SEROPREVALENCE OF CYTOMEGALOVIRUS, EPSTEIN-BARR VIRUS AND HERPES SIMPLEX VIRUSES IN CHILDREN BORN HIV POSITIVEAT THE YAOUNDÉ UNIVERSITY TEACHING HOSPITAL, CAMEROON

ABSTRACT

Aims: The aim of our study was to determine the seroprevalence of four herpes viruses that are cytomegalovirus (CMV), Epstein-Barr virus (EBV), Herpes Simplex virus 1 (HSV-1) and 2 (HSV-2) in HIV-positive patients in Yaoundé.
Study design: It was a prospective cross-sectional study.
Place and Duration of Study: Sample: Yaounde University Teaching Hospital and Department of Microbiology, Faculty of Sciences, University of Yaounde I, between November 2020 and April 2021.
Methodology: We included 74on people living with HIV born HIV positive, on antiretroviral treatment (23men, 51 women; age range 3-19 years), and whose medical file was complete and available within the ATC. IgG/IgM antibodies against HSV-1, HSV-2, CMV, and IgM against EBV were qualitatively determined by Rapid Diagnostic Tests, for the detection of these pathogens. The statistical analysis was done using IBM SPSS version 22.0, the Fischer exact, the Khi-square and the Mann–Whitney tests were used.
Results:A total of 74 participants were enrolled in the study with a female predominance of 68.92% (n=51/74).The average age of our serie was 9.05±5.09years, and a majority of participants was under 10 years old(56.76%, n=42/74).HSV-1, HSV-2, EBV and CMV Seroprevalences were 93.24 %, 93.24 %, 22.97 % and 12.2 % respectively. Other parameters such as sex, age, stage of disease, smoking and alcohol consumption were significantly associated with the seropositivity of these *herpesviridae*.
Conclusion: Despite the absence for most of the clinical manifestations related to HSV-1 and HSV-2, it was strong to note a high circulation of those virus in HIV infected patients, mainly in bi and tri co-infections.

Comment [J.1]: Lack of background at Abstract, study design : better to describe analysis data used, population and sample

Keywords:Children, HIV, EBV, CMV, HSV-1, HSV-2, herpesvirus, seroprevalence.

1. INTRODUCTION

Human Immunodeficiency Virus Infection (HIV) remains a real health problem, from the discovery of HIV in 1981, and particularly in sub-saharan Africa, and according to the data of the National AIDS Control Committee (CNLS), Cameroon in 2021, the prevalence of HIV infection was 3.1% [1]. HIV infection promotes exogenous infections or reactivation of solely controlled infections, with the LTCD4+ lymphopenia. With the weakening of the immune system, the reactivations concern more tuberculosis and the oncogenic viruses such as herpes virus [2].
Herpesviridae are a family of managerial virus such as Kaposi Sarcoma and lymphomas, opportunistic infections of HIV/AIDS [3]. The Epstein-Barr virus (EBV)and cytomegalovirus (CMV) are involved in infectious monocleosis and associated lymphomas, while the type 8 human herpes virus (HHV8) enters I the occurrence of Kaposi Sarcoma (KS) and associated

Comment [J.2]: It would be better to add information on how phenomena from other studies on the contents of CYTOMEGALOVIRUS, EPSTEIN-BARR VIRUS AND HERPES SIMPLEX VIIRUSES in HIV patients

lymphomas. The immunosuppressionof the individual, obesity, excessive alcohol and smoking considers as risk factors for the emergence of these viruses [4,5]. Although Cameroon is an endemic zone for human herpes virus, and the work done by Njiki et al., In 2015 showing that there is very little information on the epidemiology of HHV8 infection particularly that associated with HIV infection [6], the finding remains with other viruses of the same family. The purpose of our study was therefore to determine the seroprevalence of four HSV-1, HSV-2,EBV and CMV in patients born HIV positive at the Yaounde University Teaching Hospital (YUTH).

2. MATERIAL AND METHODS

2.1STUDY DESIGN AND CONTEXT

It was a prospective cross-sectional study, performed for a period of 6 months, from November 2020 and April 2021, at the YUTH, on patients who came for consultation or were followed at the Approved Treatment Center (ATC). For every participant who completed the inclusion criteria, a written informed consent was obtained from the parents, and a technical sheet had to be filled by each participants, providing the socio-demographic and clinical status as age, sex and HIV infection.

Comment [J.3]: How about ethical clearance in this study?, and then, in the Material a method better to describe about the population and sample

2.2 DATA COLLECTION TOOL AND PROCEDURE

These data were completed and/ or confirmed by the patient's medical record. Then a sampling of venous blood into an EDTA tube of 5 ml was made and the samples taken then transported to the Microbiology Laboratory of the Faculty of Science. At the laboratory, afer centrifugation (at 1300 tours/min for 10 min, between (18-24°C), the plasma obtained was kept in a freezer at -25°C, for the later serological research of the infectious agents [7]. According to the manufacturer's instructions, the kit and samples to be tested were first brought to room temperature. For the detection of IgM and IgG antibodies directed against CMV, HSV-1 and HSV-2 micro-organisms, the *OneStep TORCH IgM/IgG Kit(TOX IgM/IgG, RV IgM/IgG, CMV IgM/IgG, HSV-1/-2 IgM/IgG (Bioneavanco.LTD., NO.18 KeYuanLU, GongYeKaiFaQu, Huang Cun Zhen AaXing County, Beijing) was used, and for the detection of IgM antibodies directed against EBV, the kit Diagnostic Rapid Epstein-Barr(EB)-IgM antibodies was used according to the kit manufacturer's instructions (Bioneavanco.LTD., Beijing).* The test card was placed on a dry horizontal work surface, then 30 µl of sample plasma added on top. When the sample migration was found to be difficult, 20 µl of sample dilution solution was added immediately, and an additional 50 µl of the same solution 5 minutes later. 15 to 20 minute after the addition of the plasma, the different results were observed [8].

2.3 Data Management and Analysis

For each participant, data on parameters of interest gathered through interviews and by blood analysis were recorded and processed using Excel 2016, and the statistical analysis was done using IBM Statistical Package for Social Science Version 22.0. on the one hand, we used the Fisher exact and the Khi-sqaure tests to compare qualitative variables between groups, while on the other hand, we used the Mann-Whitney test to compare quantitative variables. All *P*values below 0.05 were considered significant.

3. RESULTS

3.1 *Sociodemographic and clinical parameters:*

The average age in the study was 9.05±65.09 years, the children were in majority (56.76%, n=42/74) under 10 years old and female gender (68.92%, n=51/74).18/74 children (24.32%)

were smoke and 17/74 concerned by alcohol consumption (22.97%). HIV-1 infection was the most encountered in our cohort, with 94.60% of participants at WHO stage I of the disease. According to medical records, the most commonly used protocol was Tenofovir-Lamivudine-Efavirenz (TDF/3TC/EFV) with 79.73% of participants.

Table 1: Baseline characteristics of the participants

Characteristics	Number	Percentage(%)
Sexe		
Male	23	31.08
Female	51	68.92
Ages (Years)		
]0-5[	17	22.97
[5-10[	25	33.78
[10-15[	16	21.62
[15-20[	16	21.62
WHO stage		
I	70	94.6
II	4	5.4
III	0	0
IV	0	0
Type of HIV		
HIV I	70	94.6
HIV II	4	5.4
HIVI +HIV II	0	0
Protocol of treatment		
Frist measure		
TDF/3TC/EFV	59	79.73
TDF/3TC/ATV	5	6.76
TDF/3TC/NVP	1	1.35
TDF/3TC/D	0	0
TDF/3TC/LPV	0	0
AZT/3TC/EFV	4	5.4
AZT/3TC/NVP	5	6.76

3.2 Seroprevalence of *Herpesviridae*:The seroprevalence of cytomegalovirus was 12.2% (n=9/74), that of HSV-1 at 93.24%(n=69/74), that of HSV-2 at 93.24% (n=69/74) that of EBV was 22.97%(n=17/74). Seropositivity for HSV-1 and HSV-2 was statically associated with HIV infection (*P*<.05) (Table 1). Our participants presented multi-infections to *herpesviridae*. The majority of co-infections found was HSV-1/HSV-2 93.24 % (n=69) (Table 2). The co-infections found concerned all age groups(Table 3). Ages ranging from 10 to 19 years concentrate the greatest number of co-infections, and all the consumption of alcohol(n=17/74) and tobacco (n=18/74) (Table 3).

Table 2: Distribution of participants according to IgM/IgG antibodies against HSV-1, HSV-2, CMV and IgM against EBV results

Infections agent	Result	Number(n)	Percentage (%)	$IC_{95\%}$	*P*Value
CMV(IgG	Positive	9	12.2	[5.6-22.6]	0.8
	negative	65	87.84	[78.16-94.29]	

EBV (IgM)	Positive	17	22.97	[13.99-34.21]	0.6
	Negative	57	77.03	[65.79-86.01]	
HSV-1(IgG)	Positive	69	93.24	[84.93-97.77]	0.04
	Negative	5	6.67	[2.23-25.07]	
HSV-2(IgG)	positive	69	93.24	[84.93-97.77]	0.04
	Negative	5	6.76	[2.23-15.07]	

Table 3: Distribution of participants according to *Herpesviridae* co-infections

Infections	**N(%)**	**$IC_{95\%}$**
HIV-1	5(6.8)	[2.23–15.07]
HIV-1/CMV/EBV/HSV-1/HSV-2	2(2.70)	[0.33–9.42]
HIV-1/CMV/HSV-1/HSV-2	6(8.1)	[3.03–16.82]
HIV-1/CMV/RV/HSV-1/HSV-2	1(1.35)	[0.03–7.30]
HIV-1/EBV/HSV-1/HSV-2	11(14.86)	[7.66–25.04]
HIV-1/HSV-1/HSV-2	43(58.1)	[46.06–69.49]
HIV-1/RV/EBV/HSV-1/HSV-2	1(1.35)	[0.03–7.30]
HIV-1/RV/HSV-1/HSV-2	1(1.35)	[0.03–7.30]
HIV-2/CMV/HSV-1/HSV-2	1(1.35)	[0.03–7.30]
HIV-2/EBV/HSV-1/HSV-2	1(1.35)	[0.03–7.30]
HIV-2/HSV-1/HSV-2	1(1.35)	[0.03–7.30]

Legend : HSV-1/-2 : Herpès simplex Virus-1/-2 ;HIV-1: Human immunodeficiency virus type 1; HIV-2: Human immunodeficiency virus type 2 ; CMV : Cytomegalovirus ; EBV: Epstein-Barr virus, RV: Rubella virus

Table 4: Frequency of HIV infection according to age group and comorbidities

Age group (years)	**Number n (%)**	**Number of co-infection found**	**Alcohol consumption n (%)**	**Tobacco intake n (%)**
] 0-5[	17 (22.97)	17	0	0
[5-10[	25 (33.78)	24	0	0
[**10-15**[	16 (21.62)	16	3 (4.05)	9 (12.16)
[15-20[	16 (21.62)	16	14 (18.91)	9 (12.16)
		Total 74 (100)		

3.2 DISCUSSION

Our study revealed a female predominance (68.92%, n=51/74) with an average age of 9.05±5.09 years, the majority of participants were under 10 years. A study conducted by Njimba et al., at the cite verte subdivisional Medical Centre of Yaounde in 2016, reported 66% of women [9]. This obervatio corroborates the feminization of the HIV pandemic, which is a major trend. Currently 50% of people living with HIV in the worl are women, with this rate

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reaching 59% in sub-saharan Africa, the region most affected by the epidemic. Certainly, the risk of contamination during sexual intercourse is greater among theme, but they are also in a

situation of greater social and economic vulnerability, and therefore greater exposure to risks, particularly in relation to AIDS [10]. The age groups obtained during our study follow the concerned population trend of PLHIV in Cameroon [11]. Most of our participants were under TDF/3TC/EFV treatment protocol (79.73%), a first-line regimen. This protocol is a preferred option in countries with limited resources, because it is simple, inexpensive, in combined form and can be used in HIV/HBV, HIV/BK and in pregnant and breastfeeding women [1].

In our study, IgG seroprevalence were 93.24% for HSV-1,93.24% for HSV-2, 12.20% for CMV, IgM seroprevalence was 22.97% for EBV. This high antibody seroprevalence demonstrates the widespread circulation of these viruses in the population, confirming the status of an endemic area for herpes viruses [6]. Also to date, population changes her sexual practices, such as oral sex associated with sociocultural changes, may explain the increasing trend of these infections [5]. The majority of co-infections between *herpesviridae* found concerned HSV-1, HSV-2 and EBV. EBV and CMV co-infections appear to be more frequent in the literature. A possible explanation is that most of the patients in this cohort, although hospitalized, were seen in outpatient care [12]. Testing for the presence of CMV infection is particularly important for HIV-positive patients to assess disease severity and monitor response to treatment. The influence of factors not investigated in this study such as genetics, nutritional status, socio-economic conditions could explain these a priori weight results concerning the prevalence of CMV [13].

Ages ranging from 10 to 19 years concentrate the greatest number of co-infections, and risk factors for the occurrence of these co-infections (alcohol and tobacco consumption). If alcohol acts as a behavioral risk factor in acquisition of HIV, it also acts at the biological level through its immuosuppressive role increasing susceptibility to infections by reducing the inflammatory response[14], thus finding the smoking which is also associated with the metabolic complications of certain antiretroviral[3]. These data underline the need to implement preventive actions, particularly with regard to the consumption of alcohol and increased dietary support when stopping smoking [15].

4. CONCLUSION

Our study allowed us to evaluate the co-infection of four *herpesviridae* (EBV, CMV, HSV-1 and 2) in children born HIV positiveat the YUTH. This study highlighted a high risk of herpesvirus infections among PLHIVborn HIV positive**,** in ages ranging from 3 to 19 years,

especially among women. The seroprevalences of these viruses were high and their association with children clinical profile highlights their risk factors. HSV-1, HSV-2 and EBV seroprevalences were lower in coinfection than in monoinfection. The prevalence of these viruses demonstrates their high endemicity in Cameroon.

CONSENT

As per international standards or university standards, participants written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

It is applicable

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