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Research Article

Seroprevalence and Associated Risk Factors for Human Herpesvirus 8 Infection among People Living with HIV in Pointe-Noire and Dolisie, Republic of Congo

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ABSTRACT

Background: Human herpes virus-8 (HHV-8) is a tumor virus causing Kaposi's sarcoma, primary effusion lymphoma, and multicentric Castleman's disease. The seroprevalence of HHV-8 infection varies in various geographical areas, and HIV infection is a major risk factor that promotes the reactivation of HHV-8 after establishment of the latent phase. Despite the HIV burden in Congo, limited data exist on HHV-8 seroprevalence and its associated risk factors. This study aimed to determine the seroprevalence of HHV-8 and identify risk factors for human herpesvirus 8 infection among people living with HIV in Pointe-Noire and Dolisie.

Methods: A cross-sectional study was conducted between september 2023 and june 2024 among HIV patients receiving highly active antiretroviral therapy. Participants were recruited from Adolphe Sicé Hospital and the Regional Military Hospital in Pointe-Noire and Dolisie, respectively. Blood samples were collected, and all plasma were tested for anti-LANA-1 IgG using a commercial ELISA kit. HIV viral load was quantified using the GeneXpert system. Statistical analyses were performed using SPSS Statistic version 27.0.1 software, with $p < 0.05$ considered statistically significant.

Results: A total of 412 PLWH were recruited with an average age 47.18 ± 11.79 years, and female were more represented 75.1% (n=310). The overall seroprevalence of HHV-8 was 12.83% (53/413). HHV-8 seroprevalence was higher in Pointe-Noire 11.86% (49/413) compared to Dolisie 0.97% (4/413). HHV-8 seropositivity was significantly associated with employment status (aOR = 2.48, 95% CI: 1.04–5.91, p = 0.04) and condom use (aOR = 4.91, 95% CI: 1.1-21.85, p = 0.03). There were no significant associations of HHV-8 infection with age, sex, marital status, education level, blood transfusion, multiple sexual partners and injecting drug use.

Conclusion: Our study demonstrated the presence of HHV-8 in these locations. These findings indicate that employment status and occasional condom use influence HHV-8 transmission in this population and highlight the need for targeted preventive strategies.

Keywords

Seroprevalence, HHV-8, Risk factors, People living with HIV.

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Introduction

The human herpesvirus type 8 (HHV8), also known as Kaposi's sarcoma-associated herpesvirus (KSHV), is an oncogenic virus belonging to the Herpesviridae family [1]. It was first identified from kaposi's sarcoma (SK) tissue in a patient with acquired immunodeficiency syndrome (AIDS) [2]. HHV-8 is the causative agent of malignancies and lymphoproliferative disorder, including all forms of KS (classic, endemic, iatrogenic and epidemic), primary effusion lymphoma (PEL), multicentric Castleman's disease (MCD), and is also implicated in immune reconstitution inflammatory syndrome (IRIS) and kaposi sarcoma inflammatory cytokine syndrome (KICS) [3-6].

Globally, HHV-8 seroprevalence varies widely depending on the geographical area and sub population, with a North–South gradient [7]. In sub-saharan Africa, 30-50% of the population is infected with HHV-8 [8]. HHV-8 infection is endemic in many countries in this region, for example, epidemiological studies have reported HHV-8 seroprevalence in general population of 50% in Uganda, 48.3% in Gabon and 37.2% in Cameroon [9-11].

HHV-8 infection can be transmitted via both sexual and non-sexual routes. HHV-8 can be found in the peripheral blood mononuclear cells (PBMCs), saliva, oropharyngeal mucosa, semen, cervico-vaginal secretions, and prostate glands, which may represent the source of both vertical and horizontal transmission [12].

HIV infection is a main risk factor for the development of HHV-8-associated malignancies [8,13]. The interaction between HIV and HHV-8 leads to increased HHV-8 viral load and enhances the risk of complications, including rapid progression to KS and other related tumors [13]. People living with HIV (PLWH) are approximately 800 times more likely to develop KS compared to the general population, making KS the most common cancer among PLWH [14]. In Republic of Congo, the prevalence of HIV among people aged 15 to 49 years is 3.2% [15], while HHV-8 seroprevalence among PLWH in Brazzaville has been reported at 19 % [16].

Despite these findings, data on HHV-8 infection remain unknown in some regions. To address the lack of data of HHV-8 infection in this population group in Pointe-Noire and Dolisie, we investigated on the seroprevalence of HHV-8 infection and associated risk factors among people living with HIV in these two urban cities.

Material and Methods

Study Areas

The study was conducted in two cities, Pointe-Noire and Dolisie, located in the south part of the Republic of Congo (Figure 1). Pointe-Noire, the second-largest city lies on the Atlantic coast and Dolisie is the third-largest city in the Republic of Congo, it is located in the northeast of Pointe-Noire. Participants were recruited the at Adolphe Sicé Hospital and the Regional Military Hospital in Pointe-Noire and Dolisie respectively.

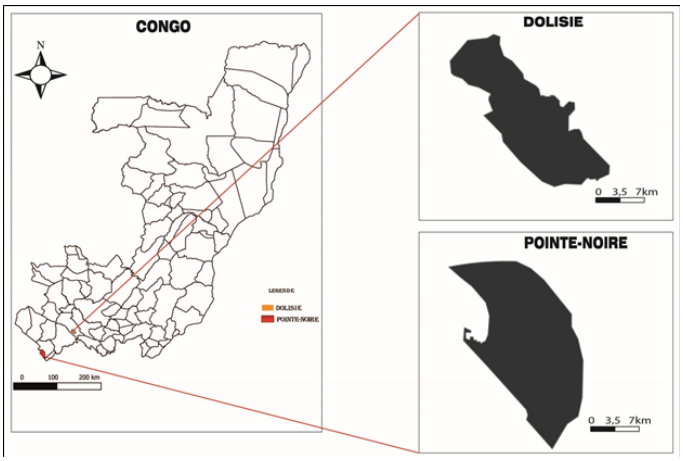

Figure 1: Map indicating the study areas (Pointe-Noire and Dolisie).

Study Population

A descriptive cross-sectional study was carried out between September 11, 2023 and June 2024. In total, 413 particpants (≤ 18 years) under highly active antiretroviral therapy (HAART), including 318 from Pointe-Noire and 95 from Dolisie.

Data and Sample Collection

A questionnaire interview was conducted for all participants to collect information on sociodemographic characteristics and sexual behaviors. For each participant, blood samples were collected in two EDTA (Ethylene Diamine Tetraacetic Acid) tubes. One tube was used for HIV viral load testing, which was performed directly at different collection sites using the GeneXpert system. The second tube was transported to the molecular biology and virology laboratory of the Marie Madeleine Gombes Foundation, where all analyses were performed. Plasma was obtained after centrifugation and stored at -20°C until analyses.

HHV-8 Serelogy

All plasma samples were tested for the presence of HHV-8 antibodies using a commercial enzyme linked immunosorbent assay (ELISA) kit (anti-HHV-8 IgG ELISA kit cat: SL2685Hu, Sunlong Biotech, Hangzhou, China) following the manufacturer's instructions. The ELISA is based on the qualitative enzyme immunoassay technique. The microplate provided in this kit has been pre-coated with the latency associated nuclear antigen -1 (LANA-1), make it to solid-phase antigen. Negative and positive controls were included in the kit. The cut-off value was calculated by this formula: average OD values of the negative controls + 0.15. Samples were considered positive if the sample OD value was above the cut-off value. The equivocal HHV-8 serology results were re-tested and interpreted according to the cut-off value.

Ethics Statement

This study received authorization from the faculty of health sciences of Marien Ngouabi University, Adolphe Sicé Hospital and the Regional Military Hospital. Before enrollment, written informed

consent was obtained from each participant. Approvals were obtained from the Health Sciences Research Ethics Committee (reference number: 089 / MESRSIT /DGRST/ CERSSA/-25).

Statistical Analysis

Statistical analyses were performed using SPSS Statistic version 27.0.1 software. Qualitative variables were expressed as numbers and percentages, whereas quantitative variables were presented as mean, standard deviation (SD) and numbers. Associations between HHV-8 seropositivity and qualitative variables were evaluated by chi-square (χ^2) test, and quantitative variables were assessed using the Student's t-test. To identify risk factors associated with HHV-8 infection, univariate and multivariate analyses were carried out based on logistic regression models. Results were presented using odds ratio (OR) with 95% confidence intervals (CI), and p-value of less than 0.05 was considered statistically significant.

Result

Sociodemographic characteristics, behavioral factors and HHV-8 seroprevalence

A total of 413 participants were recruited in the study, included 77% (n=318) in Pointe-Noire and 23% (n=95) in Dolisie. The mean age of participants was 47.18 ±11.79 years and 75.1% (n=310) were female. Most of participants 97.8% (n=404) were Congolese nationality, and 61.5% (n=254) were single. Additionally, 65.4% (n=270) had attained the secondary level, and 65.4% (n=270) were employed. The large majority of them, 68.5% (n=283) reported using occasionally condoms before HIV diagnosis. Furthermore, 92% (n=380) did not receive a blood transfusion and 99.76% (n=412) did not use intravenous drugs. However, half of the participants reported having at least two sexual partners and 61.5% (254) presented with an HIV viral load of less than 1,000 copies/ml (Table 1). The overall seroprevalence was of 12.83% (53/413).

Risk Factors Associated with HHV-8 Infection

Multivariate analysis, with ORs adjusted for age, education level, and multiple sexual partners in the final model, showed no statistically significant association between HHV-8 seropositivity and the variables tested. However, the univariate analysis showed that employed participants were less likely to be HHV8 positive compared to unemployed individuals (OR = 0.40, 95% CI: 0.19 - 0.81, p = 0.012). However, after adjustment, the association reversed, with employed participants showing a significantly higher odd of HHV8 infection (aOR = 2.48, 95% CI: 1.04–5.91, p = 0.04). They had had two fold risks to be infected compared to unemployed participants. Furthermore, participants who reported "sometimes" using condoms had seven folds risk to be infected compared to those who mentioned "always" (OR = 6.70, 95% CI: 0.83 –22.04, p = 0.012). After adjusting, the association remained significant (aOR = 4.91, 95% CI: 1.1 - 21.85, p = 0.03).

Discussion

Studies on HHV-8 infection are important in regions, such as Africa, where a significant proportion of the continent is infected with immunosuppressive agents, such as HIV [17]. In Brazzaville, previous studies showed a prevalence of HHV-8 infection at 19% among PLWH [16] and 4.9% among blood donors [18]. Nevertheless, the seroprevalence of HHV8 in Pointe-Noire and Dolisie did not determine. This study is the first to provide important insights into the seroprevalence and associated risk factors of HHV-8 infection among PLWH in these two cities of Congo.

We found an overall seroprevalence of 12.83%, with a higher prevalence in Pointe-Noire (11.86 %) compared to Dolisie (0.97%) (p= 0.004). These findings demonstrate a geographical disparity in HHV-8 distribution and this can be explained by imbalance in sample size.

Our findings highlight the presence of HHV-8 in this population and suggest a risk of HHV-8-related complications, particularly in the context of immunosuppression. Our result is in agreement with the previous studies in Brazil (13.9%) and Japan (12%) among HIV/AIDS patients [19,20], and in Mali (10.4%) among blood donors [21]. It is relatively close to that reported in Brazzaville [16], but higher than that reported in Turkey (3%) [22] among PLWH. However, in other sub-Saharan African countries, where both HIV and HHV-8 are endemic, HHV-8 seroprevalence rates among PLWH exceed 50% [23,24] and our findings are not consistent with those previously reported. The observed differences in these studies could be due to the fact that they employ different serological assays with different sensitivity and specificity to detect HHV-8 antibodies and different antigens, either lytic or latent. This may also be explained by the timing of the tests. It is possible that infection was recent or in the seroconversion phase, a period during which antibodies (IgG) are not yet detectable by standard serological assays, thus leading to an underestimation of the true seroprevalence. But, there is currently no gold standard serological assay for HHV-8.

Moreover, our study demonstrated that HHV8 seroprevalence was associated with employment status. Univariate analysis indicated that being employed was associated with a lower risk of infection (OR = 0.40, p = 0.012). However, multivariate analysis revealed a **reversal of this association**, with employed participants being more than twice as likely to be infected (aOR = 2.48, p = 0.04).

HHV-8 infection was also associated with high risk sexual behavior such as inconsistent condom use. This association between the inconsistent condom use and HHV-8 seroprevalence has previously been observed in others studies [25]. Although HHV-8 is not exclusively a sexually transmitted infection, this result supports the role of sexual behavior as a key transmission route, particularly in HIV-infected individuals where immunosuppression may increase susceptibility.

One key limitation of this study is the absence of CD4 count data, which is a critical marker of immune status in people living with HIV and strongly influences the reactivation and progression of

Table 1: Sociodemographic characteristics and behavioral factors according to HHV-8 serological status.

Characteristics	Total n (%)	HHV8-seropositive n(%)	HHV8-seronegative n (%)	p-value
All	413 (100)	53 (12.83)	360 (87.17)	
Age				
(mean ± SD), years	47.18 ± 11.79	50.26 ± 11.15	46.72 ± 11.83	
Cities				
Pointe-Noire	318 (77)	49 (11.86)	269 (65.13)	0.004
Dolisie	95 (23.0)	4 (0.97)	91 (22.04)	
Sex				
Male	103 (24.9)	13 (3.15)	90 (21.8)	0.941
Female	310 (75.1)	40 (96.8)	270 (65.37)	
Age group, years				
18 - 38	99(24)	9 (2.18)	90 (21.79)	0.039
39 - 58	239 (57.9)	29 (7.02)	210 (50.85)	
> 58	75 (18.7)	15 (3.63)	60 (14.53)	
Nationalities				
Congolese	404 (97.8)	50 (12.11)	354 (85.72)	0.189
DR Congolese	5 (1.2)	2 (0.48)	3 (0.73)	
Cameroonian	1 (0.2)	0 (0)	1 (0.24)	
Rwandan	2 (0.5)	1 (0.24)	1 (0.24)	
Malian	1 (0.2)	0 (0)	1 (0.24)	
Marital status				
Single	254 (61.5)	32 (7.75)	222 (53.75)	0.98
Married	95 (23)	13 (3.15)	82 (19.85)	
Widown	58 (14)	7 (1.7)	51 (12.35)	
Divorced	6 (1.5)	1 (0.24)	5 (1.21)	
Education level				
Uneducated	10 (2.4)	0 (0)	10 (2.42)	0.044
Primary	54 (13.1)	4 (0.97)	50 (12.11)	
Secondary	248 (60)	41 (9.92)	207 (50.12)	
Superior	101 (24.5)	8 (1.94)	93 (22.52)	
Employment				
Unemployed	143 (34.6)	10 (2.42)	133 (32.2)	0.01
Employed	270 (65.4)	43 (10.41)	227 (54.97)	
Condom use (before knowing the HIV status)				
Sometimes	283 (68.5)	47 (11.38)	236 (57.14)	0.002
Always	104 (25.2)	3 (0.73)	101 (24.45)	
Never	26 (6.3)	3 (0.73)	23 (5.57)	
Multiple sexual partners (at least 2)				
Yes	201 (48.7)	43 (10.41)	158 (38.26)	< 0.001
No	212 (51.3)	10 (2.42)	202 (48.91)	
Blood transfusion				
Yes	33 (8)	4 (0.97)	29 (7.02)	0.899
No	380 (92)	49 (11.86)	331 (80.15)	
Injecting drug use				
Yes	1 (0.24)	1 (0.24)	0 (0)	0.09
No	412 (99.76)	52 (12.6)	360 (87.17)	
HIV viral load (copies/ml)				
ND	118 (28.57)	9 (2.18)	109 (26.4)	0.434
< 1000	254 (61.5)	42 (10.17)	212 (51.33)	
1000 - 10000	14 (3.38)	0 (0)	14 (3.4)	
> 10000	27 (6.53)	2 (0.48)	25 (6.05)	

Table 2: Univariate and multivariate analyses of associations between selected variables and HHV-8 infection.

Variables	HHV8 infection n (%)	Univariate analysis		Multivariate analysis	
		OR (95% CI)	p-value	aOR (95% CI)	p-value
Age group, years					
18 - 38	9 (2.18)	Referent		Referent	
39 - 58	29 (7.02)	1.38 (0.62 - 3.03)	0.42	1.16 (0.5 - 2.67)	0.71
> 58	15 (3.63)	2.5 (1.02 - 6.079)	**0.04**	2.10 (0.8 - 5.53)	0.13
Education level					
Uneducated	0 (0)	Referent		Referent	
Primary	4 (0.97)	0	0.99	0	0.99
Secondary	41 (9.92)	0.93 (0.26 - 3.24)	0.9	1.05 (0.27 - 4.09)	0.94
Superior	8 (1.94)	2.3 (1.03 - 5.10)	**0.04**	1.82 (0.79 - 4.34)	0.15
Employment					
Unemployed	10 (2.42)	Referent		Referent	
Employed	43 (10.41)	0.397 (0.19 - 0.81)	**0.012**	2.48 (1.04 - 5.91)	**0.04**
Condom use (before knowing the HIV status)					
Always	3 (0.73)	Referent		Referent	
Sometimes	47 (11.38)	6.70 (2.03 - 22.04)	**0.002**	4.91 (1.1 - 21. 85)	**0.036**
Never	3 (0.73)	4.39 (0.83 - 23.16)	0.081	2.42 (0.39 - 14.93)	0.34
Multiple sexual partners (at least 2)					
Yes	43 (10.41)	Referent		Referent	
No	10 (2.42)	0.182 (0.89 - 0.37)	< **0.001**	0.49 (0.19 - 1.29)	0.152

HHV-8 infection.

Conclusion

In conclusion, our results highlight the presence of HHV-8 among PLWH in these localities. Employed participants and those with inconsistent condom use were more likely to be HHV-8 seropositive, indicating that socioeconomic and sexual behaviors factors may play key roles in transmission. These findings emphasize the need for targeted preventive strategies and improved monitoring, particularly given the lack of CD4 data, which limits understanding of the immunological context of HHV-8 infection in this population.

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