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HIV Care Patterns among Inhabitants of Urban and Rural Areas at the Time of the 90-90-90 Goal Adoption in Gabon, Central Africa

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ABSTRACT

Introduction: *Antiretroviral treatment (ART) and the prevention of opportunistic diseases are key factors in assessing the effectiveness of HIV control programs. This study assessed the level of ART and cotrimoxazole coverage, and associated factors in HIV-infected persons (PLHIV) in Gabon.*

Methods: *This was a retrospective study which included data from PLHIV aged over 15 years and attending their routine follow-up visits from February to June 2018 at three HIV care and treatment outpatient centers. The use of antiretroviral treatment (ART) and cotrimoxazole (CTX) prophylaxis, age, gender, the time from diagnosis to the last visit were recorded.*

Results: *Data of 927 PLHIV were analyzed. More than two-thirds were women. The median age was 43 [35-52] years, the median CD4+T cell count was 352 [177-533]/mm^3. ART and CTX chemoprophylaxis coverage were 83.9% and 39.2% respectively. Among the 778 PLHIV on ART, 68.8% had recent CD4+T cell measurements, whereas this proportion was higher (78.5%) in the absence of ART ($p=0.01$), and 19.2% ($n=60/324$) were eligible for ART. A higher proportion of PLHIV in the rural city received second-line treatment ($p<0.01$). Rural participants more frequently received CTX prophylaxis (49.7% vs. 37.1% in the urban city; $p<0.01$). Overall, 53.1% of patients with recent HIV diagnosis, 26.9% of those with an opportunistic infection and 16% of the immunosuppressed ones were not on ART nor under CTX chemoprophylaxis*

Conclusion: *ART coverage is still under 90% and CTX chemoprophylaxis coverage is still low in Libreville. HIV testing and early ART initiation of should be promoted at outpatient center.*

Keywords

ART, Cotrimoxazole, USS, Gabon.

List of abbreviations

ART: Antiretroviral therapy, PLHIV: People living with HIV, CTX: Co-trimoxazole, CTA: Outpatient Treatment Center.

Introduction

The current decrease in HIV mortality is mainly attributed to HIV care and the increased use of antiretroviral treatment (ART). Indeed, when diagnosed early, a young HIV-infected person can live a normal life if ART is promptly started [1,2]. In 2014, the United Nations' program on HIV and AIDS (UNAIDS) and its partners proposed a program made up of three 90-90-90 [3,4] targets with the ambition of ending the HIV/AIDS epidemic by 2020. The goals of the program stipulate that 90% of all persons living with HIV will know their HIV status, 90% of them will receive antiretroviral treatment (ART), and among the latter, 90% will have viral suppression [3,5-7]. Thus, each person with HIV (PLHIV) must be included in and follow the HIV care continuum (also known as the HIV treatment cascade) which includes, after a positive HIV diagnosis, a link to care, ART initiation and retention which leads to viral suppression for adults and adolescents [8]. This cascade can be used to evaluate HIV care performances and track progress towards the 90-90-90 targets. A review on the availability of national HIV care continuum highlighted the lack of data from sub-Saharan Africa despite the fact that this area continues to carry the highest HIV/AIDS burden. Indeed, the data is available for less than 10 countries outside Southern and Eastern Africa, and among the 19 countries with viral suppression estimates, only four were from Western and Central Africa [9].

Like many other African countries, Gabon has also adopted the gold-standard policy of test and treat in 2022. In 2022, according to the Health and Demographic Survey of Gabon, the global prevalence of the HIV among 15- to 49- years-old adults was 2.9%, 4.5% being women and 1.4% men [10]. This prevalence, wich varies by province, was lower in the province of Ogooue-Ivindo (3.2%) and Woleu-Ntem (3.5%) [11]. This prevalence is close to the 2.1% reported 20 years ago, and despite the fact that HIV/AIDS care treatment centers (CTC) have been implemented in the nine provinces of the country [12]. Moreover, reports from public health centers frequently highlight the significant number of individuals hospitalized in emergency units or patients in the late stage of AIDS hospitalized in internal medicine departments (unpublished data).

Although efforts in HIV care and control are led locally, very few or no data regarding the national care continuum are available in the public domain and therefore cannot be used in a comparison at the regional level. Moreover, providing national or local collective data with a worldwide recognized collecting methodology such as the HIV continuum indicators will not only be useful for program monitoring and evaluation, but also help to identify lacks, to set priorities or adapt strategies to achieve the 90-90-90 targets of the UNAIDS program.

This study reports HIV care and treatment coverage as well as immunological and demographic factors of PLHIV who were aware of their HIV status in urban and rural care treatment centers of Gabon.

Materials and Methods

This prospective cross-sectional study was conducted from February to June 2018 in urban (Libreville) and rural (Koulamoutou) areas of Gabon.

Study type and areas

The population of this country, located in Central Africa, was estimated at 1.865.058 between inhabitants in 2018, with more than 52% living in urban and semi-urban areas. According to an UNAIDS report, there were approximately 3000 new infections and 1300 AIDS related deaths each year in Gabon at the time of study periods [10].

The study sites were:

- The Tropical Infectious Disease Centre and the Military Hospital in Libreville, the capital city located in the Estuaire province where HIV prevalence was estimated at 4% [11].
- The Ambulatory Treatment Center of Koulamoutou, a rural town located in the south-east of Gabon. In this area, the population is estimated at 16,222 inhabitants and HIV prevalence is estimated at 2.5% [11].

Study population and data

This was a prospective and cross-sectional study. Patients aged above 15 years old living with HIV (PLHIV) and attending their routine follow-up visits in the three HIV care and treatment centers (CTC) were invited to participate in the study. Informed consent was obtained and then eligible participants completed the questionnaire which was administered by trained reviewers during face to face interviews. Recorded information included demographic characteristics, education and date of HIV diagnosis. The CD4+ cell counts from the last three months were obtained from patient files. Anti-retroviral treatment (ART) type and duration, cotrimoxazole (CTX) use and duration of prophylaxis were also recorded. According to the national guidelines, the drugs administered as first line ART were Zidovudine or Tenofovir plus Lamivudine plus Efavirenz or Nevirapine. Abacavir or Zidovudine plus Didanosine plus Lopinavir/r were the second line treatments.

The CD4 cell count was performed at each CTC using a FACSCaliburt Machine (BD Biosciences). CD4 T-cell counts were categorized according to the Ministry of Health and HIV national control program guidelines at the time of the study, as low or advanced stage (<200/µL), moderate or chronic stage (200–350/µL) and high or asymptomatic stage (≥350/µL). CTX prophylaxis was recommended for patients with less than 350CD4+cells/µL at the time of the study.

Sampling

Sample size estimation was performed according to the CTX and ART coverage of 50% and 80% previously reported in Gabon (Janssen, 2015). The sample size calculation was based on 5% precision with 95% level of confidence and an expected prevalence of 50% and 80%, by using the following formula for sample size calculation for prevalence study[22]: $N= (Z^2x\ p(1-p))/d^2$ with Z=1.96; p = previous coverage d= precision. Therefore, a

minimum of 385 screened individuals was necessary. Considering the cross-sectional design of the study and taking into account the fact that the absence of health worker training on specific data record during PLHIV routine visits would be responsible for missing information, an increase of 20% of the needed sample size was adopted. Therefore, a minimum of 462 PLHIV should be included.

Data management and statistical analysis

The generated data were entered into an excel file, reviewed, then imported and analyzed using STATA 13.0 (Statacorp, College Station, USA). Patient characteristics were summarized using medians and interquartile ranges for continuous variables and proportions for categorical variables. Differences between groups were assessed using the chi-squared or Fisher's exact tests if there were less than five expected values for proportions. Student's *t*-test and analysis of variance (ANOVA) or the Kruskal-Wallis test were used, as appropriate, for continuous variables.

According to the IAPAC guidelines, PLHIV linked to care were those who sought care for their HIV infection upon diagnosis; newly diagnosed patients were those who entered HIV care within one month after their HIV diagnosis and at the time of the study period; late presenters where those who had their first visit more than one year after their HIV diagnosis and were at the WHO clinical stage 3 or 4 and/or with a CD4 cell count below 200/mm^3; patients "on ART" were those on ART the day of the interview; patients "not on ART" or "not on CTX" were those who had not been on ART or CTX the last 12 months preceding the interview; immunosuppressed individuals were those with a CD4 cell count below 200/µL.

Ethical approval

This study was part of an evaluation regarding the coverage of an antiretroviral treatment with cotrimoxazole in the HIV population and received the approval of the Ministry of Public Health and the National Ethics Committee (**PROT N°003/2018/SG/CNE**). Participation was fully anonymous and written informed consent was obtained before data record and analysis.

Results

General characteristics of the population living with HIV

A total of 927 patients living with HIV were enrolled in the study and interviewed. More than two thirds were women (Table 1). Median age was 43[35-52] years, significantly lower in women (40[33-50] years) compared to men (48[31-56] years (p<0.01), and the elderly approached 20%. Half (53.7%; n=492/917) were officially single. The majority resided in the capital Libreville, an urban area, and had received a secondary education level or more (76.3%, n=664/870). HIV infection had been newly diagnosed for 81 participants.

Apart from those attending the CTC for the first time, 79.0% (n=652/825) had a recent CD4+ cell count measurement, among them 30.1% (n=196) had a count below 500/mm^3 and 54.4% were late presenters. Overall, 28.7% of participants were immunosuppressed, and this value was more significant among the newly diagnosed (34.1%, n=62/182) compared to the others (26.8%; n=123/459; p=0.04). Indeed, quantitative analysis showed that the median CD4+T cell count was 352[177-533]/mm^3 and also significantly lower among the newly diagnosed (260[126-446]/mL *versus* 355[181-533]/mL; p<0.01).

After compiling the data generated by the interviews and the patient files, it was found that 83.9% of participants were on ART and 39.2% under CTX prophylaxis (Table 1). The majority (84.7%) was on first line treatment and 15.3% on second line ART.

Table 1: General characteristics of the population living with HIV.

Variables	N	%
Gender (N=927)		
Men	296	31.9
Women	631	68.1
Age group (N=927)		
< 20 years	16	1.7
20 – 54 years	747	80.6
≥ 55 years	164	17.7
Area of residence (N=927)		
Rural area	179	19.3
Urban area	748	80.7
Marital status (N=917)		
In Couple	425	46.3
Single	452	49.3
Divorced	21	2.3
Widowed	19	2.1
Highest education achieved (N=870)		
Primary or less	206	23.7
Secondary	474	54.5
High school	190	21.8
Time from diagnosis to present visit (N=906)		
Month of interview	81	8.9
≤ 1 year	168	18.5
2 – 5 years	315	34.8
6 – 10 years	221	24.4
> 10 years	121	13.4
CD4+ T-cell count measurement (N=652)		
< 200/mm^3	187	28.7
200-350/mm^3	137	21.0
> 350/mm^3	328	50.3
Treatment (N=927)		
ART only	458	49.4
CTX only	43	4.6
ART + CTX	320	34.5
1st line ART	659	84.7
2nd line ART	119	15.3
None	106	11.5
Opportunistic infection (N=927)		
No	608	65.6
Yes	290	34.4

ART and CTX coverage according to the residing areas

Regarding the area of residence, ART coverage was comparable between urban and rural centers. However, a higher proportion of

PLHIV from the rural city were on second line treatment (p<0.01; Table 2). Likewise, participants from these settings were more frequently receiving CTX prophylaxis (49.7% vs 37.1% in the urban city; p<0.01) (Table 2).

Table 2: ART and CTX coverage according to the residence areas.

	RURAL AREA N(%)	URBAN AREA N(%)	*P*
ART	154 (86.0)	624 (83.4)	0.29
1rst line	99 (64.3)	560 (89.7)	<0.01
2nd line	55 (39.7)	64 (10.3)	<0.01
CTX	86 (48.0)	277 (37.1)	<0.01
ART + CTX	79 (44.1)	241 (32.2)	<0.01

Characteristics of PLHIV according to ART and CTX intake

No significant association was found between age, education level and ART or CTX use (Table 3). One third of the participants were on ART and CTX prophylaxis (Table 1). Women (not significantly) received more frequently ART and CTX. These treatments were also more frequent among the younger patients (not significantly) with a 2-5 years HIV infection duration (Table 3). The rate of participants under CTX prophylaxis was significantly higher in the group with an HIV infection diagnosed less than 6 years ago and those with a low CD4+T cell count (p<0.01). The second "90" target was only achieved in participants with an HIV infection diagnosed for more than two years (Table 3). Among the 778 PLHIV on ART, 68.8% had recent CD4+T cell measurements while this proportion was greater (78.5%) in the absence of ART (p=0.01), although 19,2% (n=60/324) where eligible to ART. Furthermore, the rate of immunosuppressed individuals was also greater in this group (41/0%, n=48/117) compared to those on ART (26.0%; n=139/535) (p=<0.01). 12.6% of patients with a CD4+ cell count below 200/mm^3 were on second line treatment.

All the participants with a CD4+T cell count between 200 and 350/mL who were on ART were also under CTX, while 18.7% and 15.0% of immunosuppressed PLHIV or with a high count, respectively, were under CTX without ART.

The proportion of participants without any treatment was the highest among those with opportunistic infection and/or a CD4+T cell count below 200/mL, the newly diagnosed patients and men (Table 3).

Table 3: Characteristics of HIV-infected patients who were currently receiving ART and/or CTX.

Variables	On ART only			On CTX only			On ART+CTX			Not on ART nor CTX		
	N	%	*p*	N	%	*p*	N	%	*p*	*N*	%	*p*
Gender			0.16			0.47			0.89			0.09
Men	146	48.8		13	4.3		98	32.8		42	14.1	
Women	315	49.9		30	4.8		222	35.2		64	10.1	
Age group			0.91			0.33			0.08			0.83
< 20 years	8	50.0		1	6.2		6	37.5		1	6.2	
20 – 54 years	363	48.6		36	4.6		264	35.3		84	11.3	
≥ 55 years	87	53.0		7	4.3		49	29.9		21	12.8	
Marital status			0.56			0.04			0.16			0.32
Married or in a relationship	226	53.2		11	2.6		136	32.0		52	12.2	
Single	202	44.7		28	6.2		170	37.6		52	11.5	
Divorced	13	61.9		2	9.5		6	28.6		0	0.0	
Widowed	10	56.6		1	5.3		6	31.6		2	10.5	
Highest education achieved			0.63			0.07			0.89			0.45
Primary	107	51.9		8	3.9		68	33.0		23	11.2	
Secondary	211	45 .3		26	5.3		175	36.9		57	12.0	
High school	107	56.3		8	4.3		55	28.9		20	10.5	
Time from diagnosis to present visit			<0.01			<0.01			<0.01			<0.01
Month of interview	13	16.1		13	16.1		12	14.7		43	53.1	
≤ 1 year	79	47.1		12	7.1		57	33.9		20	11.9	
2 – 5 years	166	52.4		9	2.9		130	41.3		11	3.5	
6 – 10 years	126	57.0		4	1.8		74	33.5		17	7.7	
> 10 years	69	57.0		4	3.3		42	34.7		6	5.0	
CD4+ T-cell count			<0.01			<0.01			<0.01			<0.01
< 200	61	32.6		18	9.6		78	41.7		30	16.1	
200-350	58	62.3		0	0.0		65	47.5		14	10.2	
> 350	188	57.3		15	4.6		85	25.9		40	12.2	
Opportunistic infection			0.01			0.99			<0.01			<0.01
No	390	64.2		127	20.9		111	18.3		28	4.6	
Yes	5	1.0		0	0.0		209	72.1		78	26.9	

Opportunistic infection

WHO clinical stage was recorded for 350 PLHIV, the majority of them (n=266; 76.0%) were in the WHO clinical stage 3 or 4 at the time of the visit, with no difference regarding the HIV infection duration (Table 1). A proportion of 77.2% were also considered as late presenters. Opportunistic infections was the cause of HIV diagnosis in 30.9% (n=64/249) of the newly diagnosed patients (Table 1). Tuberculosis (n=110; 31.4%), zona (n=62; 17.7%) and candidiasis (n=30; 8.6%) were the main opportunistic infections.

Discussion

The HIV continuum of care, which includes HIV diagnosis, linkage to HIV medical care and maintaining viral suppression, is essential for the monitoring of HIV and for the prevention of transmission of the virus [13]. This study assessed ART and CTX coverage and associated immunological and demographic factors in PLHIV living in Gabon.

HIV infection predominates in the sexually active young population, aged 15 to 49 years old. Studies in Côte d'Ivoire and Burkina Faso have reported similar age groups [14,15]. A non-negligible proportion of patients over 55 years of age (17.7%) was also found in the study population. This is in accordance with current epidemiological data on HIV aging in the elderly [16]. In addition, women were predominantly represented (68.1%; n = 631/927). These results are comparable to those found elsewhere, where female predominance was also recorted (77.7%) [14]. Indeed, anatomical, physiological, sociocultural and economic factors, the prevention of mother-to-child transmission intervention that allows the screening and care of pregnant women, poverty and prostitution contribute to the feminization of HIV infection [17].

ART coverage was high (83.9%). Moreover almost all patients under 20 years of age were on ART with or without co-trimoxazole chemoprophylaxis. The majority were children born from HIV-infected mothers, as mother-to-child transmission being the primary mode of HIV transmission among children under 15 in sub-Saharan African countries [19]. These children are likely to benefit from DOT supervised by their parents. Furthermore, adolescents are more exposed to factors of poor continuum of care, including poor adherence to treatment and follow-up, poor retention in care, lower virologic suppression rates and higher mortality rates [20,21].

The majority of patients on ART had at least of secondary school level. The proportion of patients receiving co-trimoxazole alone was higher in this group. These results are consistent with other studies which report that a low level of education is an obstacle to starting treatment [22,23]. In addition, more than half of the patients (53.1%) who had been in care since less than one month were not on CTX or ART. Despite the 2017 WHO recommendations to initiate treatment on the day of diagnosis or within seven days, this delay in initiating antiretroviral therapy seems to be common like observed in Uganda and South Africa where only 35% of patients were on treatment, nine months after starting treatment [24,25]. The delay found in Libreville could be explained by an entry into care at an advanced stage of the disease, mostly with the presence of opportunistic infections, which must be treated initially before the initiation of the ART. Indeed, Gabon and Sierra Leone, reports from Gabon and elsewhere highlighted that almost 30% of PLHIV who enter into care are at who stage 3 or 4 or with CD4 cell count be low 100/mm3 [26,27]. ART coverage was 93.7% ($p < 0.01$) for patients followed between 2-5 years of age reaching the second UNAIDS population target of 90%. These results are similar to those found by other authors in sub-Saharan Africa [28,29]. More than half of the PLHIV (62.3%) with CD4 cell count between 200 and 350/mm^3 were on ART and without CTX chemoprophylaxis. Other wiser Of the 187 severely immunocompromised patients, 9.6% were only on CTX and 16% (n=30) had no therapeutic management.

This underlines the non-compliance with the 2014 and 2018 guidelines on the initiation of prevention with cotrimoxazole and ART regardless of CD4 cell count and WHO stage, in settings where malaria and/or severe bacterial infections are widespread [18,24]. Tugume et al. in Uganda also reported a high failure of early initiation of ART [30].

More than half of the patients who were on the combination ART and cotrimoxazole had opportunistic infections (n=209; 72.1%) ($p < 0.01$) according to Ousley at al. [31]. The latter certainly motivated this practice. The occurrence of these opportunistic diseases may also be related to immune reactivation syndrome in these immunocompromised patients. However, the absence of ART and CTX would explain the existence of opportunistic infections in the 78 patients presented in Table 3. It therefore appears that the initiation of ART and CTX remains more after motivated by the occurrence of opportunistic infections and a CD4 cell count < 200/mm3. Indeed, Table 3 shows that only 25.9% of patients with CD4 counts > 350/mm3 benefit from these treatments.

Limitations

This study, which is the first in Gabon, has limitations. It concerned two PLHIV outpatient ambulatory units, therefore the results cannot be extrapolated to the general population. However, the size of the population studied already allows to consider the present data. Likewise, the retrospective design of the study did not provide reliable information on the duration and adherence to treatment, as well as on economic and psychological factors that could explain that ART coverage still below the objectives. However, this present results could serve as baseline data, which can be compared with other regional settings and which can be and used by public health decision makers. There is a need for multi-center studies in the country to update algorithms for the achievement of 95-95-95 targets by 2030.

Conclusion

ART coverage is still below the second target at the ''90, 90, 90''. HIV testing and early initiation of ART would reduce the high coverage prevalence of opportunistic infections and

immunosuppression. The Factors associated with low coverage this be highlighted in order to improve the continuum of care of PLHIV from Gabon and to reach the'95, 95, 95'.

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