

Primary and tertiary management of ocular surface lesions in HIV-infected patients in Ehlanzeni, Mpumalanga Province

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Background. In sub-Saharan Africa, ocular surface squamous neoplasia (OSSN) is the most common ocular surface tumour and is strongly associated with HIV infection. This range of ocular malignancies can be managed early to prevent large tumours requiring invasive treatment, facial disfigurement and mortality. Primary healthcare workers (HCWs) play a critical role in the early identification of the lesion. In addition, the ocular lesion can also be the presenting sign of HIV infection in individuals who have not yet been diagnosed. The aim of the present study was to assess the management of suspicious conjunctival growths in HIV-infected patients in primary health facilities and a specialist eye clinic in South Africa.

Objectives. To assess the knowledge, attitude and current practice of HCWs working in HIV clinics regarding ocular surface lesions and to evaluate the management of patients with ocular surface lesions at a tertiary hospital.

Methods. A cross-sectional study design was used (November 2020 - May 2021), for which 149 HCWs were invited to assessments about their knowledge, attitudes and practices regarding ocular surface lesions. In addition, files of patients with ocular surface lesions who presented between January 2018 and August 2020 to the eye clinic were reviewed using a data extraction sheet.

Results. One hundred-and-three HCWs agreed to participate in the survey (response rate 69.1%). Of these participants, 84.5% were experienced professional nurses (6 - 15 years of work experience) but had minimal experience with detection and management of eye complaints and lesions. Twenty-seven (26.2%) of the participants recognised some ocular surface lesions and 86 (83.5%) reported that they would refer patients with suspicious lesions. Sixty-two files were reviewed and 51 (82.2%) of the patients had an HIV-positive diagnosis. Fifty percent had carcinoma-in situ and squamous cell carcinoma of the conjunctiva. Thirty-one (50%) of the patients were lost to follow-up.

Conclusion. OSSN is an important manifestation of HIV infection. It would be beneficial for patients to receive a basic ocular examination as part of the baseline clinical evaluation; this may contribute to early referral to an eye care facility. The health system would benefit from establishing an eye health support system with the nearby health facilities, thereby educating primary HCWs about the association between HIV and OSSN.

S Afr Med J 2024;114(6b):e1310. <https://doi.org/10.7196/SAMJ.2024.v114i6b.1310>

The human immunodeficiency virus (HIV) is associated with numerous ocular diseases including ocular malignancies. These include Kaposi's sarcoma, conjunctival lymphoma and ocular surface squamous neoplasia (OSSN). OSSN is a range of ocular surface tumours of the conjunctival and corneal epithelium characterised by dysplastic changes involving partial to full thickness epithelium and invasion into the globe, orbit and surrounding structures.^[1-4]

In sub-Saharan Africa, OSSN is the most common ocular surface tumour and is strongly associated with HIV infection.^[4-6] The aetiology of OSSN is unknown but various studies have identified HIV, human papillomavirus (HPV) and ultraviolet (UV) light exposure as major risk factors.^[2,3] Primary healthcare workers (HCWs) need to be able to identify suspicious lesions in the presence of the above risk factors and refer appropriately in a timely manner.^[7-9]

Primary HCWs are usually the first point of contact for individuals with OSSN and therefore need to be able to recognise the lesion early and refer to the relevant level of care for early treatment. It has been shown that early diagnosis and appropriate management will reduce morbidity by saving vision, preventing extensive cancer and facial disfigurement, and reducing mortality.^[2,3,8,11-17] It is often difficult for

HCWs to differentiate between benign and malignant lesions in their early stage, which may lead to poor management and delayed referral, especially in borderline cases.^[3,12,14,17]

An ocular lesion can be the presenting sign of HIV infection in individuals who have not yet been diagnosed.^[18] It would be beneficial for patients to receive a basic ocular examination as part of the baseline clinical evaluation to detect ocular manifestations of HIV that could be present. This check may contribute to early referral to an eye care facility, early diagnosis and treatment.^[10,19] Primary HCWs (especially those working in the HIV clinic) should be educated about the association between HIV and OSSN. In tertiary settings, HIV testing needs to be part of assessment and early management of ocular surface lesions.

Despite being enrolled in an HIV programme, patients with HIV do experience delays in management for ocular surface neoplasia. This can be attributed to limited awareness about OSSN among HCWs, stigma associated with facial disfigurement and difficulty in seeking care for OSSN.^[20] Incorporating ocular surface screening in patients presenting for HIV care programmes may also assist with reducing the number of delayed referrals.^[13]

The aim of the present study was to assess the management of suspicious conjunctival growths in HIV-infected patients in primary health facilities and a specialist eye clinic in South Africa.

Methods

A descriptive cross-sectional study design was used. A file review of patients and telephonic surveys were done from November 2020 to May 2021.

Sixty-two files were selected for file review from the clinic and theatre registers for participants with conjunctival growths and surgical procedures for suspicious lesions between February 2018 and August 2020. The files selected were of participants who were diagnosed with conjunctival growth or mass, and the files that were excluded were those of participants diagnosed specifically with pterygium or pinguecula. Demographic data that were extracted from theatre preparation forms included smoking history and employment status (Table 1).

Telephonic surveys of HCWs were conducted using a pretested questionnaire to evaluate their knowledge, attitude and practice regarding OSSN. Consent was obtained telephonically prior to the survey and an electronic form was also sent for signing. Data were entered into EpiData 3.1 using double entry and analysed with Stata 15.1.

The study received approval from the Faculty of Health Sciences Research Ethics Committee (605/2020) of the University of Pretoria, the Mpumalanga Provincial Department of Health and the tertiary hospital.

Results

From the file review, the ages of participants ranged between 18 and 80 years, with a mean of 43 years. Females comprised two-thirds of the sample. Forty-six (82.3%) of the 51 participants diagnosed with HIV were on antiretroviral treatment (ART).

Nineteen (30%) participants had a growth only on the conjunctiva, 21 (34%) participants had involvement of the cornea and limbus, and 19 (30%) participants presented with intraocular and orbital extension of the growth. Twenty-four (39%) participants had near normal vision and 30 (48%) participants had near-total to total blindness.

All participants who had clinically suspicious growths had interventions planned as soon as possible but 9 (15%) participants were lost to follow-up after the first visit and did not have any procedure done. Thirty-eight (61%) participants had a biopsy done. Nineteen

participants had an exenteration, 6 of whom had extensive limbal and corneal involvement and 11 had intraocular and orbital extension. Seven (11.3%) participants received topical 5-fluorouracil.

Thirty-one (50%) participants had squamous cell carcinoma and carcinoma in situ, 1 participant had malignant peripheral nerve sheath tumour, 6 (9.6%) participants had severe dysplasia and 7 had mild to moderate dysplasia.

The final outcome of the participants was recorded based on the last interaction that the participant had with the eye clinic. Thirty-one (50%) participants were lost to follow-up. Fig. 1 illustrates the outcome of the participants reported in the files.

Regarding the HCWs who were surveyed, 149 HCWs were invited and 103 (69.1%) participated. The median age was 43 years (range 25 - 64 years). The highest qualification was professional nurse (84.5%), some with specialisation in Primary Health Care and Management. Nine (8.7%) of the participants were student nurses and 7 (6.8%) had other qualifications. Forty-nine (47.6%) of the participants had 6 - 15 years of experience. One clinic reported having an ophthalmic nurse and three clinics in the Nkomazi district reported that there was an outreach by an ophthalmic nurse.

Most HCWs reported that they had no experience with patients presenting with visual symptoms and could not conduct a basic eye examination. Sixty (58.3%) HCWs stated that they had no experience with conjunctival growths. Forty-two (40.8%) HCWs said that conjunctival growths were diagnosed clinically. Table 2 lists the frequencies of responses of HCW to the knowledge questions.

The attitude towards working with patients who have conjunctival growths was based on hypothetical scenarios of patients who present with a condition that requires urgent attention. Ninety-five (92.2%) HCWs said they would enquire from a patient about a conjunctival growth instead of waiting for a patient to present with it as a complaint. Ninety-six (93.2%) HCWs expressed that they would refer a patient to the next level. Two HCWs said they would attempt first to treat, then refer, and 92 (89.3%) said they would send the patient to the eye clinic urgently. Fifty-nine (57.3%) HCWs

Table 1. Demographic information of participants obtained from file review

Variables	Female (n=41)	Male (n=21)
HIV		
Negative	2 (5%)	2 (10%)
Positive	34 (83%)	17 (80%)
Unknown	5 (12%)	2 (10%)
Smoke		
Yes	0	3 (14%)
No	16 (39%)	9 (43%)
Missing information	25 (61%)	9 (43%)
ART		
Yes	30 (73%)	16 (76%)
No	5 (12%)	3 (14%)
Unknown	6 (15%)	2 (10%)
Working outdoors		
Yes	2 (5%)	1 (5%)
No	39 (95%)	20 (95%)

ART = antiretroviral therapy.

Table 2. Healthcare workers' knowledge about conjunctival growths (N=103)

Question	n (%)
Know any types of growths?	
Yes	27 (26.2)
No	16 (15.5)
No experience	60 (58.3)
How are growths diagnosed?	
Surgically	3 (2.9)
Clinically	42 (40.8)
No experience	58 (56.3)
What is the growth rate of growths?	
Gradual	19 (18.5)
Quick	1 (0.9)
Depends on type of lesion	2 (1.9)
No experience	81 (78.6)
What are the treatment options for growths?	
Surgery	19 (18.5)
Medication	11 (10.7)
Refer	5 (4.9)
No experience	68 (66.0)
What are features of malignancy?	
Protrusion	12 (11.7)
Dark lesion	12 (11.7)
White lesion	2 (1.9)
Redness	5 (4.9)
No experience	72 (69.9)

admitted to not following up with patients once referred.

The practice responses were based on interaction with patients with eye problems and hypothetical scenarios. Five (4.9%) HCWs said they would ask for help to manage a patient with growths. Eighty-six (83.5%) said they would refer, 40 (46.5%) of whom would give topical treatment and 9 (10.5%) would give analgesia. Thirty-one HCWs said they could conduct a basic eye examination which meant using the visual acuity chart and crude ocular surface examination. Seventy-five (72.8%) HCWs refer using referral letters and 15(14.6%) call to book an appointment for the patients. Fifty-three (51.5%) HCWs give health education as part of advice which includes avoiding over-the-counter medication, using protective gear such as hats and sunglasses against sun exposure, and 41 (39.8%) emphasise urgent presentation to hospital.

Discussion

OSSN is an important manifestation of HIV with the risk of vision loss and death. Various studies have demonstrated that there is 60 - 77% increased risk for OSSN among HIV-infected individuals, and it may be the presenting sign in 50 - 86% of cases.^[2,6,12,21,22] If recognised early, patients with OSSN can be managed effectively and morbidity and mortality be reduced.^[15]

As in other studies, the present study comprised more females than males who had been diagnosed with OSSN.^[11,2,11,23,24] The mean age of the study population was 43years. Loss of vision in this economically active age group poses a negative impact on families and the workforce.^[25,26]

Most (82.3%) patients were HIV positive, of whom 72.5% had histological changes ranging from mild dysplasia to squamous

cell carcinoma of the conjunctiva. Two of the 7 patients had mild to moderate changes on histology and 2 patients had squamous cell carcinoma of the conjunctiva.

Ultraviolet radiation is among the main risk factors for OSSN.^[3,11] In the present study, information about UV radiation was in the form of sun exposure to the eye based on the location of work. Three (4.8%) patients declared working outdoors, of whom 2 (66.7%) had mild to moderate dysplasia and squamous cell carcinoma. There was no information about duration in the sun and use of protective gear to limit sun exposure. Studies conducted in Kenya and Uganda revealed limited association with smoking and low prevalence of smoking among participants, respectively.^[6,10,11,22] Smoking history was available in this study although limited to information from theatre preparation notes. The prevalence of smoking was also low at 3 (4.8%) and all 3 patients had changes in their histology – mild dysplasia, severe dysplasia and squamous cell carcinoma.

Diagnosing OSSN begins with clinical suspicion based on typical features that are suggestive of OSSN.^[3,27,28] This suspicion warrants further investigation using either non-invasive methods or biopsy.^[29] In the present study, 61.3% patients had a biopsy done to confirm histological changes, and none of the non-invasive methods was used for diagnosis as they were not available during the timeline of this study. Since then, an optical coherence tomography machine has been acquired and efforts are being made to include it as part of diagnosing OSSN.

Management of OSSN is divided into surgical and medical. Medical therapy involves using a topical chemotherapy agent over a period of months with frequent visits

for follow-up.^[27,30,31] Surgical treatment aims to remove the growth in one piece and exenteration is used for extensive and invasive tumours.^[3,12,32] In the present study, most patients had surgical intervention as it would serve as both a diagnostic and treatment measure. This approach allowed fewer visits and patients could receive further management as warranted. Seven (11.3%) patients had incompletely excised lesions and were put on adjuvant topical chemotherapy, 5-fluorouracil. There was no information on how well the patients tolerated the drug as they were yet to return for follow-up.

Patient outcomes were based on the last interaction recorded in the file. Thirty-one (50%) patients were lost to follow-up. Although eye care services were available, they were not easily accessible for 36 (58%) patients who were referred from surrounding hospitals. The cost of travelling to the tertiary hospital may have been a challenge that led to poor follow-up rates. Lack of awareness and understanding of their eye condition may be another reason for not following up. Despite being told the diagnosis during consultation, patients may have cultural beliefs and personal factors that influenced poor follow-up.^[33] A high number of patients did not return despite having serious findings on histology (1 (3.2%) severe dysplasia, 2 (6.4%) carcinoma in situ, and 11 (35.5%) squamous cell carcinoma).

Primary eye care services in South Africa are limited and face numerous challenges including a poor level of clinical knowledge regarding eye care among primary HCWs.^[34,35] This raises concern as primary health facilities are the first point of contact for most South Africans.

The study showed a lack of knowledge and experience in primary eye care. This was demonstrated by 'no experience' being the most frequent response for the knowledge questions.

Knowledge of conjunctival growths consisted mainly of benign conjunctival growths, and only a third said they could recognise features suggestive of malignancy. The lack of adequate training on primary eye health care makes most HCWs rely on the limited exposure from training at bigger health facilities and their experience from managing patients who present with eye problems.^[35]

Forty-two HCWs said conjunctival growths were diagnosed clinically and treated surgically. Early recognition and timeous referral initiate the process that leads to diagnosing and treating, and these are possible without specialised equipment.

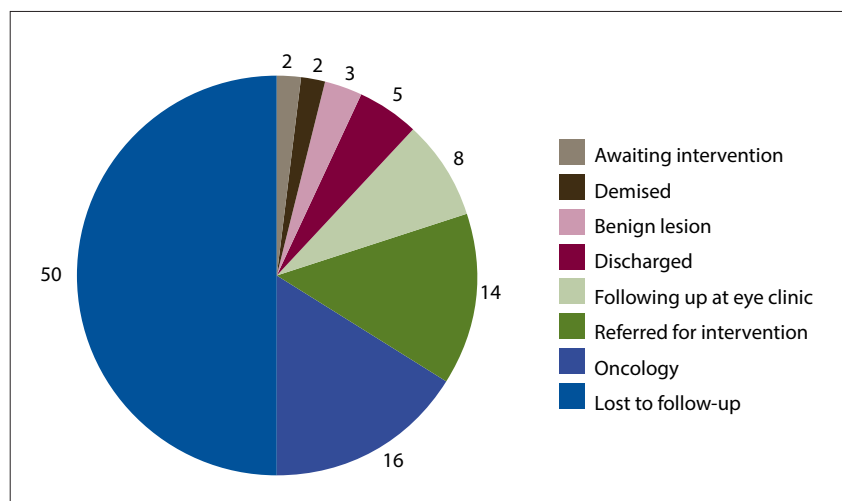


Fig.

Primary HCWs form the primary point of care and they need to be able to direct patients where to go and educate them about their condition to allow better compliance and follow-up. Despite being known at the referral institution, patients will return to the primary health facility for advice and continued care, which means the primary HCW must at least have basic knowledge to identify conjunctival growths, and be able to educate patients and recognise instances that require urgent referral.

Most of the HCWs reported they would refer patients with conjunctival growths rather than treat and then refer. This may be because they were not confident in managing eye problems and chose not to delay appropriate management. Referring patients was said to be easy and patients were sent using referral letters, but a few HCWs had difficulty with referring.

Most HCWs reported they would ask about a lesion in a patient's eye even if the patient did not complain about it. For this practice to be effective in preventing advanced ocular surface lesions, the HCW needs to enquire about growths that seem small or negligible which are detected by examining the eye. However, many HCWs lack experience in basic eye examination.

Most HCWs reported that they did not follow up with patients they had referred. This was attributed to lack of written feedback from the referral hospitals. Those who followed up with patients relied on verbal feedback from patients and this information may not be complete.

In the present study, a third of the HCWs reported they could conduct a basic eye examination which included assessing visual acuity and crude examination of the ocular surface. However, most HCWs would refer the patient without reporting physical findings from examination, and the referral letter therefore mentions only the symptoms. Similar findings were found in a study conducted in Nigeria where eye examination was not routinely done and all the primary healthcare centres studied would refer patients to the next level of care.^[36]

The present study had several limitations. The file selection was based on diagnoses written on clinic and theatre registers which may have been recorded erroneously. The limited study sample combined with telephonic surveys in the coronavirus disease 2019 (COVID-19) environment may affect the generalisability of the study findings. Furthermore, social desirability bias was a concern as the researcher was a healthcare professional but this was mitigated by the assistance of two health sciences students with data collection in the survey component.

Conclusion

There is a significant association between HIV infection and OSSN as most of the patients who were diagnosed with OSSN had HIV infection. This finding highlights the importance of testing for HIV in all patients with suspicious conjunctival growths and screening for OSSN in patients who have been diagnosed with HIV.

Half the patients managed at the eye clinic were lost to follow-up among whom there were changes in the conjunctiva that warranted further treatment and management. These patients may present at a later stage with advanced ocular malignancy requiring invasive intervention. Patients need to be educated extensively about the clinical findings and the importance of follow-up to ensure appropriate care is given.

There is a significant lack of knowledge and experience regarding conjunctival growths among primary HCWs. This is concerning, given that primary health facilities are the first point of care for most of the population. There needs to be education and training of primary HCWs to improve recognition and appropriate management of patients with OSSN.

It may be beneficial to establish an eye health support system between the tertiary hospital and nearby primary health facilities to facilitate appropriate and efficient management of patients with suspicious conjunctival growths. This could be assessed through a study determining the necessity, feasibility and accessibility of such a system to assist with timeous intervention and prevention of vision loss and disfigurement.

Declaration. None.

Acknowledgements. The authors thank Vanessa Gxewa and Lehlohonolo Chueu from the Tuks Undergraduate Research Forum, Faculty of Health Sciences, University of Pretoria, who assisted with data collection.

Author contributions. SL assisted in formulating the study question, drafting the research protocol, gathering information by reviewing files and conducting telephonic interviews. AT and SB supervised the protocol drafts and edited the manuscript. All authors contributed to writing and editing the manuscript and approved the final version.

Funding. None.

Conflicts of interest. None.

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Accepted 5 December 2023.