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Research Article

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Associated factors with mortality in people living with HIV in Ziguinchor, Southern-region, Senegal: about 804 cases.

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Abstract

Background: *The generalization of antiretroviral treatment to all People living with HIV (PLHIV) contributes to the considerable decrease of HIV-related mortality. However, this remains higher than in the general population, hence the importance of identifying its determining factors. The objective of our study was to determine the factors associated with death in PLHIV followed in Ziguinchor.*

Patients and method*: This was a cross-sectional, descriptive and analytical study on the cohorts of PLHIV followed in the health districts of Ziguinchor and Bignona in Senegal over a period of 5 years. We included all the patients infected with HIV, aged 15 years and over, regularly followed and under antiretroviral treatment during the study period.*

Results: *Of the 804 patients included, 597 (74.25%) were female, i.e. a sex ratio (F/M) of 2.88. The average age was 45.61 ± 13.01 years [15 to 96 years]. The diagnosis was made at WHO stages 3 and 4 in 286 patients (35.58%). The predominant serotype was HIV-1 (82.34%) followed by HIV-2 (15.17%) and HIV-1+2 (2.49%). Lethality was 6.34% after 12 months of follow-up under treatment. In multivariate analysis, death was associated with: age over 65 years (p=0.027), treatment duration < 12 months (p<0.005), insufficient immunological restoration (CD4+<500/mm3; p=0.001) and a viral load > 1000 copies (p=0.000).*

Conclusion: *Advanced age and insufficient immunovirological response are the main factors associated with death in our patients. The introduction of more effective treatments based on integrase inhibitors, good therapeutic education and better monitoring of seniors will improve their prognosis.*

Introduction

Human Immunodeficiency Virus (HIV) infection remains a global public health problem. In 2020, the World Health Organization (WHO) estimated the number of people living with HIV worldwide at around 37.7 million, including 1.5 million new infections [1]. In Senegal, 0.4% of women and 0.3% of men aged 15-49 are HIV positive (UNAIDS Spectrum, 2020). In Senegal in 2020, the number of PLHIV (people living with HIV) was around 39,400 people. The latest Spectrum in 2020 estimates show a gradual decline in prevalence among people aged 15-49 year-old since 2005, dropping from 0.7% to 0.3% [2].

The effectiveness and increasingly easy access to highly active antiretroviral treatment (ART) have contributed to an important drop in HIV-related mortality, from 1.2 million in 2015 to 680,000 in 2020 [1,3]. However, the mortality of HIV-infected adults remains globally higher than in the general population [3]. According to several studies, the reasons of death are

dominated by opportunistic infections (11-71.4%) in developing countries [5, 6] and by cardiovascular diseases (6.5-19%) and cancers in developed countries (11.8-19%) [7.8]. History of opportunistic infections, a delay in initiation of ART, a duration of antiretroviral triple therapy < 12 months are among the main factors associated with mortality in Africa [5, 6].

The objective of this study was to determine the factors associated with the occurrence of death in patients living with HIV followed in the Ziguinchor, southern region of Senegal, in order to improve the care of these patients in our context.

Patients and method

This was a cross-sectional, descriptive and analytical study on the cohorts of people living with HIV (PLHIV) followed in the health districts of Ziguinchor and Bignona in Senegal from January 1st, 2014 to December 31st, 2018 (5 years). We included all patients infected with HIV aged 15 years and beyond, regularly followed under antiretroviral treatment during the study period of the two following clinics: Health district of Ziguinchor and Health district of Bignona. Patients whose records were unusable were excluded.

Data were collected from patient follow-up records using a pre-established questionnaire with the following aspects

- Socio-demographic age, gender, marital status
- Clinical, Circumstance of discovery, clinical state according to WHO, types of opportunistic infections diagnosed
- Paraclinical CD4 count, viral load
- Therapeutic and evolutive, ARV therapeutic regimen, evolution under treatment.

Patients were considered:

- Lost to follow-up after at least 3 missed appointments
- Transferred, when notified in the follow-up file
- Deceased, if notified in the file and
- Active follow-up for the rest of the cases

Therapeutic failure was defined as a viral load greater than 1000 copies/ml after at least 6 months of well-conducted ART in an observant patient and outside of any context of drug interaction or intestinal absorption defect.

Data were entered using Epi Data 3.1 software and analyzed using Stata16 software. The comparison of proportions was performed using Fisher's exact test, the chi-square test and the linear trend chi-square test, as indicated. The level of significance was 0.05 and the confidence interval 95%. Associated factors with death in patients living with HIV were determined by univariate analysis using binomial regression. The multivariate model was constructed from variables with a significance level less than or equal to 0.05 in univariate analysis due to the exploratory nature of our study. The final model consisted of the variables that in the multivariate model had a value less than 0.05. Local ethical committees of all participating study sites approved the study and written informed consent was obtained from all participants.

Results

Epidemiological data

Of the 804 patients included, 494 (61,44%) were followed in the health district of Ziguinchor and 310 (38,56%) in the health district of Bignona. Majority of patients were female (597/804) (74,25%), i.e. a sex ratio (F/M) of 2.88. The average age was 45.61 years ± 13.01 years with extremes of 15 to 96 years. The 46-60 age group was the most represented, 36.94% or 297 cases. Patients were married in 56.2% of cases, 42% among them were polygamous. Widowers accounted for 16.42% of cases. Table 1 shows the epidemiological profile of PvHIV in our study.

Table 1: Epidemiological aspects of people living with HIV

Variables	n =804	Percent ( )
Sex		
Male	207	25,75
Female	597	74.25
Age		
14-30	112	13,93
31-45	282	35,07
46-60	297	36,94
> 60	113	14.05
Marital status		
Married	494	61,44
Widows	132	16,42
Single	115	14,30
Divorced	63	7,84

Circumstances of discovery of HIV		
Infections opportunistes	536	66.92
Pregnancy	93	11.61
Drugs consomption	81	10.11
Tuberculosis	61	07.55
Family screening	24	03,00
Blood donation	02	0.25
Clinical stage according to WHO		
1	307	38.18
2	211	26.24
3	241	29.98
4	45	5.60

Clinical data

We had 286 patients (35.58%) who were diagnosed at stages 3 and 4 according to WHO. In 358 patients (44.52%), opportunistic infections were the circumstance of discovery. They were dominated by chronic gastroenteritis (29.51%), recurrent non-specific or community-acquired bacterial pneumonia (29.23%), tuberculosis (20.11% with 12.5% of extra-pulmonary forms), oral or oropharyngeal candidiasis (09.17%), shingles (07.16%), Kaposi (1.15%). A carriage of AgHbs was noted in 10.11%.

According to the virological profile, 82.34% were infected with HIV1. Type 2 was found in 122 (15.17%) patients and the dual profile found in 20 cases (2.49%). The average CD4 count was 327±295/mm3 with extremes of 1 and 2156/mm3. Two hundred and thirteen(213) patients (40.73%) had a CD4 count below 200/mm3 and 117 patients (22.37%) had a CD4 count above 500/mm3 (see table 2).

Table 2: Immunological and virological data of PvHIV

Variables	Headcount (n =804)	Pourcentage (%)
Viral load (copies/ml)		
Undetectable < 20	8	2,29
20 - 1000	320	91,69
1001 - 10000	8	2,29
10001-100000	7	2,01
>100000	6	1,72
LTCD4+ count (cell/mm3)		
< 500	406	50,50
≥ 500	398	49,50

Therapeutic and evolutionary data

Antiretroviral treatment was initiated in 791 patients (98.38%). The antiretroviral regimen combined 2 NRTIs (nucleoside reverse transcriptase inhibitor) with 1 NNTI (non-nucleoside reverse transcriptase inhibitor) in 82.71% of cases. The average duration of follow-up was 3.22±1.33 years (range 1 to 6 years). After 12 months of therapeutic follow-up, the viral load (VL) was carried out in 349 patients and 6.02% had virological failure (CD4 > 1000 copies) with a mean of 3061 copies/mL. Four hundred and ninety (60.95%) patients were regularly followed. Lost to sight and deaths accounted for 25.25% and 6.34% of cases respectively (see Table 3).

In multivariate analysis, the occurrence of death was associated with age greater than 65 years (p = 0.027), treatment duration < 12 months (p 0.005), a delayed ARV treatment (CD4 at baseline less than 500 cells/mm3 (p=0.001) and high viral load greater than 1000 copies/mL (p=0.000) at baseline).

Table 3: Therapeutic and evolutionary aspects of people living with HIV.

Variables	Headcount (n =804)	Pourcentage (%)
Therapeutic regimen		
2INTI* +1NNTI**	665	82,71
2INTI +1IP***	138	17,16
2INTI	1	0,12
Evolution aspects		
Active follow-up	489	60,90
Lost of sight	203	25,28
Transferred	60	7,47
Deceased	51	6,35

*Nucleoside Reverse Transcriptase Inhibitor
** Non-nucleoside reverse transcriptase inhibitor
***Protease inhibitor

Table 4: Bivariate analysis of factors associated with lethality in PLHIV

Variables	Deceased n (%)		P-value
	YES Headcount (%)	No Headcount (%)	
Sex			
Male	16 (7,73)	191 (92,27)	0.342
Female	35 (5,86)	562 (94,14)	
Age at enrollment (years)			
< 65	43 (5.80%)	699 (94,20)	0,027
≥ 65	8 (12,90)	54 (87,10)	
Stages according to WHO			
1-2	248 (85,52)	505 (98,25)	0,000
3-4	42 (14,48)	9 (1,75)	
LTCD4 + count (cell/mm3)			
<500	37 (9,11)	369 (90,89)	0.001
≥500	14 (3,52)	384 (96,48)	
Treatment's length (months)			
< 12	44 (14,47)	260 (85,53)	0.000
≥ 12	7 (1.40)	493 (98,60)	
Viral load			
<1000	4 (1,17)	339 (98,83)	0.000
≥1000	47 (10,20)	414 (89,80)	

Table 5: Multivariate analysis of factors associated with lethality in PLHIV

Associated factors	Odds ratio	P-value	IC 95%
Age>65 ans	3,81	0,052	0,98 -14,7
WHO stage 3-4	6,73	0,000	2,60-17,38
TARV Length< 12mois	4,59	0,008	1,49- 14,15
CD4 < 500	2,24	0,305	0,47-10,50
CV> 1000 cp/mm3	3,10	0,135	0,70-13,69

Discussion

This study, conducted in Ziguinchor, southern region of Senegal at the health districts of Ziguinchor and Bignona, allow a better understanding of the problem with care and the epidemiological, clinical and immuno-virological factors associated with the mortality of patients living with HIV in decentralized settings. The population oh this study is comparable to data from the African literature [9,10, 11] with a predominance of women (72.4%) and young adults with an average age of 45.61 years ± 13, 01 years old. Regarding the serological profile, the predominance of type 1 was noted in our study (82.34%). In the work of the infectious diseases department at the University Hospital of Fann in Dakar, type 1 was found in 85%, Mboup et al. [12], in Senegal the sentinel surveillance, found type 1 in 84.5% of cases. It should

be noted that HIV 2 only exists in Africa and the rare cases observed in the Occident are imported cases. In our study, we noted an important delay in diagnosis that can be explained on the one hand by insufficient accessibility to care, on the other hand by the fact that patients prefer to consult traditional healers first and arrive to the health settings only when their state deteriorates. This delay in diagnosis could be a factor of poor prognosis for HIV infection [9, 13]. Awareness of the need for voluntary testing should be strengthened.

Of the 349 patients in our cohort, the viral load (VL) was detectable, greater than 1000 copies/ml in 21 patients, i.e. 6.02% of cases considered to be in virological failure. This result is similar to the one found in several studies [8] but remains lower than the data from De Beaudrap [16] and Douara [15] in different cohorts in Senegal. In two studies conducted in Togo and Nigeria, the virological failure rate was 42% and 23.4% respectively [16, 17]. In Cameroon, after 36 months of ARV treatment, 77.1% of patients enrolled had a VL below the detection limits (< 300 copies/ml) and 17.6% of patients had virological failure [11]. This could be explained by a higher proportion of patients screened (11.6%) of cases in the context of PMTCT and thus benefiting from the advantage of reinforcement of compliance.

The fatality rate was 6% and three factors were identified in multivariate analysis as associated with the occurrence of death. This was delayed screening (cd4<500, duration of ART <12 months). Our results are similar to those of a study carried out in the United Kingdom where delayed diagnosis was a strong predictor of death. Those diagnosed earlier had a lower risk of death.

This fatality rate found in our study is consistent with the scientific literature showing that mortality among HIV-positive people has decreased over the past 20 years. [18, 19] The improvement in survival recorded in this study is the result of improvements in treatment and its earlier initiation [20]. Indeed, the early initiation of ARV treatment with regular monitoring and good therapeutic compliance makes it possible to obtain lasting viral suppression leading to improved survival with a better quality of life and a reduction in viral transmission. This objective can be achieved on the one hand by better access to care with a reasonable prescription of antiretrovirals and on the other hand by the implementation of a screening strategy allowing early knowledge of the patient's serological status with a prompt referral to a proper care service.

Conclusion

Our study shows that the deaths of HIV-infected patients occur within the first 12 months after the ARV treatment starts and are significantly associated with delayed diagnosis and late initiation of antiretrovirals. Strengthening screening, early initiation of ART, strengthening the therapeutic arsenal of antiretrovirals, are the main factors to be taken into consideration in order to reduce mortality in HIV-infected patients.

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