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Original Research Article

THE SPECTRUM OF CLINICAL CHARACTERISTICS IN OCULAR SURFACE SQUAMOUS NEOPLASIA: A COMPREHENSIVE ANALYSIS

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ABSTRACT

Background

Ocular surface squamous neoplasia (OSSN) is the most common non-pigmented malignancy of the ocular surface and is represents with a wide morphological types and clinical symptoms. Along with that it has wide range of histologic diagnoses, ranging from mild epithelial dysplasia to invasive squamous carcinoma. The diagnosis rely on histopathological examination of the excised mass and imaging to rule out infiltration.

Aim

The aim to study the demographics, presenting features, different morphological types, histopathological types and associated risk factors of ocular surface squamous neoplasia (OSSN)

Methods

This was a prospective case study of 27 cases with conjunctival masses suspicious of OSSN presenting to our centre between November 2022 and October 2023.

Results

Among 27 cases 17 (62.96%) males and 10 (37.03%) females, with a mean age of 54.3 years (range 22–68 years). The main presenting symptoms were a mass or growth on the eye, followed by eye irritation or pain, pigmentation and visual impairment. The

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associated risk factors included chronic sun exposure, smoking and tobacco usage, HIV serology positive, and Ocular trauma. The lesions were most common near the limbus, most commonly seen in the interpalpebral area, nasal quadrant. Among the lesions 59.25% had less than 3 clock hours of limbal involvement. The most common presenting clinical morphological feature of the tumor was a leukoplakic lesion, followed by papilliform, nodular, gelatinous, pigmented and mixed morphology accordingly. Vascularization, hyperpigmentation and pterygium was the most common association. Conjunctival or corneal intraepithelial neoplasm (17) was most common in comparison with squamous cell carcinoma (10)

Conclusion

OSSN in our study mainly presented with leukoplakic variant, most commonly involving limbus with a feeder vessel. Most common in males .HIV serology was positive in younger patients. Larger lesion, papilliform variant most commonly showed squamous cell neoplasia in histology.

Keywords: Ocular surface squamous neoplasia (OSSN), Intra-epithelial neoplasia, Squamous cell Carcinoma, Demography, Histopathology,

INTRODUCTION

The spectrum of OSSN varies widely. Ocular surface squamous neoplasia (OSSN) is an umbrella term for a group of conjunctival tumours that include conjunctival intraepithelial neoplasia (CIN) and squamous cell carcinoma (SCC) described by Lee & Hirst in 1995. It is the most common ocular surface tumour with incidence rates ranging from 0.03–1.9 per 100,000 persons/year [1].

OSSN presents with non-specific symptoms such as ocular irritation and redness. If the lesion is too large, it may cause visual impairment by obstructing the visual pathway or inducing astigmatism [1]. The incidence increases with decreasing latitude, being higher in countries located close to the equator [2,3]. The average age of presentation is usually at sixth and seventh decades of life. However, in immunocompromised individuals, OSSN might occur at a younger age [2]. The two leading risk factors that have been associated with OSSN are HIV infection and ultra-violet-B radiation (UVB). Several other associated risk factors include smoking, vitamin A deficiency, exposure to petroleum products, hepatitis B and C infection, chronic ocular surface inflammation, ocular injuries, and immunodeficiency other than HIV [2-4]

OSSN is suspected in patients who presents with conjunctival masses that are raised, gradually increasing in size and having feeder vessels. The tumour is most often located near the corneal limbus within the interpalpebral fissure and unilateral[5]. Morphologically they are classified into leukoplakic, gelatinous, papilliform, nodular and diffuse lesions (Fig. 1). An OSSN lesion may exhibit more than one morphology. [1]

Diagnosis in clinical practice is mainly by slit-lamp examination. But the gold standard for confirmation of the diagnosis and histological grading is a biopsy with histological evaluation. Histologically, OSSN includes epithelial dysplasia, carcinoma in situ, and invasive squamous cell carcinoma (SCC)[4]. Data reveals that an epithelial tumor diffusely infiltrating the surface of the eye, measuring greater than 10 mm diameter and 1mm thickness, and with regions of pigmentation, carries 4.33 greater chance to develop

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SCC rather than CIN.[5]

The standard modality for treatment of OSSN has been wide surgical excision with "no-touch" technique and adjunctive cryotherapy. [2]
Amidst evolving trends in the prevalence and therapeutic modalities for Ocular Surface Squamous Neoplasia (OSSN), there exists a notable dearth of understanding regarding the clinicodemographic characteristics and treatment efficacy within the Indian context. In this study, we aim to elucidate the clinicodemographic profile among individuals presenting with OSSN at a tertiary eye care facility. Our objective is to explore the histopathological findings and demographic distribution of patients with conjunctival masses suspected of malignancy, as ascertained through slit-lamp bio microscopy.

METHODS AND METHODOLOGY

An interventional prospective case study of patients presenting with conjunctival masses to KR Hospital, Mysore, Karnataka. Ethical committee approval was taken and the study adhered to the tenets of the declaration of Helsinki. Patients that presented with conjunctival masses suspicious of OSSN between November 2022 and October 2023 were considered for inclusion in the study. Conjunctival masses were considered to be suspicious of OSSN if they had morphology typical of OSSN and/or had feeder vessels, increasing in size and had excess pigmentation.
Patients were included after informed consent. Sociodemographic data was collected from all patients. Detailed history was taken Systemic risk factors, if any, were recorded. Main focus of associated risk factors included: HIV and the use of ARVs; other systemic conditions or medications associated with immunosuppression; use of tobacco products or smoking. Comprehensive ophthalmic examination was done.

A slit-lamp examination was performed to identify the clinical characteristics like: dimensions, tumor laterality, tissue involved, quadrant of involvement and presence of feeder vessels. The dimensions were recorded as the largest two perpendicular dimensions with rose Bengal staining for proper demarcation. The amount limbal involvement was documented in clock hour. Each tumor was morphologically classified into Leukoplakic, gelatinous ,papilliform, nodular, diffuse, pigmented OSSN. Any clinically palpable preauricular, submandibular, or cervical (regional) lymph nodes were noted. Anterior segment photo was taken for documentation. Patients were also evaluated for presence of any systemic predisposing conditions and routine blood examination for surgery[1]

All patients with suspicion of OSSN underwent wide local excision of 4mm clearance with "no touch technique". The excised biopsy was sent for histopathological evaluation.

Statistical Analysis

Windows SPSS version 20 was used for all statistical analyses, and a p value </=0.05 was considered statistically significant. data was analysed using the statistical software SPSS for Windows v28. The result was calculated in the form of descriptive statistics in tabular forms expressed as numbers and percentages (%), and numerical variables as

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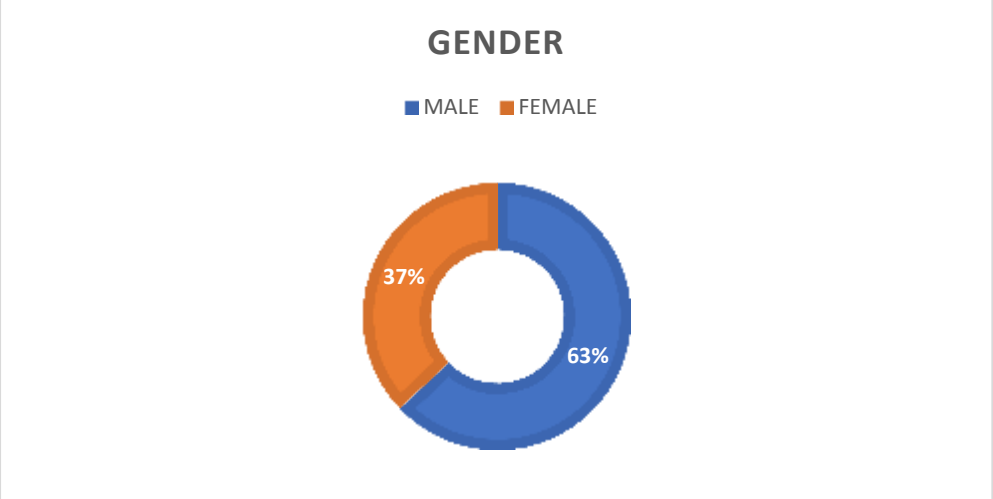
mean ± std.. The non-parametric data was analysed by Chi square test.

RESULTS

Patients' demographics data and presenting symptoms

A total of 27 OSSN patients were reviewed. There were 17 (62.96%) males and 10 (37.03%) females (Fig. 1), with a mean age of 54.3 years (range 22–68 years). The main presenting symptoms were a mass or growth on the eye, followed by eye irritation or pain, pigmentation and visual impairment. The mean duration of the symptoms was 5 months (range 1-14 months). The lesion involved right eye in 16(59.25%) and left eye in 11(40.74%) patients. The associated risk factors included chronic sun exposure (84%), smoking and tobacco usage (53%), HIV serology positive (30%), and Ocular trauma (7%). 1 patient was treated for the recurrent OSSN which was treated elsewhere.

Figure 1: Gender distribution



OSSN characteristics and pathological study

Among 27 eyes the location of the lesions was at limbus in 17(62.96%), the conjunctiva 6(22.22%) and the cornea 4(14.81%) (Fig. 2). The lesion was most commonly seen in the interpalpebral area, that is in nasal quadrant 19 (70.37%), temporal quadrant 7(25.92%) and superior quadrant in 1(3.70%) eye. Among the lesions with limbal involvement, 16 eyes (59.25%) had less than 3 clock hour, 7 eyes (25.92%) 3-6 clock hours and 4 eyes (14.81%) had more than 6 clock hours of involvement (Figure 3). In suspected OSSN cases, there was a strong co-relation with the amount of limbus involvement and OSSN confirmation by histopathology.

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Figure 2: Location of lesion

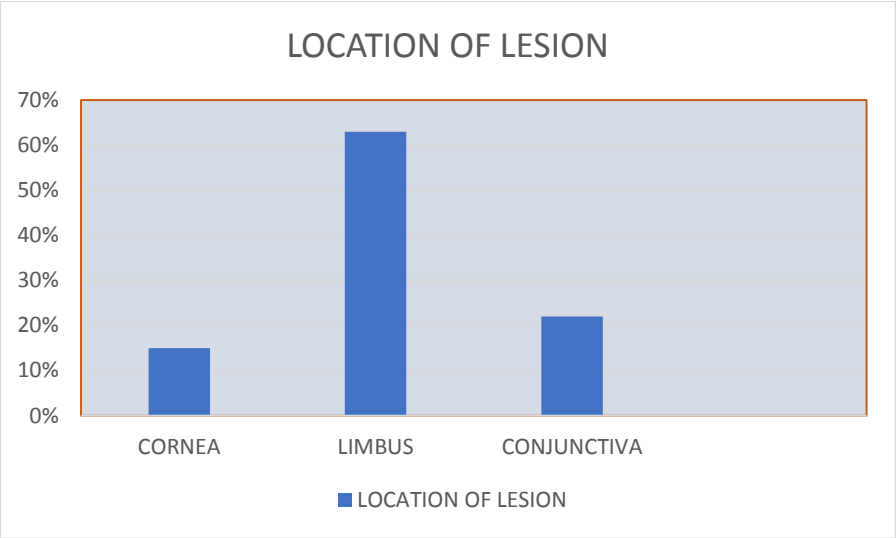
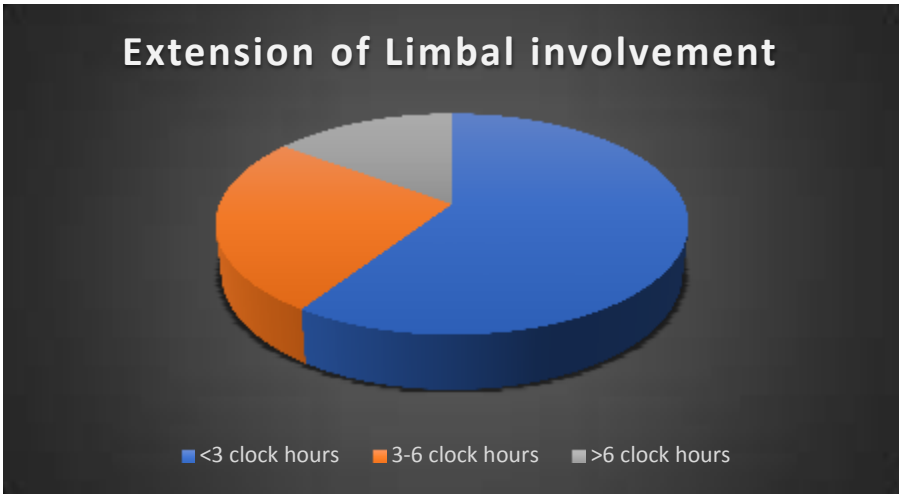


Figure 3: Extension of limbal involvement



The most common presenting clinical morphological feature of the tumor was a leukoplakic lesion in 10 eyes (37.03%), followed by papilliform mass in 7 eyes (25.92%), nodular in 4 eyes (14.81%), gelatinous mass in 2 eyes (7.4%), pigmented in 1 eye (3.73%) and mixed morphology in 3 eyes (11.11%) (Fig. 4). Among these lesions, Vascularization (feeder vessels) was associated with 22 eyes, hyperpigmentation was found in 11 eyes and association with pterygium in 5 eyes (Figure 5).

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Figure 4: Different morphological presentation

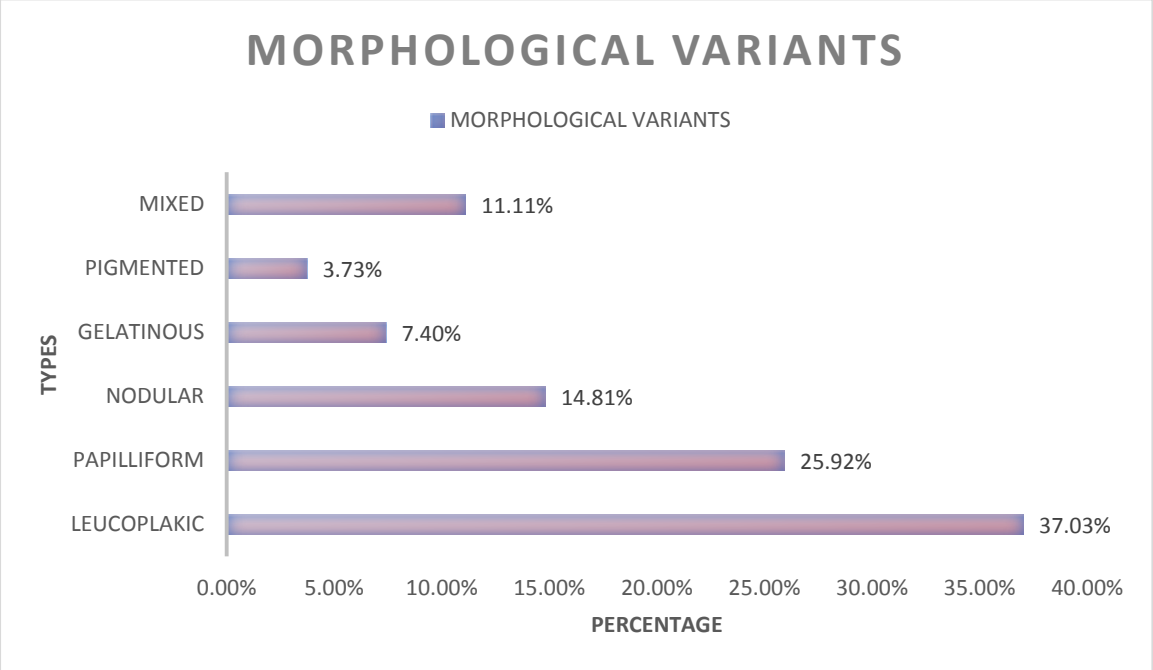
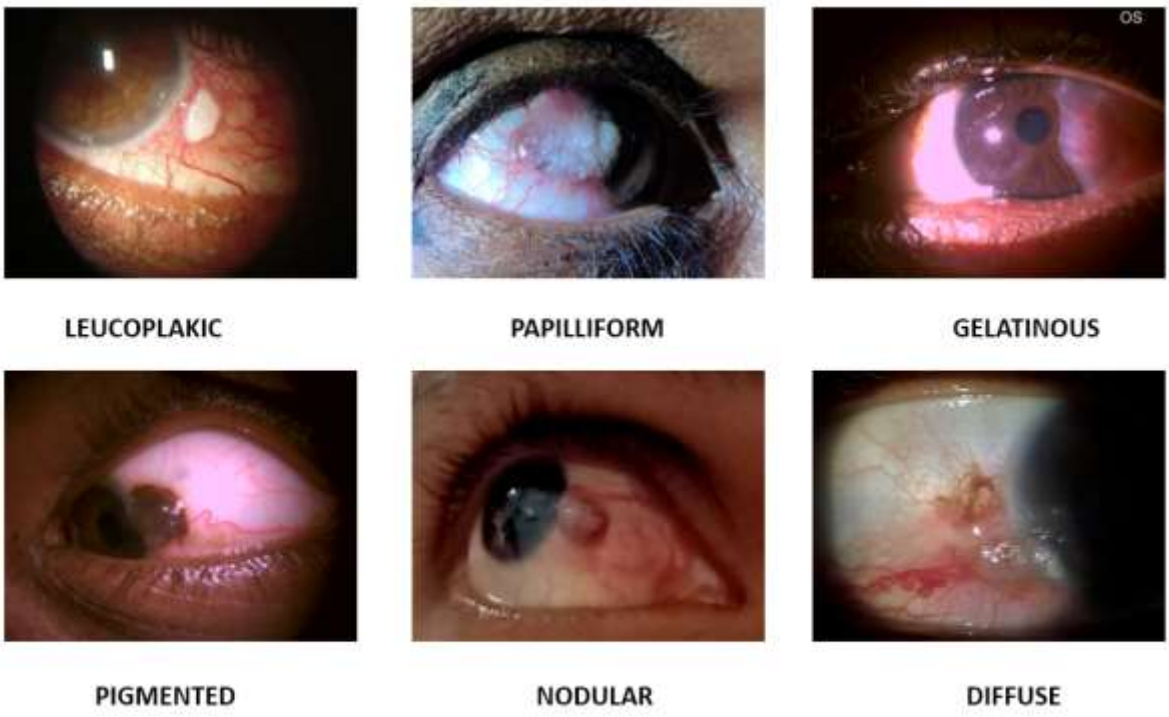


Figure 5: Morphological variants



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All lesions were treated with en-bloc excision and cryotherapy. No recurrence was found during follow up.

Histologic examination revealed that 10 cases were squamous cell carcinoma (SCC) and 17 were conjunctival or corneal intraepithelial neoplasm (CIN) with dysplastic cells in the epithelium: which had mild dysplasia in 6 eyes, moderate dysplasia in 8 eyes and severe dysplasia in 3 eyes, and most of them had inflammatory infiltrates (Table 1). SCC was most common in Papilliform variant.

Table 1: Comparison of histopathological findings

Histopathologic and cytologic findings	Number	Percentage
Squamous cell neoplasia (SCC)	10	37.03%
Corneal or Conjunctival intraepithelial neoplasia	17	62.96%
• Mild dysplasia	6	
• Moderate dysplasia	8	
• Severe dysplasia	3	

DISSCUSSION

Ocular surface squamous neoplasia (OSSN) is the most common malignancy of the ocular surface[6]. The mean age at presentation was 54 years with a male preponderance (62.96%) similar to Meel et al, Tananuvat et al [2,7]. However, studies from Africa report a younger age of onset and female predominance that has been linked with high HIV prevalence[6,8]. This finding was consistent with previous reports that OSSN in HIV-infected patients has been found to affect younger populations with a mean age at presentation in the third to fourth decade. [8,9]

The pathogenesis of OSSN is multifactorial. Risk factors for OSSN in our study were similar to those reported in the literature, including ultraviolet radiation, cigarette smoking, old age, male gender, ocular trauma/ surgery, and immunosuppression [2,6,10]. Invasive OSSN was associated with smoking and alcohol consumption (p = 0.04 and 0.03, respectively) [10].

The most common location of the lesion was limbus. This is similar to other studies and follows the pathophysiology of OSSN, which is thought to originate from the limbal stem cells [1,6,7,11]. Indicating the location of more exposure to the ultraviolet (UV) light and the harbour site of stem cells which have unlimited regenerative capacities.

OSSN is also most commonly reported to affect the interpalpebral space, with the nasal quadrant being affected the most [7,11,12]. This is hypothesised to be due to the amplification of UVB radiation on the nasal limbus [12]. Similar to these study, even our study showed nasal quadrant being the most affected one, followed by temporal.

This study found that the main presenting symptom was mass or growth on the eye, followed by eye irritation or pain, pigmentation and visual impairment.

Meel et al [2], Chauhan et al. [13] and Dandala et al.[14] reported nodular form as the most common morphological growth pattern. Kaliki et al. [11] in India and Tananuvat et al.[7] in Thailand found papilliform lesions to be the most common morphological type, whereas Gichuhi et al. [15] in Kenya found more prevalance of leukoplakic lesions.

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Studies from the Middle East and Indian populations reported that nodular gelatinous mass was the most common form [16-18]. Contradictory to many studies we found that Leukoplakic mass was the most common presenting morphological form, followed by papilliform, nodular, gelatinous and pigmented form accordingly.

On clinical examination most consistent findings associated with OSSN was a mass with feeder vessels, and pigmentation. Sheilds et al postulated that the pigmentation may be due to intra-tumoral pigmented dendritic melanocytes [19].

Clinically it's often difficult to clearly differentiate dysplasia, carcinoma in situ, and SCC based solely on clinical features. Interpretation Shields et al. data reveals that an epithelial tumor diffusely infiltrating the surface of the eye, measuring >10 mm in diameter and 1 mm in thickness, and with regions of pigmentation, carries 4.33 greater chance to represent SCC rather than CIN [20,21].

All the histopathological reporting should use AJCC 8 recommendation which helps in proper staging and management [22] (Figure 6). In our study most lesions were CIN, but the lesions with SCC showed higher corelation with papilliform variant, size >10mm in diameter and hyperpigmentation similar to Ma IH et al [23].

Since the diagnosis of OSSN cannot be completely made based on clinical appearance, the gold standard for definite diagnosis remains the histopathological examination. This helps to distinguish between benign, pre-invasive, and invasive lesions, which guides for the further management of the patient.

This study mainly aimed at finding out the clinical presentation, morphological characteristics, risk factors associated, histopathological types and the surgical outcome of suspected OSSN. However, there were some limitations to be addressed, that is small study population, screening with ultrasound bio microscopy pre operatively, study on action of newer antimetabolites on managing OSSN and lastly short follow up.

CONCLUSION

In conclusion, ocular surface squamous neoplasia (OSSN) represents a significant ocular health concern, with multifactorial pathogenesis and diverse clinical presentations. While typically presenting in older males, variations in demographics and risk factors are noted, particularly in regions with high HIV prevalence. Understanding OSSN's association with UV radiation, smoking, and immunosuppression is crucial for early detection and intervention. Clinically, OSSN manifests predominantly as a limbal lesion, often presenting with mass, pigmentation, and visual impairment. Histopathological examination remains the gold standard for definitive diagnosis, guiding appropriate management strategies. Despite advancements, challenges persist in accurately differentiating between benign and malignant lesions solely based on clinical features. Further research addressing these limitations, including larger sample sizes and longer follow-up periods, is warranted to enhance diagnostic and therapeutic approaches for OSSN.

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Conflicts of interest: There are no conflicts of interest.

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REFERENCES

1. **Höllhumer R, Michelow P, Williams S. Demographics, clinical presentation and risk factors of ocular surface squamous neoplasia at a tertiary hospital, South Africa. Eye (Lond). 2023 Dec;37(17):3602-3608. doi: 10.1038/s41433-023-02565-1. Epub 2023 May 31. PMID: 37258660; PMCID: PMC10686408**
2. **Meel R, Dhiman R, Vanathi M, Pushker N, Tandon R,Devi S. Clinicodemographic profile and treatment outcome in patients of ocular surface squamous neoplasia. Indian J Ophthalmol 2017;65:936-41.**
3. **Ramberg I, Heegaard S, Prause JU, Sjö NC, Toft PB. Squamous cell dysplasia and carcinoma of the conjunctiva. A nationwide, retrospective, epidemiological study of Danish patients. Acta Ophthalmol. 2015 Nov;93(7):663-6. doi: 10.1111/aos.12743. Epub 2015 Apr 22. PMID: 25903169.**
4. **Alharbi I, Alfawaz AM, Otaif W, Al-Dahmash SA, Alkatan HM. Variable presentations of six conjunctival/limbal ocular surface squamous neoplasia (OSSN) cases: How good is our clinical judgment evidenced by the correlation to the histopathological findings and diagnosis? Int J Surg Case Rep. 2024 Mar;116:109359. doi: 10.1016/j.ijscr.2024.109359. Epub 2024 Feb 6. PMID: 38330700; PMCID: PMC10864213.**
5. **Shields CL, Alset AE, Boal NS, Casey MG, Knapp AN, Sugarman JA, Schoen MA, Gordon PS, Douglass AM, Sioufi K, Say EA, Shields JA. Conjunctival Tumors in 5002 Cases. Comparative Analysis of Benign Versus Malignant Counterparts. The 2016 James D. Allen Lecture. Am J Ophthalmol. 2017 Jan;173:106-133. doi: 10.1016/j.ajo.2016.09.034. Epub 2016 Oct 8. PMID: 27725148.**
6. **Gichuhi S, Ohnuma S, Sagoo MS, Burton MJ. Pathophysiology of ocular surface squamous neoplasia. Exp Eye Res 2014;129:172‑82.**
7. **Tananuvat N, Niparugs M, Wiwatwongwana D, Lertprasertsuk N, Mahanupap P. Ocular surface squamous neoplasia in Northern Thailand: a 16-year review. BMC Ophthalmol. 2022 Mar 12;22(1):121. doi: 10.1186/s12886-022-02340-y. PMID: 35279126; PMCID: PMC8918314.**
8. **Julius P, Siyumbwa SN, Moonga P, Maate F, Kaile T, Kang G, West JT, Wood C, Angeletti PC. Clinical and Pathologic Presentation of Primary Ocular Surface Tumors among Zambians. Ocul Oncol Pathol. 2021 Mar;7(2):108-120. doi: 10.1159/000511610. Epub 2021 Jan 21. PMID: 33869164; PMCID: PMC8024974**
9. **Rathi SG, Ganguly Kapoor A, Kaliki S. Ocular surface squamous neoplasia in HIV-infected patients: current perspectives. HIV AIDS (Auckl).2018;10:33–45.**
10. **Lee GA, Hirst LW. Ocular surface squamous neoplasia. Surv Ophthalmol. 1995;39:429–50.**
11. **Kaliki S, Vempuluru VS, Ghose N, Gunda S, Vithalani NM, Sultana S, et al. Ocular surface squamous neoplasia in India: a study of 438 patients. Int Ophthalmol. 2022**
12. **Coroneo M. Ultraviolet radiation and the anterior eyei. Eye Contact Lens Sci Clin Pr. 2011;37:214–24.**
13. **Chauhan S, Sen S, Sharma A, Tandon R, Kashyap S, Pushker N, et al. American**

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 5, 2024

joint committee on cancer staging and clinicopathological high‐risk predictors of ocular surface squamous neoplasia: A study from a tertiary eye center in India. Arch Pathol Lab Med 2014;138:1488‐94

14. **Dandala PP, Malladi P, Kavitha. Ocular Surface Squamous Neoplasia (OSSN): A retrospective study. J Clin Diagn Res 2015;9:NC10‐3.**
15. **Gichuhi S, Macharia E, Kabiru J, Zindamoyen AM, Rono H, Ollando E, et al. Clinical presentation of ocular surface squamous neoplasia in Kenya. JAMA Ophthalmol.2015;133:1305.**
16. **Asadi-Amoli F, Ghanadan A. Survey of 274 patients with conjunctival neoplastic lesions in Farabi Eye Hospital, Tehran 2006–2012. J Curr Ophthalmol. 2015;27(1–2):37–40**
17. **Chauhan S, Sen S, Sharma A, et al. American Joint Committee on Cancer Staging and clinicopathological high-risk predictors of ocular surface squamous neoplasia: a study from a tertiary eye center in India. Arch Pathol Lab Med. 2014;138(11):1488–94.**
18. **Ma IH, Hu FR, Wang IJ, et al. Clinicopathologic correlation of ocular surface squamous neoplasia from a university hospital in North Taiwan 1994 to 2014. J Formos Med Assoc. 2019;118(4):776–782.**
19. **Shields CL, Manchandia A, Subbiah R, Eagle RC Jr, Shields JA. Pigmented squamous cell carcinoma in situ of the conjunctiva in 5 cases.Ophthalmology. 2008;115(10):1673–8.**
20. **Shields CL, Alset AE, Boal NS, Casey MG, Knapp AN, Sugarman JA, et al. Conjunctival tumors in 5002 cases. Comparative analysis of benign versus malignant counterparts. The 2016 James D. Allen Lecture. Am J Ophthalmol. 2017;173:106–33**
21. **Honavar SG. Ocular surface squamous neoplasia: Are we calling a spade a spade? Indian J Ophthalmol. 2017 Oct;65(10):907-909. doi: 10.4103/ijo.IJO_971_17. PMID: 29044051; PMCID: PMC5678322**
22. **Amin MB, Edge SB, Greene FL, Schilsky RL, Gaspar LE, Washington MK, et al., editors. AJCC Cancer Staging Manual. 8th ed. New York: Springer; 2017**
23. **Ma IH, Hu FR, Wang IJ, Chen WL, Hsu YJ, Chu HS, Yuan CT, Hou YC. Clinicopathologic correlation of ocular surface squamous neoplasia from a university hospital in North Taiwan 1994 to 2014. J Formos Med Assoc. 2019 Apr;118(4):776-782. doi: 10.1016/j.jfma.2018.09.001. Epub 2018 Sep 25. PMID: 30266199.**