

Original Research Article

# Ocular surface squamous neoplasia

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## Abstract

**Background:** It describes a spectrum of conjunctival and corneal epithelial neoplasia, manifesting as Dysplasia, Carcinoma in Situ and Ocular squamous cell neoplasia (OSSN).

**Aim:** To study the association between human immunodeficiency virus and ocular surface squamous neoplasia.

**Materials and methods:** It was a prospective interventional study on total 60 eyes of 60 patients with Ocular squamous cell neoplasia (OSSN) was included in this study diagnosed Histopathologically. Bilateral and recurrent OSSN cases, which were diagnosed by repeat excision biopsy and HPE were included only once to exclude HIV statistics.

**Results:** A total of 72 patients of clinical OSSN attended, the OP Department of Occuloplastics. 3 patients did not consent for surgery and were dropped from the study (2 HIV reactive 1 HIV non-reactive). 9 patients HPE negative for OSSN and were dropped from the study. 60 eyes of 60 patients were included in the study all had histopathologically confirmed diagnosis of OSSN. Minimum age was 6 years and maximum age was 80 years. HIV reactive and HPE positive OSSN was 12. 1 patient had lower lid palpebral conjunctival tumor OSSN – A typical presentation. CD4+ T lymphocytes of the patients were around 250 cells / cuml and below in all HIV positive patients. OSSN can occur from 6 years to 80 years Common age group for affection was 51 - 60 years i.e. above 50 years but it can affect any age group. This disease has male preference. HIV association was 20% of cases. Neglected old patients reported late i.e. 3.3% had radical surgery. Recurrence of the tumour was 3.3% so regular follow up is needed. OSSN develops when the CD4 counts were less than 250cell/cu ml.

**Conclusion:** It can be concluded from the study that there is an association between HIV infection and OSSN.

## Key words

Ocular squamous cell neoplasia, HIV infection, Xeroderma pigmentosa.

## **Introduction**

It describes a spectrum of conjunctival and corneal epithelial neoplasia, manifesting as Dysplasia, Carcinoma in Situ and Ocular squamous cell neoplasia (OSSN). It is a rare benign or slowly progressing unilateral or asymmetrical bilateral growth with low malignant potential. Squamous cell carcinoma is the late manifestation in this condition. The occurrence of OSSN has a wide geographical variation, declining with the increase in latitude [1]. It is the disease prevalent in tropics. Population survey in Sub Saharan Africa (Uganda) it is 0.13 per 1,00,000 population and that in Australia it is 1.9 per 1,00,000 population. It is third most common tumour of the eye after melanoma and retinoblastoma (all though it may rank higher in some geographical region). Sex distribution of this disease is such that males are affected more than females. However in Sub Saharan African town Malawi, a HIV endemic area the incidence in females is ever increasing. In 1989 only 46 cases per year of OSSN were reported but 2008 the number has swollen to 469 cases per year. The commonest age of presentation is sixth and seventh decade, but no age is bar from occurrence. The disease was reported from 2 years up to 97 years [2]. Younger age of presentation have associated immuno deficiency or associated with Xeroderma pigmentosa - An autosomal recessive condition with pre disposition for dermal and ocular surface tumour. The predisposing causes are exposure to ultraviolet and other radiations, HIV an HPV infection, chronic irritation and exposure to petroleum products etc. Clinically the term leukoplakia or Bowens disease is used to describe the lesion of OSSN Clinically Dysplasia carcinoma in situ and invasive squamous cell carcinoma cannot be distinguished they are pathological diagnosis. Leukoplakia is white patch on mucous membrane which may be microscopically carcinoma Leukoplakia is clinical description. It can be benign hyper keratosis or acanthosis. OSSN can present as a growth in the limbal area, there may be decreased vision or ocular irritation due to

watering itching etc. A chronically inflamed red eye may be presentation at times [3]. Some patients may remain asymptomatic and the tumour may be detected routinely during eye examination. Very late presentation is large necrotic mass with destruction of the eye ball. Morphologically there are three type of lesions (1) Gelatinous which include leukoplakia and papilliform lesion (2) Nodular are growths on the surface and (3) diffuse i.e., generalized inflamed red eye. Gelationous lesion is common and has thick plaque like lesion with shiny velvety surface; there can be tufts of vessels and there can be white patches sometime [4]. Nodular type is circumscribed elevated focal mass with mulberry appearance. The lesions have sharp margins and can be pearly gray or reddish gray, depending on vascularization due to feeder vessel. The diffuse type is one which is not having distinct margins; it grows readily and has deceptive appearance of chronic inflamed red eye to delay the diagnosis or chronic blepharo conjunctivitis. There can be appearance resembling like local sclera involvement or local corneal lesion. In old patients with chronic conjunctivitis, unilatal diagnostic cytology is mandatory [5]. OSSN tumor may sometimes be pigmented due to the presence of melanocytes, melanosomes or melanin granules with in the neoplastic cells. The tumor OSSN is characteristically located at the limbus and encroaches on the corneal surface. It may occur elsewhere on conjunctiva also. Very rarely they are confined to cornea. Bulbar conjunctiva is predominant site but it may be confined to palpebral conjunctiva also as occurs in diffuse variety [6]. The tumor is mostly unilateral but rarely it may be bilateral simultaneous presentation or sequential presentation. OSSN on cornea presents usually as elevated gray intraepithelial plaque with fabricated margin and also isolated clusters of gray spot that has beaten metal appearance under retroillumination. Fluorescein and rose bengal dye cause diffuse punctuate staining of the tumour surface.

## Materials and methods

It was a prospective interventional study done at Department of oculoplastics: Sarojini Devi Eye Hospital, Hyderabad a Tertiary eye care centre. A total of 60 eyes of 60 patients were included in this study. Detailed history of patients was taken, best corrected visual acuity was recorded, Slit lamp examination was done, Fundus examination was done, intraocular pressure was measured by applanation tonometry.

### Inclusion Criteria

All Histopathologically diagnosed cases only were included in this study. Bilateral and recurrent OSSN cases, which were diagnosed by repeat excision biopsy and HPE were included only once to exclude HIV statistics.

### Exclusion Criteria

All such clinical suspected OSSN cases who were Histopathology for squamous carcinoma HPE negative were excluded from the study. All cases who refused HIV testing.

All the suspected patients were routinely investigated preoperatively. 3 patients were taken up for surgery with the following parameters which were taken normal Hb 10 gms/dl and above, RBS 160 mg/dl. and below. CUE nil for albumin and sugar. CT below 7 minutes, BT below 5 minutes. BP below 140/90, diabetic FBS below 110 mg/dl). The presenting complaints were mass in the inter Palpebral area on the conjunctiva near the limbus extending onto the cornea 24 patients. (12 of the above masses had feeding vessels and 5 of the masses were pigmented). Episcleritis like Nodule superficial painless not responding to oral and topical NSAIDS 12 patients. Recurrent OSSN presented with simple redness of the eye but earlier HPE diagnosis as OSSN helped (Chronic conjunctivitis like) 2 patients. Pterygium like growth with pearly excrescences near corneal end growing rapidly 4 patients. (6 patient between 25 years to 50 years and 12 patients above 50 years had diminution of vision 11 had Nuclear Sclerosis, 2 refractive error corrected

with Spectacle to BCVA 6/12-,6/12.) All such patients who were fit for excision were subjected to HIV infection Serology test by ELISA method at VCTC centre. All the HIV Positive patients were simultaneously advised CD4+ T lymphocyte count and referred to ART centres for further management. All the clinically diagnosed cases were subjected to excision of the lesion with 3 mm of surrounding margin and double freeze thaw procedure under local or general anesthesia and the excised tissue was sent for biopsy and HPE to the hospital pathology laboratory. Extensive intraocular extension and extra ocular extension had enucleation and exenteration respectively. The tissue was sent for HPE. Routine post operative treatment with topical and systemic antibiotic systemic analgesic and topical lubricants. Post operatively patients were reviewed after one week to see the wound, then two weeks and one month thereafter for complete healing. Latter they were advised to report if similar complaints recurred. One eye was enucleated for invasive SCC after HPE report. One eye was exenterated for invasive SCC after HPE report.

## Results

Demographic distribution of study was as per **Table – 1**. Sex distribution of HIV affected patients was as per **Figure – 1**. Distribution of dysplasia and incidence of xeroderma pigmentosum was as per **Table – 2**. Other findings of study were as per **Table - 3**.

## Discussion

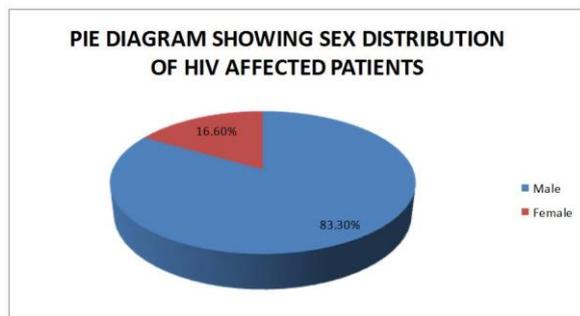
In our study, 12 out of 60 patients were HIV reactive i.e. 20%. A similar study was also conducted in Sub Saharan Africa's HIV endemic area - Malawi by Spitzer, Martin S, et al. [6] and found 30 out of 38 patients of OSSN were HIV reactive i.e. 79% (**Table – 4**).

In our study we found 3 patients out of 12 were detected HIV reactive (25%) for the first time. The rest were already diagnosed as HIV+ve and were followed regularly at ART Centre.

**Table – 1:** Demographic distribution in study.

Age Group	Number of eyes	%
0-10	2	3.3
11-20	1	1.6
21-30	8	13.3
31-40	10	16.6
41-50	9	15
51-60	18	30
61-70	9	15
71-80	3	5
<b>Distribution of OSSN patients who were HIV reactive</b>		
21-30	4	33.3
31-40	2	16.7
41-50	4	33.3
51-60	2	16.7
Total	12	100

**Figure – 1:** Pie diagram showing sex distribution of HIV affected patients.



**Table – 2:** Distribution of dysplasia and incidence of xeroderma pigmentosum(XP).

Histopathology	Number of Eyes	%
Dysplasia	15	25%
CIS	12	20%
SCC	33	55%
	60	100%
<b>Incidence of xeroderma pigmentosum (XP)</b>		
Number of eyes		
60	2	3.3%

In similar study done at Blantyre Malawi in Sub Sahara Africa by Spitzer, Batum ba also reported that out of 30 HIV Reactive OSSN patient, 70%

were detected HIV+ for the First time which is 21 patients [6].

**Table - 3:** Findings in study.

Findings in study	No of Eyes	%
HPE report + Pterigium	7	11.6%
Number of recurrent OSSN	2 (1HIV+, 1HIV -)	3.3%
Number of palpebral conjunctival mass	1	1.6%

The above results are not comparable because the population under study is living in different condition (1) HIV endemic area (2) HIV non endemic area in our study. In our study we also came across a case of palpebral conjunctival tumour which turned out be OSSN. A similar finding was also made by Desilva, Don Julian; they described it as "Conjunctival squamous cell carcinoma Atypical presentation".

In our study various CD4 cell count of 12 cases of OSSN HIV reactive were 155/cuml, 181/cuml, 178/cuml, 56/cuml, 265/cuml, 91/cuml, 147/cuml, 212/cuml, 128/cuml, 145/cuml, 256/cuml,112/cuml. The mean was 151.5/cuml.

We have observed that the age distribution of OSSN is very wide ranging from 6 years to 80 years. The younger age group patients were mostly HIV reactive between 21-50 years, male are more prone to develop this tumor than females probably because they are more exposed to ultraviolet rays compared to females, by virtue of habit. HIV and OSSN association is more common in male population. Thus, strengthening the belief that HIV and OSSN have male preference. We observed that SCC was the commonest HPE finding i.e. 55% and was more than Dysplasia which was 25% and this was more than CIS 20%.

1 - 10 years age group two patients of Xeroderma pigmentosum occurred which constituted about 3.3% of the above study population. The findings further strengthened the belief that these

patients are predisposed to develop dermal and conjunctival tumours. Pinguecula a degenerative condition of the conjunctiva caused by exposure

to ultra violet rays was associated findings in HPE 11.6% probably because both shared a common etiology.

**Table - 4:** Comparison with other studies.

Authors	Total No of patients with OSSN	No of HIV Reactive OSSN	% of HIV reactive OSSN
Spitzer, et al. [6]	38	30	79%
Our study	60	12	20%

Many studies have shown the association between HIV infection and Ocular squamous cell neoplasia. Stephen Gichuhi, et al. [7] conducted a study to determine modifiable risk factors of ocular surface squamous neoplasia (OSSN) in Kenya using disease-free controls. Adults with conjunctival lesions were recruited at four eye care centres in Kenya and underwent excision biopsy. A total of 131 cases and 131 controls were recruited. About two-thirds of participants were female, and the mean age of cases and controls was 42.1 years and 43.3 years, respectively. Risk factors for OSSN were HIV infection without antiretroviral therapy (ART) use (OR = 48.42; 95% CI: 7.73–303.31) and with ART use (OR = 19.16; 95% CI: 6.60–55.57), This study concluded that measures to prevent and control HIV, reduce sun exposure such as wearing hats and control allergic conjunctivitis are recommended.

Govardhanan Nagaiah, et al. [8] conducted a study in which ocular surface squamous neoplasia (OSSN) in sub-Saharan countries is an aggressive tumor that affects younger patients and appears to be increasing in incidence. Data suggest the association of this disease with solar radiation exposure, HIV, and human papilloma virus (HPV). This trend possibly reflects the association of the high incidence of HIV, concomitant high incidence of exposure to HPV, and the solar radiation exposure that people in this region of the world receive. There is increasing evidence of a significant association between HIV seropositivity and OSSN. Patients

with conjunctival cancer in sub-Saharan Africa are typically younger and more than 50% have underlying HIV infection. Initial presentation can be asymptomatic; however, many of these patients have advanced disease before they seek medical help and OSSN appears to have a more aggressive clinical course in sub-Saharan Africa. P. Padmavathi, et al [9] conducted a study to study the clinical behaviour of Ocular Surface squamous neoplasia (OSSN) in HIV positive patients. This is a retrospective study done at the department of the oculoplastics and orbital diseases, Sarojini Devi Eye Hospital Hyderabad over a period of three years from February 2012 to January 2015. 26 cases of HIV positive patients with OSSN were included in the study, 26 cases 17 were males and 9 were females and average age of presentation was 34 years 10 to 15 years younger than non HIV cases. Histopathologically 18 cases were squamous cell carcinoma, 5 cases were carcinoma in situ and 3 cases were with moderate to severe dysplasia. Recurrence was seen in 8 cases (32.1%). OSSN presents at a younger age in HIV positive patients with aggressive behaviour clinically and histopathologically with more chances of recurrence.

Ruchi C Khabra, et al. [10] compared any statistically significant difference in patient demographics, clinical features and pathological findings in HIV infected and non-HIV infected histologically proven cases of ocular surface squamous neoplasia (OSSN). 48 patients, 11 were HIV positive and 37 were HIV negative. Age of the patients ranged from 14-66 years in

HIV and 22-66 years in non HIV group with a preponderance of younger age patients in HIV positive group. 54.5% patients with lesion having base more than 5mm were observed at the time of presentation in HIV positive population as compared to 21.6% in non HIV cases. Feeder vessels were seen in all HIV patients and a significantly greater degree of fornicial involvement was noted in comparison with non-HIV group. Histopathological analysis showed 63.63% of cases to be of invasive carcinoma amongst the HIV positive group and 54.05% of invasive carcinoma in non HIV group. Younger age and aggressive looking tumour at presentation should caution ophthalmologist to look for an un- diagnosed HIV infection in OSSN patients.

K T Steele, et al. [11] Ocular surface squamous neoplasia (OSSN) is a group of ocular tumours that has been rising in incidence among HIV-infected individuals in sub-Saharan Africa. Surgical excision is the mainstay of treatment for OSSN in this region. The mean age of the patients in the study was 38 years (interquartile range 30 - 44), and 53.9% were women. Of the patients, 48.5% were known to be HIV-infected, 1.5% were HIV-uninfected, and 50.0% had unknown HIV status. Among HIV-infected patients with CD4 counts, the median CD4 count was 192 cells/ $\mu$ L. As initial OSSN treatment, 20.7% of patients received simple surgical excision, 70.9% received surgical excision with adjunctive beta radiation, 0.9% received evisceration, 1.3% received enucleation, and 6.2% underwent surgical removal of unknown type. The overall rate of known recurrence was 7.1%; however, among those with at least 6 months of follow-up, the recurrence rate was 24.2%. Rates of known recurrence after simple surgical excision and surgical excision with adjunctive beta-radiation were 10.3% and 5.4%, respectively. This study confirms the high incidence of OSSN among young individuals in Botswana. Further investigation is warranted to determine the most effective treatment modalities to prevent

recurrence of OSSN among patients in sub-Saharan Africa.

## Conclusion

It can be concluded from the study that there is an association between HIV infection and OSSN. OSSN can occur from 6 years to 80 years. Common age group for affection is 51 - 60 years i.e. above 50 years but it can affect any age group. This disease has male preference. HIV association is 20% of cases. It may be the first manifestation of HIV and considered a HIV marker in young individuals. Although tumour is a malignant it is surface neoplasia and presents early and has good prognosis. Neglected old patients reported late i.e. 3.3% had radical surgery. Recurrence of the tumour is 3.3% so regular follow up is needed. OSSN develops when the CD4 counts are less than 250cell/cuml.

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