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Ocular Findings in HIV-Positive Children in Two Hospital Facilities in Yaoundé, Cameroon

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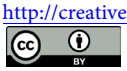

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Abstract

Background: HIV infection in children as well as adults remain a disease with potential multisystemic disorders despite the increased use of Highly Active Antiretroviral Therapy (HAART). The aim of this work was to determine the profile of eye diseases among HIV-positive children aged 5 to 15 years in the Mother and Child Centre of the Chantal Biya Foundation and the University Hospital Centre (UHC) in Yaoundé. **Materials and Methods:** an analytical study was conducted from June 1, to July 31, 2019. Our sample consisted of all children aged 5 - 18 years who were HIV positive and whose parent or legal guardian gave his or her consent. A complete clinical examination was performed. The following variables were collected: socio-demographic data, Immunological data. A comprehensive eye exam was also performed. Data were analysed by the Epi info 3.5.4 software. **Results:** A total of 53 children were retained for the study. The population consisted of 28 boys (52.3%), for a sex ratio of 1.12. The mean age was 12.7 ± 4.2 years [5 - 18 years]. And 84.9% of children had normal immune status. The average duration of HAART was 8.3 ± 3.9 years [0 to 16 years] with more than half (50.9%) of the children on treatment for more than 8 years. The main eye complaints were pruritus (11.32%), eye pain (11.32%) and tingling (9.43%). The frequency of ophthalmological manifestations was 52.8% with adnexal involvement the most frequent (34%), followed by anterior (7.5%) and posterior segment involvement (1.9%). Anterior segment involvement was marked by granulomatous anterior uveitis, keratouveitis and corneal ulcer. A cytomegalovirus retinitis and a macular scar of a unilateral retinitis were found in 2 patients. In a multivariate analysis, elevated CD4 count (>500) was associated with ocular manifestations. **Conclusion:** In the HAART era, an ocular examination is mandatory to prevent harmful eye diseases among children because ophthalmological

diseases remain frequent. Although they are most often lesions of the annexes, corneal and chorioretinal involvement can be detrimental for the vision.

Keywords

HAART, Children, HIV, Retinitis, Uveitis, Eye, CD4

1. Introduction

HIV infection leads to the destruction of immune system cells, resulting in the deterioration of the immune system and the development of opportunistic infections, the most advanced of which is acquired immunodeficiency syndrome (AIDS) [1].

In 2018, according to UNAIDS, 37.9 million people worldwide were living with HIV, including 1.7 million children under the age of 15 [2]. In the course of HIV infection in children as well as adults, there is a multisystemic approach to the disease. The ocular complications of HIV in adults are well described in the literature in contrast to the few studies in children. Nevertheless, the prevalence of ocular involvement during HIV infection in children varies from 20% to 54% depending on the study [3]. These show that the risk for these children to develop ophthalmological diseases is higher in cases of severe immunodeficiency and/or high viral load [3] [4]. In addition, the profile of these manifestations in children differs from that in adults with a predominance of opportunistic infections [5].

Awareness of these complications is important as they can lead to uni- or bilateral blindness, which severely impairs the quality of life of these children, who may not always be able to express their visual discomfort [6]. They can occur at any stage of the disease course, with prognosis depending on early diagnosis and prompt management [3].

Thus, the objective of this work is to determine the frequency and describe the ophthalmological manifestations in HIV-infected children aged 5 to 18 years in hospital settings in Yaoundé.

2. Materials and Methods

After obtaining the ethical authorizations, an analytical study was conducted from June 1 to July 31, 2019 at the Mother and Child Centre of the Chantal Biya Foundation (CME-FCB) and at the Paediatrics Department of the University Hospital Centre (CHU) in Yaoundé. Our sample consisted of all children aged between 5 and 18 years tested positive for HIV and whose parent or legal guardian had given free and informed consent. The exclusion criteria was any child who did not have a follow-up check-up no more than 6 months ago.

Procedure

A complete clinical examination was performed. The following variables were collected: socio-demographic data, age of discovery of HIV disease, level of im-

munosuppression at the time of diagnosis of HIV disease, last CD4 count, last viral load, clinical grade of the HIV infection according to WHO, duration of the highly active antiretroviral treatment (HAART), current protocol and current complaints.

The ophthalmological examination consisted of a measurement of distance visual acuity with and without an optical correction using a Monoyer chart, the study of ocular motricity, the Schirmer I test. The examination of the adnexa and anterior segment as well as the fluorescein test were performed using a slit lamp. The examination of the fundus was performed with the VOLK 90D lens after pupillary dilation with Tropicamide 0.5% eye drops. Retinophotography was performed in patients with posterior segment lesions using a Topcon retinograph.

Statistical analysis

The data collected was analysed by the Epi info 3.5.4 software. The comparison of proportions was done using the Chi2 test and for small numbers, the exact Fischer test. The OR was used to measure the association between binary qualitative variables. For the multivariate analysis, the logistic regression test was used. The significance level was for a value of $p < 0.05$.

3. Results

A total of 53 children were included in the study. The population consisted of 28 boys (52.3%), for a sex ratio of 1.12. The mean age of the children was 12.7 ± 4.2 years with extremes ranging from 5 to 18 years. The age group 15 years and older was the most represented (Figure 1).

Immunological features

At the time of the ophthalmologic examination, 45 (84.9%) children had no immune deficiency, 4 (7.5%) had moderate and 2 (3.8%) had advanced immune deficiency (Table 1).

At the time of diagnosis, 47.2% of children had normal immune status compared to 84.9% at the time of ophthalmological examination (Figure 2).

The grade of the disease

At the time of diagnosis of HIV infection, 32 (60.3%), 10 (18.9%), 10 (18.9%), and 1 (1.9%) children were at grade I, grade II, grade III, and grade IV respectively. However, at the time of the ophthalmologic examination, 52 and 1 children were in grade I and grade IV respectively. The child in grade IV was not yet on second-line HAART.

The average duration of antiretroviral treatment was 8.3 ± 3.9 years with extremes ranging from 0 to 16 years. More than half (50.9%) of the children were on treatment for more than 8 years.

Ophthalmological diseases

The main eye complaints were pruritus (11.32%), eye pain (11.32%) and tingling (9.43%) (Table 2).

All patients had uncorrected visual acuity in the better eye greater than 0.3.

The frequency of ophthalmological manifestations was 52.8%.

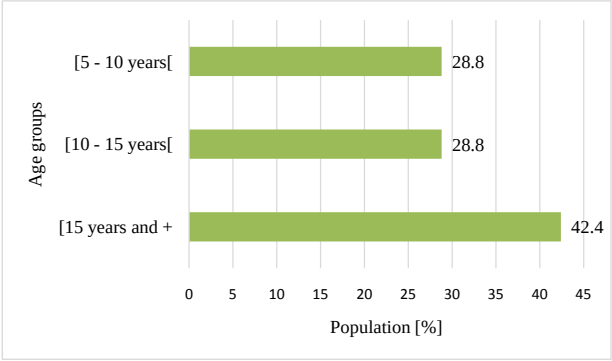

Figure 1. Distribution of children according to age groups.

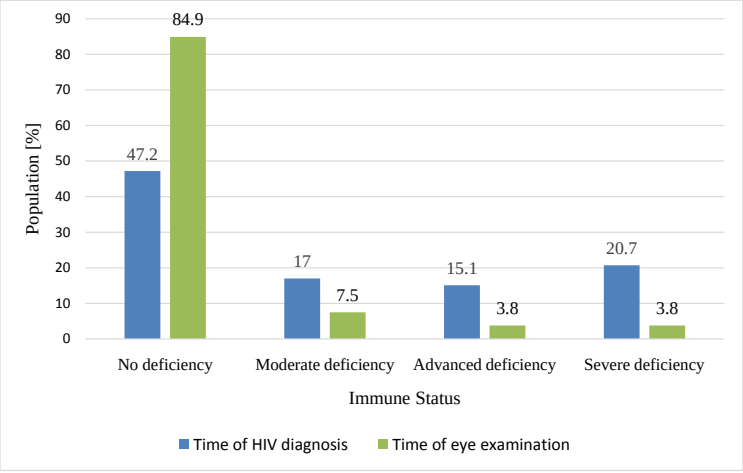

Figure 2. Distribution of children by immune status at the time of HIV diagnosis and at the time of the eye examination.

Table 1. Immunological grading at the time of ophthalmological examination.

Immune deficiency	Number (n)	Percentage (%)
Absent: >500 cell/mm^3	45	84.9
Moderate: 350 - 449 cell/mm^3	4	7.5
Advanced: 200 - 349 cell/mm^3	2	3.8
Severe < 200 cell/mm^3	2	3.8
	53	100.0

Table 2. Distribution of eye symptoms in the study population.

Plaintes oculaires	Number (n =53)	Percentage (%)
Eye pruritus	6	11.32
Eye discomfort	6	11.32
Eye tingling	5	9.43
Tearing	4	7.55
Decreased distance visual acuity	3	5.66
Eye redness	1	1.89
Photophobia	1	1.89
Headache	1	1.89

Adnexal involvement was most frequent (n = 36; 34%), followed by anterior and posterior segment involvement in 8 (7.5%) and 2 (1.9%) eyes respectively.

Adnexal disease was dominated by dry eye and allergic conjunctivitis in 32 and 8 eyes respectively (Table 3).

Anterior segment involvement was marked by unilateral granulomatous anterior uveitis, unilateral keratouveitis with severe immune deficiency with CD4 = 52 cell/mm^3, unilateral corneal ulcer. The other 3 presented bilateral superficial punctate keratitis (KPS) in 2 children and unilateral in 1 child. KPS was associated in 2 cases with dry eyes and in 1 case with allergic conjunctivitis.

Two patients had posterior segment involvement: unilateral cytomegalovirus retinitis (Figure 3) and a macular scar of unilateral chorioretinitis (Figure 4). The child with CMV retinitis had a severe immune deficiency with CD4 counts of 20 cells/mm^3 and was not yet on HAART.

Factors associated with ophthalmologic manifestations in uni- and multivariate analyses are shown in Table 4 and Table 5. The univariate analysis (Table 4) showed that sociodemographic variables (age and sex) were not associated with ophthalmological manifestations in HIV-infected children. In addition, viral load was not related to ocular findings. Concerning the immune status, only a CD4 count higher than 500 was linked to ophthalmological disorders as a protective factor (p = 0.04; OR = 0.13).

In the multivariate analysis (Table 5), the CD4 count was associated with ocular manifestations (p = 0.028).

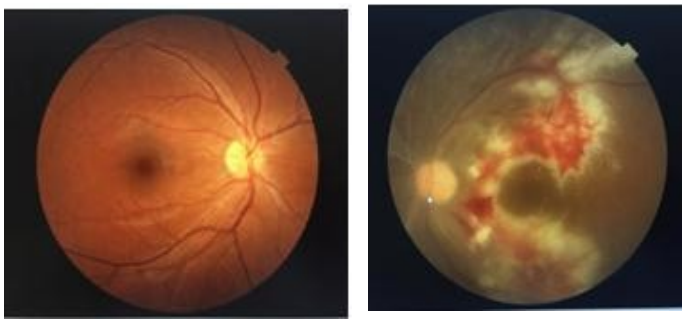

Figure 3. A Patient with CMV retinitis.

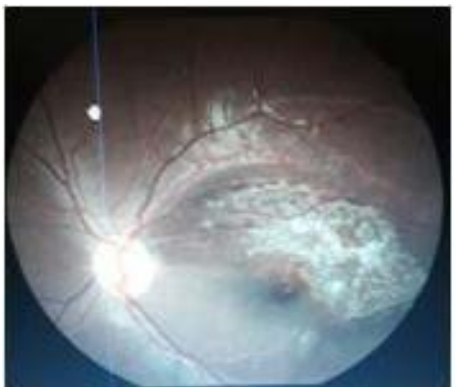

Figure 4. A patient with a cicatricial site of CMV retinitis.

Table 3. Distribution of ophthalmological manifestations.

Ophthalmological manifestations	Number (N = 106)	Percentage (%)
Dry Eye syndrome	32	30.1
Allergic conjunctivitis	8	7.5
Purulent conjunctivitis	2	1.9
Tropical endemic limbo-conjunctivitis	4	3.8
Superficial punctate keratitis	5	4.7
Anterior granulomatous uveitis	1	0.94
Keratouveitis	1	0.94
Corneal ulcer	1	0.94
Cytomegalovirus retinitis	1	0.94
Macular scar of retinitis	1	0.94

Table 4. Factors associated with ocular manifestations (univariate analysis).

	Ocular manifestations				
	Yes	No	Total	OR (IC 95%)	p value
	N = 28	N = 25			
Variables	**n (%)**	**n (%)**	**n (%)**		
Sex					
Male	15 (53.6)	13 (46.4)	28 (52.8)	1.07 (0.35 - 3.2)	0.560
Female	13 (52)	12 (48)	25 (47.2)	0.94 (0.31 - 2.83)	0.560
Age (ans)					
[5 - 10]	9 (60)	6 (40)	15 (28.3)	1.5 (0.44 - 5.33)	0.360
[10 - 15]	10 (66.7)	5 (33.3)	15 (28.3)	2.22 (0.63 - 8.33)	0.170
[15 et +]	9 (39.1)	14 (60.9)	23 (43.4)	0.37 (0.12 - 1.16)	0.070
Duration of treatment (years)					
[0 - 5]	6 (75)	2 (25)	8 (15.1)	3.14 (0.58 - 24.16)	0.160
[5 - 10]	14 (53.8)	12 (46.2)	26 (49.1)	1.08 (0.36 - 3.26)	0.550
[10 et Plus]	8 (42.1)	11 (57.9)	19 (35.8)	0.51 (0.16 - 1.63)	0.190
CD4 (cell) count					
[20 - 200]	2 (100)	0 (0)	2 (3.8)	-	0.270
[200 - 350]	2 (100)	0 (0)	2 (3.8)	-	0.270
[350 - 450]	3 (75)	1 (25)	4 (7.5)	2.88 (0.28 - 78.76)	0.350
[500 et +]	21 (46.7)	24 (53.3)	45 (84.9)	0.13 (0.01 - 0.93)	0.040
Viral load (particles)					
0	20 (57.1)	15 (42.9)	35 (66)	1.67 (0.52 - 5.4)	0.280
[1 - 100,001]	5 (45.5)	6 (54.5)	11 (20.8)	0.69 (0.17 - 2.74)	0.420
[10,001 - 50,000]	1 (33.3)	2 (66.7)	3 (5.7)	0.43 (0.01 - 6)	0.460
[50,001 et +]	2 (50)	2 (50)	4 (7.5)	0.88 (0.09 - 9.09)	0.650

Table 5. Factors associated with ocular manifestations (multivariate analysis).

CD4 (cell) count	Odds Ratio (ajusted)	95%	C.I.	p value
[500 et +]	0.0761	0.0076	0.7571	**0.028**

4. Discussion

The authors report the frequency and ocular diseases in children aged 5 to 18 years with HIV in hospital settings in Yaoundé. The present study reveals a frequency of manifestations of 52.8% comparable to the data in the literature which indicates that the frequency of ophthalmologic manifestations in HIV-infected children ranges from 20% to 54% [3]. However, this is still low compared to the adult population, where it varies between 50% and 90% [3]. Nevertheless, the frequency of eye involvement reported in the present study and in some African ones [4] [7] are higher than those reported in studies carried out on other continents: 7.7% for Esposito in Italy [8], 19.8% for Almeida in Brazil [9], 20% for Dehenny in the United States of America [10].

The mean age of the children was 12.7 ± 4.2 years. This mean age is higher than that found by Nsiangani *et al.* who found an mean age of 8.32 ± 4 years [4] and in many other studies [3] [5] [7] [10] [11]. This discrepancy could be explained by the fact that in other studies, ophthalmological examination of children was performed at the time of diagnosis of HIV infection. This was not the case in the present study.

HAART is currently available for children aged 0 - 14 years, although only 54% (37% -73%) had access to HAART in 2018 [2]. In the present study, the vast majority of children were in a clinical grade 1 of the WHO classification, and had a normal immune status. Viral load was undetectable in 33 children (62%). This result is similar to that of Yonaba, who found 43% of children with undetectable viral load and 69.6% of the children in his study did not have an immune deficiency [12]. Children in the Nsiangani series had normal immune status in 45.5% of cases, and 12.5% of children had severe immune deficiency [4]. In the present study, children with CD4 > 500 (normal immune status) had fewer ophthalmologic diseases and the difference was statistically significant. Two children with severe immune deficiency (CD4 = 20 and 52 cells/mm^3) had CMV retinitis and keratouveitis, respectively, both of which were severe ophthalmologic diseases with an ocular morbidity. There was no correlation between viral load and ophthalmologic diseases. This may be justified by the fact that the children in our series were already on a second-line protocol after treatment failure. The mean duration of antiretroviral treatment in the children was 8.3 ± 3.9 years. This average duration of treatment is higher than that found in other African studies where it varies between 2 and 5 years [4] [7]. A duration of antiretroviral treatment of >10 years was a protective factor against the development of ophthalmological diseases but the difference was not statistically significant. This could be explained by the small sample size. The aim of antiretroviral treatment

is to restore immunity by inhibiting viral replication, which would reduce the occurrence of ophthalmological diseases.

Adnexal involvement in 1 eye out of 3 in this series, as found in several other studies [4] [12] [13], is by far the most frequent ocular manifestation. Of these, dry eye syndrome is the most prevalent. According to the studies, 20% to 25% of HIV-infected children have lacrimal hyposecretion, which may be explained by HIV-mediated inflammation of the lacrimal glands. However, this lacrimal hyposecretion is not associated with the severity of the HIV infection [5]. Tropical Endemic limboconjunctivitis found in 3 eyes is an entity described by several other African authors [4] [12] to varying degrees, this form of allergic conjunctivitis is self-sustained by lacrimal hyposecretion which slows the elimination of allergenic substances that bind to the ocular surface. Padhani in 2000 [13] noted that HIV-infected children were 22 times more likely to develop conjunctival xerosis, which was favoured by a background of malnutrition and vitamin A deficiency. No cases of conjunctival xerosis were recorded. This is probably due to the systematic administration of vitamin A to these children at 6 and 11 months. Similarly, *Molluscum contagiosum* infection and conjunctival microvasculopathy described in other African studies [4] [12] [14] were not found in our study. This may be justified by the fact that the majority of our children were at grade 1 of the WHO clinical classification (98%). In addition, 84.9% of the children in our series had normal immune status.

Anterior segment involvement was present in six children (granulomatous anterior uveitis, keratouveitis, corneal ulcer and 3 cases of superficial punctate keratitis). It was associated in two cases with a dry eye syndrome and in one case with an allergic conjunctivitis. Ikoona in her study found corneal ulcers predominantly as anterior segment involvement [7]. Nsiangani in his series found only one case of anterior uveitis in a child with severe immune deficiency [4]. In our study, the child who had keratuveitis also had a severe immune deficiency with CD4 levels of 52 cells/mm^3, two of the three cases of KPS were associated with a dry eye syndrome and the third case with allergic conjunctivitis. This is a consequence of corneal exposure due to the instability of the tear film. The cases of uveitis found were not associated with immune reconstitution syndrome, the duration of HAART was 7 and 9 years respectively.

Involvement of the posterior segment was found in 2 children. Our results are similar to those of Ikoona, where CMV retinitis was found in only 4% of cases [7], Kestelyn in Rwanda recorded 3 cases (1.9%) [5]. On the other hand, in the work of Biswas in India, CMV retinitis was the most frequent ocular manifestation, accounting for 33% of cases [15]. The low frequency of CMV retinitis is thought to be justified by the increasing accessibility to antiretroviral treatment in children, which improves immune response and quality of life. The isolated cotton-wool exsudate was not found in our study. Nsiangani found 2% of cases of isolated cotton-wool exsudate in his study [4], Yonaba *et al.* recorded 1 case (14.3%) [12]. Kestelyn also obtained a rate of 1.2% [5]. Retinal vasculitis, which is the most

frequent manifestation of the posterior segment in several studies [3] [5] [7] [12], was not found in the present study. Cases of oculomotor paralysis were absent in the present study, although Ikoona found 3.1% [7], Nsiangani 5% [4]. Livingstone in the United States noted 2 cases (6%) of neurophthalmological disorders [11].

5. Limitations

The main limitation is the size of the sample. However, this study provides an overview of ophthalmologic diseases in paediatric HIV patients in the era of HAART.

6. Conclusion

In this study, the frequency of ophthalmologic findings was 52%. Good immune status is associated with ocular manifestations. Adnexal involvement is the most common, followed by anterior segment involvement. Corneal and retinal damage remain the source of significant ocular morbidity.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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