

# Clinical and histopathological characteristics of ocular surface squamous neoplasia: Evidence from a tertiary eye care center, northwest Ethiopia

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## Abstract

**Background:** Ocular surface squamous neoplasia is a spectrum of diseases encompassing from mild dysplasia to invasive squamous cell carcinoma of the ocular surface.

**Patients and methods:** A series of 50 cases with suspected ocular surface squamous neoplasia presenting to Gondar University Hospital Tertiary Eye Care and Training Center, Northwest Ethiopia from January 2015 to June 2016 were enrolled. Clinical parameters were documented through interviewer administered questionnaire and ocular examination. Excisional or incisional biopsy was done on suspected conjunctival lesions and sent for histopathology examination to an experienced pathologist. Statistical Packages for Social Sciences version 21 was used to analyze data.

**Results:** Mean age of the participants was 41.26 years (age range 18-75) and 72% of the cases were males. Majority of the participants were farmers (40%). Human immunodeficiency virus (HIV) was positive in 22% of the participants. Leukoplakic appearance was the commonest (68%) and nasal side of the conjunctiva was the commonest location of the lesions (72%). Feeding vessels were observed in 84% of the participants. Histopathological examination revealed ocular surface squamous neoplasia in 96% of the participants. Among these 36% had carcinoma in situ, 36% had invasive squamous cell carcinoma, 18% had conjunctival/corneal intraepithelial neoplasia and 10% had associated pterygium clinically and on histology as well.

**Conclusion and recommendations:** Almost all the clinically suspected OSSN lesions were actual OSSN in histology. Most of the ocular surface squamous neoplasia cases in the study were non-HIV positive young males and had the lesion on their nasal side of the globe. Despite the age of the patient and status of HIV infection it is good to subject suspected OSSN lesions for histopathological examination. Most of the patients were farmers and the role of other risk factors need to be considered and large-scale studies are recommended in Ethiopia and other African countries in the future.

## Introduction

Ocular surface squamous neoplasia (OSSN) includes a spectrum of conjunctival/corneal mild dysplasia to carcinoma in situ to invasive squamous cell carcinoma that occurs mostly on the exposed part of the globe [1]. Prevalence of OSSN varies from 0.3-19 per million populations depending on the geographic location being more common in countries that are closer to the equator where excessive exposure to sunlight is more common [2-5].

Age of occurrence of OSSN is reported to be variable predominantly affecting older males in temperate climates and on the contrary in Sub-Saharan Africa it affects young males and females [6,7]. The incidence of OSSN in sub-Saharan countries is increasing and presents as an aggressive tumor affecting younger patients. This may be explained by high incidence of HIV, high incidence of exposure to human papilloma virus (HPV), and solar radiation exposure [8-10]. According to some reports, more than 50% of Sub-Saharan patients with OSSN have underlying Human Immunodeficiency Virus (HIV) infection and present with advanced disease [6]. Reports from temperate climates indicate advanced age and male gender are more associated with the diseases, however in East Africa OSSN is more associated with young age and female gender [3,6-9]. Though there are clinical signs

commonly associated with malignancy of conjunctival lesions, these signs are also reported to be clinical signs of benign lesions as well [9].

Diagnosis of invasive Squamous Cell Carcinoma (SCC) by clinical examination alone is correct only in 30% of cases even by experienced clinicians [1,11]. Correct diagnosis mainly rests on the histopathological examination of the excised lesion which is the gold standard method. The drawback with this method is its unavailability in most eye clinics of Sub Saharan African countries and most lesions are surgically excised without histopathological examination [12,13].

Published works regarding the clinical and histopathological characteristics of OSSN in Ethiopia and at the study area is not available except a report on pattern of ophthalmic lesions at histopathology centers [14]. The aim of this study was to describe the clinical and

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histopathological characteristics of OSSN at Gondar University Hospital tertiary eye care and training center.

## Patients and methods

### Study design and period

The study was clinicopathological evaluation of a series of clinically suspected OSSN cases from January 2015 – June 2016.

### Study area

The study was conducted at Gondar University Hospital tertiary eye care and training center, which is found in Gondar City, Amhara region, Northwest Ethiopia. The study setting is located at a latitude and longitude of 12°36'N 37°28'E with an elevation of 2133 meters above sea level [15]. Gondar is located 730 kilometers from the national capital; Addis Ababa with a total population of 207,044. Gondar University Hospital tertiary eye care and training center is the only tertiary center in the region with a catchment population of 14 million. The tertiary center has 6 ophthalmologists, 21 optometrists, 3 ophthalmic nurses and one cataract surgeon. The center has a postgraduate training program in ophthalmology residency training that is provided for 4 years. The center has different subspecialty clinics among these is the anterior segment clinic where patients with OSSN are referred to.

All patients clinically suspected to have OSSN and had histopathological examination of excised conjunctival lesion were included while patients who were not volunteer to have the surgery and patients who had surgery but refused to have histopathological examination of excised lesions were excluded from the study.

### Definition used in the study

Excisional biopsy with wide margin=excision of a lesion with 3-4 mm safety margin, Conjunctival intraepithelial neoplasia (CIN)=partial involvement of the corneal/conjunctival epithelial layer by neoplastic cells, carcinoma insitu (CIS) =full thickness involvement of corneal/conjunctival epithelium by neoplastic cells, invasive squamous cell carcinoma = corneal/conjunctival basement membrane invasion by neoplastic cells.

### Variables of the study

The outcome variable of the study was the presence of pathologically confirmed OSSN and the explanatory variables were age, occupation, sex, HIV infection status, pterygium, smoking, and history of eye trauma.

### Data collection procedure and instruments

Clinical data was collected from patients with suspected OSSN and were evaluated by senior ophthalmologists and each clinical parameter was documented through an interviewer administered questionnaire by final year ophthalmology residents. Clinical parameters included are demographic data of patients, history of trauma, smoking, position of lesion, lesion size (with estimated clock hours), lesion feeding vessels, pigmentation, appearance of lesion (leukoplakic, gelatinous, papilliform, fungating mass, sessile), site of involvement, local or distant metastasis, presence of associated pterygium, recurrence of conjunctival lesion after excision and HIV status. Suspected small lesions underwent 3-4 millimeters safety margin excisional biopsy and alcohol epitheliectomy of the cornea. Incisional biopsy was done for larger lesions involving most of the ocular surface area or local metastasis to the orbit and eyelid by either an ophthalmologist or final year ophthalmic resident after written consent of the patients was found. Specimen was fixed in 10%

buffered formalin and transported to a single experienced pathologist, department of pathology for histologic examination and results were filled under CIN, CIS and invasive SCC.

**Data quality assurance:** To assure the quality of data in the study, data collectors were supervised by principal investigator and senior ophthalmologists.

**Data processing and analysis:** Data was cleaned and analyzed with SPSS version 21. Tables, mean and proportion were used to describe the results.

**Ethical considerations:** Ethical clearance was obtained from the research ethical review committee of UOG. Verbal consent was taken from the participants prior to data collection and written consent was taken before doing surgery. The tenets of the Helsinki declaration of medical research were followed during the research process [16].

## Results

### Socio-demographic characteristics of study participants

A total of 50 participants were enrolled and among these 72% were males. The mean age of the patients was 41.26 year (age range 18-75 year). Majority were farmers (40%) followed by civil servants (28%) and daily laborers (14%) (Table 1).

### Clinical features of ocular surface squamous neoplasia

Leukoplakic appearance was the commonest in 30 (60%) participants followed by gelatinous in 6 (12%), papilliform in 5 (10%) and 4 cases (8%) had large elevated fungating masses. Nasal (74%) and temporal (18%) sides of the globe were the commonest location of the lesion. The size of the majority of the OSSN ranges from 1-3 clock hours (74%). Large feeder vessels occurred in 42 (84%), dark pigmentation was seen in 6%, 22% of the participants were HIV positive. The size of conjunctival involvement in participants with SCC was 6 clock hours and beyond in 55.6% of the participants. Recurrence of previously excised lesion was observed in 6 (12%) participants (Table 2).

### Histopathological diagnosis of suspected ocular surface neoplasia

The histopathology results of all participants included in the study was reported by the examining pathologist and 6 (12%) participants had CIN, 18 (36%) had CIS, 18 (36%) had SCC. Pterygium was reported in 5 (10%) together with CIN in 3 (6%) and CIS in 2 (4%) participants. It is inconclusive in one participant (Table 3).

**Table1.** Socio-demographic characteristics of patients with suspected OSSN at Gondar University Hospital tertiary eye care and training center, Gondar, Northwest Ethiopia, 2016 (n=50)

Characteristics	Frequency (n)	Percent (%)
<b>Age category (years)</b>		
18-53	43	86.0
≥ 54	7	14.0
<b>Sex</b>		
Male	36	72.0
Female	14	28.0
<b>Occupation</b>		
Farmer	20	40.0
Civil servant	14	28.0
Daily laborer	7	14.0
Housewife	6	12.0
Merchant	2	4.0
Student	1	2.0

**Table 2.** Clinical features of OSSN at Gondar university hospital tertiary eye care and training center, Gondar, Northwest Ethiopia, 2016 (n=50)

Characteristics	Frequency (n)	Percent (%)
<b>Clinical appearance</b>		
Leukoplakic	34	68.0
Gelatinous	6	12.0
Papilliform	5	10.0
Fungating	4	8.0
Sessile & strawberry like	1	2.0
<b>Site of involvement</b>		
Bulbar conjunctiva	14	28.0
Limbus and bulbar conjunctiva	8	16.0
Limbus	3	6.0
Bulbar conjunctiva, Limbus and Cornea	7	14.0
Whole globe, orbit & eyelids	16	32.0
<b>Location</b>		
Nasal	2	4.0
Temporal	37	74.0
Nasal, temporal and superior	9	18.0
All quadrants of the globe	1	2.0
<b>Size in clock hours</b>		
1-3	3	6.0
4-6	37	74.0
>6	9	18.0
<b>Pigmentation</b>		
No	4	8.0
Yes	47	94.0
<b>Feeding vessels</b>		
Yes	3	6.0
No	42	84.0
<b>Local metastasis</b>		
No	8	16.0
Yes	48	96.0
<b>HIV positive</b>		
No	2	4.0
Yes	48	96.0
<b>Smoking history</b>		
No	39	78.0
Yes	11	22.0
<b>Globe trauma history</b>		
No	46	92.0
Yes	4	8.0
<b>Previous recurrence</b>		
No	57	96.0
Yes	3	6.0
<b>Previous recurrence</b>		
No	44	88.0
Yes	6	12.0

**Table 3.** Histological diagnosis of suspected OSSN in Gondar University Hospital tertiary eye care and training center, Gondar, Northwest Ethiopia, 2016 (n=50)

Histological diagnosis	Frequency (n)	Percent (%)
CIN	6	12.0
CIS	18	36.0
SCC	18	36.0
Pterygium and CIN	3	6.0
Pterygium and CIS	2	4.0
Papilloma	1	2.0
Pinguecula	1	2.0
Inconclusive	1	2.0

## Discussion

This study described the clinical and histopathological characteristics of ocular surface squamous neoplasia among a series of patients presented at a tertiary eye care center in Ethiopia.

The mean age of participants in this study was 41.26 years which is comparable with previous reports from Sub Saharan Africa [2-4]. The majority of the participants were males which is in agreement with worldwide incidence of OSSN where males are mainly affected. However, it is unlike many other reports from Sub-Saharan Africa where both females and males are equally affected, or females are

predominantly affected by OSSN. This difference could be due to the difference of our study participants which is a single hospital-based population unlike other African studies which are multi center studies with large sample size [5,6]. In contrast, it is similar to reports from temperate climates where males are predominantly affected but in our study the males affected are relatively younger or middle aged whereas those from temperate climates are old aged males [3].

The majority of the participants affected by OSSN in our study are farmers and males which are presumed to be prone for outdoor activities and exposure to UV solar radiation. This is in agreement with previous reports where exposure to UV solar radiation is attributed as one of the major risk factors for the development of OSSN [8,17].

Among the clinical presentations the commonest is leukoplakic appearance in the majority of the participants which is similar to a report from Africa but unlike the report from Asia where the commonest presentation was gelatinous appearance [18,19]. Feeder vessels and pigmentation of OSSN lesions were also among the predominant clinical findings. Though it is important that these clinical presentations are commonly observed in OSSN, it is also important to note that they could also be the clinical presentations of benign conjunctival lesions as well. This has been reported by the study conducted in Kenya where histopathological findings revealed a high degree of overlap between benign and malignant conjunctival lesions [19].

The prevalence of HIV positivity in our study participants is unlike the reports from other Sub Saharan African countries where a high number of patients with OSSN were found to be positive for HIV infection. According to the report by S Gichuhi from Kenya the prevalence of HIV infection in patients with OSSN was 72% and similarly a report from Malawi showed that OSSN to be the first apparent manifestation of HIV infection in 72% of their patients [6,19]. In our study participants only 22% of them were positive for HIV infection similar to a report from India [20]. This may be explained by other confounding factors like UV solar radiation exposure, outdoor activities and HPV infection which are still considered to be the predisposing factors for the development of OSSN [9,17].

The commonest location of the OSSN lesions in this study is the nasal side (74%) of the globe similar to most previous reports that ranges between 61% to 78% [6,18]. This has been explained by incident temporal light being focused nasally with a 20-fold magnification on intensity affecting the nasal side of the conjunctiva according to Coroneo M [21].

Pterygium was an associated clinical and histopathological finding in (10%) of the participants. Similarly, it has also been reported from Australia where 9.8% of patients with OSSN had associated pterygium [3,22,23]. In addition to this a report from Bascom Palmer showed the presence of an associated pterygium in 1.7% of the OSSN lesions [24]. This associated presence of pterygium with OSSN could be explained by the similarity of the pathophysiology of the two lesions with similar predisposing factors like solar Ultraviolet Radiation, p53 gene mutation and Human Pailoma Virus infection [9,17,24]. This may also emphasize the importance of subjecting clinically suspicious fibrovascular growth for histopathological examination.

Almost all of the lesions with large size (4-12 clock hours) turned out to be invasive SCC complementing to the reports from sub-Saharan countries which showed that being large in size is significantly associated with invasive SCC [6,25].

Among the participants enrolled in the study with clinical suspicion of OSSN, 47 (96%) were found to have histopathological

proven OSSN. This could explain the role of histopathological examination in confirming the diagnosis of malignant lesions which could have overlapping clinical features with benign lesions so that appropriate management approach could be practiced. The high yield of this histopathology evaluation also supports the role of stereoscopic evaluation of the lesions with the slit lamp in clinically suspicious malignant lesions [26].

The strength of this study is its being a prospective one and the first report on the subject matter in Ethiopia. However, it has its own limitations because of its small sample size and absence of control group.

## Conclusions

Despite the age of the patient and status of HIV infection it is good to subject suspected OSSN lesions for histopathological examination. Most of the patients were farmers and the role of other risk factors need to be considered and large-scale studies are recommended in Ethiopia and other African countries in the future.

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