Comparison of HIV-related Ocular Involvement in HAART-naive and HAART-treated Patients

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ABSTRACT

Objective: To compare the HIV-related ocular manifestations between HAART-naïve (Highly active antiretroviral therapy) and HAART-treated patients.

Study Design: Observational (comparative) Study.

Place and Duration of the Study: Department of Ophthalmology and Family Care Centre of Hayatabad Medical Complex, Peshawar, Pakistan, from October 2019 to July 2021.

Methodology: HIV-infected patients, who were receiving HAART treatment as well as HAART-naïve, were recruited. A complete ocular examination was performed to check for HIV-related ocular manifestations. Anterior and posterior segment findings were recorded and compared between the two groups.

Results: Of the 80 participants (40 in each group), 62 (77.5%) were males and 18 (22.5) were females with no significant difference between the groups for either gender (p=1.0). A significant difference, between the two groups, was found in the mean duration (838.64 $\pm$ 908.16 days) of HIV infection at the time of recruitment (p<0.001). HIV-related ocular manifestations were found in 6 (7.5%) with no statistically significant difference between the two groups (p=1.0). Similarly, the involvement of systemic co-infections was found in 6 (7.5%) with no statistically significant difference between the groups (p=0.675).

Conclusion: There was no difference in both groups when analysed for HIV-related ocular manifestations or systemic co-infections. The authors' finding contradict with some of the previously published data. Therefore, it is recommended that further research should be carried out to reach definite conclusion.

Key Words: *HIV, Eye manifestations, Acquired immunodeficiency syndrome, Highly active antiretroviral therapy, HIV-related opportunistic infections, Pakistan*.

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INTRODUCTION

Globally, in 2020, 37.7 million (30.2 million – 45.1 million) of the population was infected with Human Immunodeficiency Virus (HIV), and 53% of them were women and girls.[1] HIV affects every organ of the body including the eye. The cumulative risk of getting ocular involvement in HIV is from 52% - 100%.[2] HIV-related ocular manifestations have been reported from the different regions but with variable results. The studies from Ethiopia have reported HIV-related ocular involvement from 25.7 % to 14.2%.[3,4]

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Pakistan, being the 5th most populous country, is put at the higher risk of HIV.[5] First case of HIV in Pakistan was reported in 1987.[6] This number has climbed to 200,000 (190,000 – 210,000) by 2020 with incidence and prevalence rates of 0.12 per 1000 and 0.2 percent, respectively.[7] Some of these ocular conditions cause irreversible visual disability or even blindness. Hence, these patients must be carefully examined for ocular involvement.

To the best of authors' knowledge, no work has been done in Pakistan to investigate this important health issue. As a result, this question remains unaddressed, and the load continues to grow without any awareness. Furthermore, a number of studies have shown that HAART (Highly active antiretroviral therapy) has reduced ocular involvement.[3,4,8,9] However, when comparing pre-HAART and HAART period patients, few researchers have observed no difference in ocular involvement.[10] Because of the disparities in reports, the need was felt to conduct a research that reflected the scope of the problem in the local population. The findings will help in developing preventive and/or treatment initiatives to assist this underserved segment of the community. This study aimed to compare the

ocular manifestations in HIV-infected patients who were HAART-naive (pre-HAART group) and those who were already receiving HAART (HAART group).

METHODOLOGY

This was an observational (comparative) study conducted at the Department of Ophthalmology and Family Care Centre of Hayatabad Medical Complex (HMC), Peshawar, Pakistan. The participants were recruited from October 2019 till July 2021 through consecutive sampling method. Ethical approval was obtained from the Ethical Committee of Hayatabad Medical Complex, Peshawar (Ref. No. 179/HEC/B&PC/19). This study adhered to the standards of the Declaration of Helsinki and informed written consent was taken from each participant. All the diagnosed cases of HIV were screened at The Family Care Centre of HMC and were enrolled if the eligibility criteria was met. Those, who were newly diagnosed and HAART-naïve, were assigned to the pre-HAART group, whereas those, who were already on HAART treatment, were assigned to the HAART group. Patients of all the genders between the ages of 18 and 60 years, patients who were newly diagnosed and had not yet started HAART therapy, as well as those who had already started HAART were eligible. Patients with diabetes mellitus or hypertension were excluded because their signs could be mistaken for HIV microangiopathy. Those with a history of ocular injuries, intraocular surgery (excluding cataract surgery), or eye injections were also excluded.

Eligible participants from both groups were examined in the Ophthalmology Department, and biodata were collected. The best-corrected visual acuity (BCVA), intraocular pressure (IOP), anterior segment examination, and posterior segment examination with a 78 dioptre condensing lens were performed. A third-year resident completed the examination and in the event of any ocular findings, the consultant's opinion was sought. All the data were recorded on predesigned proforma by the same resident.

The overall sample size was computed as 74 (37 in each group) using a 95% confidence level, 80% power, and a frequency of ocular manifestations of 60%[8] in the pre-HAART era and 25.7%[3] in the HAART era. The sample size was calculated via the OpenEpi website.

For statistical analysis, IBM SPSS Statistics for Windows, version 24 (IBM Corp., Armonk, N.Y., USA) was used. Descriptive statistics for categorical variables were calculated in the form of frequencies and percentages for both groups. For continuous variables, mean and standard deviations were calculated. An independent sample t-test was used for the comparison of means between the two groups. For comparison of categorical variables between the two groups, the chi-square test and Fisher exact tests were used to find out the association. A p-value of <0.005 was considered significant.

RESULTS

A total of 80 participants were included in the study (40 in each group). The baseline demographics are given in Table I. The majority were males 62 (77.5%) with equal distribution in each group. The mean age of the participants was 34.9 ± 10.37 years with a statistically significant difference between the two groups ($p=0.029$). There was a statistically significant difference in the duration of HIV infection between the two groups; 232.23 ± 189.1 days for pre-HAART *versus* 1445.05 ± 938.39 days for HAART ($p<0.001$). Most were illiterate 28 (35.5%), labourers 21 (26.3%), and the mode of HIV infection was unknown in 30 (37.5%).

The association of both groups with HIV-related ocular manifestations and systemic co-infections were analysed. The HIV-related ocular manifestations were present in 6 (7.5%) of the participants with no statistically significant difference ($p >0.99$). The HIV-related systemic co-infections were present in 6 (7.5%) of the participants with no statistically significant difference ($p >0.675$). Hepatitis B cases in the pre-HAART (HAART-naive) group were 2 (5%), while Hepatitis C and sexually transmitted disease cases were 1 (2.5%) each. In the group receiving HAART, there was 1 (2.5%) case of Hepatitis C, 1 (2.5%) case of pulmonary TB, and 0(0) cases of hepatitis B and STD. Ocular findings of both groups are given in Table II. There was no anterior segment abnormality in 131 (81.9%) and no posterior segment abnormality in 141 (88.1%) of the total 160 eyes.

DISCUSSION

This study compared HIV-related ocular manifestations in two groups (pre-HAART *versus* HAART). To the best of authors' knowledge, this is the first report from Pakistan that has investigated this health problem. While it is likely that the ocular involvement in the HAART group will be much lower, no difference was identified in this study. At the time of recruitment, most of the studied participants had experienced no ocular complaints. Similarly, no ocular abnormalities were found in more than 3/4th of the studied subjects in either group. However, several other ocular findings were discovered for which other consultants' expert opinion was sought.

Six (7.5%) participants in this study reported HIV-related ocular manifestations with 5 (6.25%) of them having cotton wool spots and one having Kaposi sarcoma. Vasculitis and concomitant vitreous haemorrhage with retinal detachment were also seen in two cases (one each). These were not labelled as secondary to HIV because HIV-related retinal vasculitis was still unclear. Although there have been case reports of retinal vasculitis connected to HIV in people of all the ages, more research is needed.[11,12] According to the experts, retinal vasculitis in these people may be caused by secondary infections such as syphilis rather than HIV.[13] In contrast to other studies, the prevalence of HIV-related ocular manifestations in this study is low. Previous Ethiopian research has indicated prevalence rates ranging from 21.4 to 25.7% in their community.[3,14,15] In the same country, a recent study found a prevalence rate of 14.2%.[4] These studies were conducted under different times in different populations and under different study conditions. All these differences account for the disparities in results within the same country.

Table I: Demographics of study participants.

Characteristics		Pre-HAART Group (n = 40)	HAART Group (n = 40)	p-value
Gender, n (%)	Males, 62 (77.5)	31 (77.5)	31 (77.5)	>0.99[w]
	Females, 18 (22.5)	9 (22.5)	9 (22.5)	
Mean age in years (SD)	34.9 (10.37)	32.38 (0.19)	37.43 (10.72)	0.029[Y]
Duration of HIV in days (SD)	838.64 (908.16)	232.23 (189.1)	1445.05 (938.39)	<0.001[Y]
BCVA in LogMAR (SD)	0.07 (0.17)	0.063 (0.19)	0.07 (0.11)	0.83[Y]
IOP in mmHg (SD)	13.01 (3.21)	12.7 (3.74)	13.25 (3.22)	0.48[Y]
Eye symptoms, n (%)	Absent, 57 (71.3)	31 (77.5)	26 (65)	0.323[t]
	Present, 23 (28.8)	9 (22.5)	14 (35)	
Treatment given, n (%)	No treatment is required, 44 (55)			
	Conservative, 20 (25)			
	Referred to vitreoretinal consultant, 12 (15)			
	Referred to oculoplastic consultant, 2 (2.5)			
	Referred to glaucoma consultant, 2 (2.5)			

[Y]Independent sample t-test. w = chi-square test, t = fisher's exact test. Fisher's exact test, Chi-square test. n = number of participants, % = percentage, SD = standard deviation, HAART = Highly Active Antiretroviral Therapy, BCVA = Best corrected visual acuity, LogMAR = Log of minimum angle of resolution, IOP = intraocular pressure, and mmHg = millimetre of mercury.

Table II: Ocular findings of the participants.

Ocular findings (n=160)		Frequency (n)	Percentage
Anterior segment	No abnormality	131	81.9
	Visually non-significant cataract	16	10
	Corneal opacity	3	1.9
	Visually significant cataract	1	0.6
	Blue dot cataract	3	1.9
	Bitot spots	1	0.6
	Conjunctival concretions	2	1.3
	Kaposi sarcoma	1	0.6
	Esotropia	2	1.3
Posterior segment	No abnormality	141	88.1
	Maculopathy (non-specific)	4	2.5
	Cotton wool spots	5	3.1
	Vasculitis	1	0.6
	Combined VH and RD	1	0.6
	Drusen	2	1.3
	Disc cupping	3	1.9
	Retinal lesion (non-specific)	1	0.6
	Retinal degeneration	2	1.3

n = number of eyes examined, VH = vitreous haemorrhage, RD = retinal detachment.

A study from Ghana, another African country, found a greater risk of HIV-related ocular problems despite the use of HAART. They reported that 48% of their study participants had at least one ocular complication due to the HIV.[16] Studies from Asia have published different results. A research group from Taiwan in a recent study reported a prevalence of 4.6% in their participants.[17] While results from India reported a high prevalence rate of 38% - 41.67% when they compared HAART *versus* pre-HAART group.[10] Another study of 1000 consecutive HIV patients from India reported that 68.5% of them had ocular involvement.[18] All of these published studies indicate that there is a great deal of variety globally on this topic which is why each country must research this issue on its own level and ability.

No significant difference in ocular involvement between both groups (pre-HAART *versus* HAART) was found in this study. Even though some researchers have stated that HAART therapy reduces ocular involvement, no change was noted in this study. In an Ethiopian research of 348 HIV-positive patients, the prevalence of ocular manifestations was observed to be significantly higher in the HAART (32.6%) group than in the pre-HAART (17.9%) group.[14] It is worth noting that the pre-HAART group had a lower prevalence. The authors did not provide an explanation for this difference, but it may be because the patients were recruited from the two different facilities, and treatment regimens at both centres may have differed resulting in this difference. A research from India, on the other hand, showed no difference (38% in HAART *versus* 41.6% in pre-HAART).[10] Similar findings were reported in this paper, but the PGIMER study enrolled patients at two separate times; pre-HAART from January 1999 to February 2000 and HAART from October 2009 to March 2010, whereas recruitment in this study was done at the same time. The duration of HIV infection was most likely the cause for no variation between studied groups. The HAART group may have responded to the therapy, resulting in less ocular involvement. The pre-HAART group, on the other hand, had recently been diagnosed and had a functioning immune system. Secondly, the relationship, between CD4 cell count and ocular manifestations in these groups, was not evaluated.

This study has the advantage of being the first report from Pakistan on this important health problem. It has given other researchers the opportunity to expand the scope of their work. However, there are some limitations: only one province, which has a low HIV prevalence, was studied, and so does not represent the results of the entire country. To make the results more robust, it is suggested that the similar study be reproduced in other provinces as well.

CONCLUSION

Even though the literature claims that HAART therapy reduces the prevalence of HIV-related ocular symptoms, no such difference was found. These findings encourage other Pakistani

researchers to perform their own research and compare the outcomes. This will assist government officials in prioritising ocular screening in this demographic as a part of their HIV action plan.

ETHICAL APPROVAL:
Before the commencement of the study, ethical approval was obtained from the Ethical Committee of Hayatabad Medical Complex, Peshawar (Ref. No. 179/HEC/B&PC/19).

PATIENTS' CONSENT:
An informed written consent was obtained from all the patients for the purpose of this research and its publication.

COMPETING INTEREST:
The authors declared no competing interest.

AUTHORS' CONTRIBUTION:
YJM: Contributed to the idea, design, analysis, interpretation of data, drafting of the manuscript, final approval, and agreed to be accountable.
MB, SF, MZK: Contributed to the design, acquisition of data, drafting of the manuscript, final approval, and agreed to be accountable.

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