initialtherapeutic line do not appear to significantly influence this development.

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