P-ISSN 0215-7284
e-ISSN 25279106
Accredited by KEMENRISTEKDIKTI/Sinta-3

Clinicopathological Characteristics of Ocular Surface Squamous Neoplasia in National Eye Center, Cicendo Eye Hospital Bandung from 2019 to 2022

Nia Nuraeni[1], Hermin Aminah[1], Hasrayati Agustina[1], Friska Mardianty[2]
[1]Department of Anatomical Pathology, Faculty of Medicine, Universitas Padjadjaran/RSUP dr Hasan Sadikin
[2]Department of Anatomical Pathology National Eye Hospital Cicendo Bandung, Indonesia

Correspondence author: dr. Nia Nuraeni
Department of Anatomical Pathology, Faculty of Medicine, Universitas Padjadjaran/RSUP dr Hasan Sadikin

Received : 02-10-2024
Accepted : 23-10-2023
Published : 31-05-2025

ABSTRACT

Introduction
Ocular surface squamous neoplasm (OSSN) comprises a broad spectrum of dysplastic alterations of the squamous epithelium of the conjunctiva, ranging from conjunctival squamous intraepithelial neoplasm (CSIN) to squamous cell carcinoma (SCC). The aim of this study was to describe the clinicopathological characteristics of OSSN at National Eye Center, Cicendo Eye Hospital Bandung from January 2019 to December 2022.

Methods
We collected OSSN data from 2019 to 2022. The collected data were the patient's age, gender, education, occupation, laterality, clinical features, recurrence, and classification of tumor according to the 2022 WHO classification.

Results
A total of 128 cases were collected. The most common tumor identified was SCC (48.4%), followed by CSIN with severe dysplasia (25%), moderate dysplasia, and mild dysplasia (14.8% and 11.7%, respectively). The average patient's age was 53.1 years old (M=53.1, SD=16.9), predominantly males (68%), education completed elementary school (52.3%), and more patients worked outdoor (59.4%). The most common affected site was the left eye (53.9%), and the tumor located in the nasal region (78.1%) with clinical features is papilliform (64.1%).

Conclusion
OSSN was predominant in elderly male patients. The majority of cases were seen in the left eye, primarily in the nasal area. The majority of patients had completed elementary school and worked outdoors. Additionally, the clinical symptoms showed that most patients had papilliform. In patients with OSSN, SCC was the most common anatomical pathology discovered. Moreover, recurrence was higher in SCC cases.

Keywords: Conjunctival squamous intraepithelial neoplasm, ocular surface squamous neoplasia, squamous cell carcinoma, eye

P-ISSN 0215-7284
e-ISSN 25279106
Accredited by KEMENRISTEKDIKTI/Sinta-3

INTRODUCTION

Ocular surface squamous neoplasia (OSSN) is a broad spectrum of neoplasms originating from the ocular surface squamous epithelium involving the conjunctiva, cornea, or limbus, ranging from precancerous lesions of conjunctival squamous intraepithelial neoplasia (CSIN) to squamous cell carcinoma (SCC).[1,2] CSIN consists of various degrees of histopathology ranging from mild, moderate, and severe dysplasia and carcinoma in situ (Cis), while SCC is a malignant tumor originating from the ocular surface epithelium with squamous differentiation.[3]

OSSN is the third most common ocular tumor after melanoma and lymphoma in conjuctiva.[3-5] Conjunctival OSSN is a prevalent ocular malignancy and has shown an increasing incidence in recent decades.[3] The worldwide incidence of OSSN varies widely, from 0.2 to 3.5 cases per 100,000 people. Previous epidemiologic studies reported the incidence of OSSN to be 0.2 per 1,000,000 population per year in the UK. The average incidence of OSSN of the conjunctiva and cornea was estimated to be higher, with 3.5 per 100,000 population in Uganda, Africa.[6] The incidence of OSSN increases among Caucasians and people in countries close to the equator.[6] The incidence of OSSN in Afro-Americans is around 34%, while in Asians, it happens in less than one percent of the population.[7]

OSSN disease mainly occurs in the elderly between the 6th and 7th decades and in the male gender.[6,7] A 2022 study in India reported the average age of OSSN was 49 years old in 438 patients.[8] The etiology of OSSN is influenced by several factors. The most important etiology is thought to be due to Human papillomavirus (HPV) infection and exposure to ultraviolet B (UV-B) light.[3-5] OSSN affected 16% of patients with a history of Human Immunodeficiency Virus (HIV) infection, 5% in Xeroderma pigmentosum (XP) patients, and 14% in hepatitis patients.[8]

The clinical symptoms of OSSN are similar to those of common conjunctival and corneal disorders, such as pinguecula, pterygium, conjunctival granuloma, and cysts.[1,3] OSSN has great potential to cause visual impairment and death. The main treatment option for OSSN is surgical excision. Several topical drugs have been used as adjuvant therapy, including chemotherapy, immunomodulators, antiviral drugs, and photodynamic therapy.[9] Topical immuno-modulatory therapy, interferon α-2b (IFNα-2b), mitomycin C (MMC) chemotherapy, and fluorouracil (5-FU) are therapies in OSSN.[9] Recent studies using topical antiviral treatment in HPV-associated OSSN with Cidofovir provided efficient effects.[10]

Based on the literature, the aim of this study is to determine the clinical and pathological characteristics and prognosis of OSSN patients at National Eye Center, Cicendo Eye Hospital Bandung in 2019-2022. This data can be used as a reference for scientific development at National Eye Center, Cicendo Eye Hospital and provides an overview of the prognosis of OSSN.

METHODS

This study was a retrospective observational study. The population in this study was patients with OSSN who have undergone histopathological examination from biopsy and surgery at the Department of Anatomic Pathology of National Eye Center, Cicendo Eye Hospital from January 2019 to December 2022. The number of patients enrolled in this study was 128 cases. Demographic data (gender, age, educational history, occupation) and clinical data (laterality, clinical symptoms, pathological grading, and follow-up) were based on patient visits during 2-56 months to National Eye Center, Cicendo Eye Hospital.

Statistical analysis was performed using statistical analysis software. Demographic and clinical data were compared between diagnoses (CSIN with mild, moderate, severe dysplasia and SCC) patients using ANOVA test and Chi-square test. If data was not normally distributed and chi-square assumptions were not met, the Kruskal-Wallis test and Fisher-exact probability test would be used, respectively. P-value less than 0.05 was considered statistically significant.

This study has obtained ethical approval from the Health Research Ethics Committee of National Eye Center, Cicendo Eye Hospital with number LB.02.01/2.3/8707/2023.

RESULTS

Descriptive Statistics

In the current study, we included 128 participants, with a majority of male patients (68%). The average patient's age was 53.1 years old (*M*=53.1, *SD*=16.9). Education level among the patients varied, with the highest percentage having completed elementary school (52.3%), followed by senior high school graduates (22.7%). In terms of their occupation,

Maj Patol Indones 2025; 34(2): 939-944
DOI: 10.55816/mpi.v34i2.649

P-ISSN 0215-7284
e-ISSN 25279106
Accredited by KEMENRISTEKDIKTI/Sinta-3

more patients worked outdoors, which exposed them to direct sunlight (59.4%). Furthermore, our study found that the majority of the patients had left laterality (53.9%), and a significant proportion of them had tumors located in the nasal region (78.1%). Moreover, regarding the clinical features, most of them suffered from papilliform (64.1%). Most of them suffered from this pathological grade of squamous cell carcinoma (SCC) (48.4%). Additionally, the characteristics of the participants in detail can be seen in Table 1.

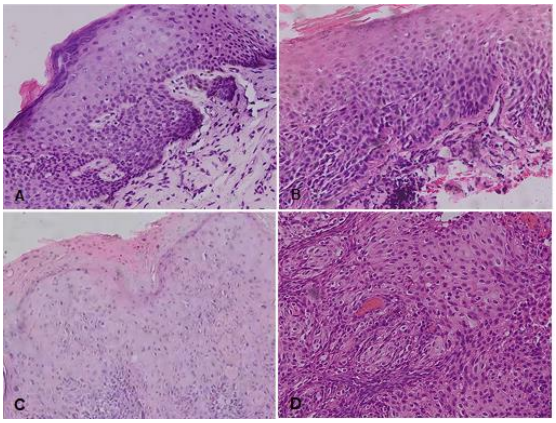

Figure 1. Pathological grading of OSSN stained with hematoxylin and eosin. A. Dysplastic cells confined to basal layer (CSIN with mild dysplasia). B. Dysplastic cells involving middle third of the conjunctiva (CSIN with moderate dysplasia). C. Dysplastic cells invading upper third of the conjunctiva (CSIN with severe dysplasia). D. Squamous cell carcinoma.

Table 1. Patient's characteristics.

Characteristics	N = 128	
	n	%
Age (in years old)		
Mean (SD)	53.1 (16.9)	
Gender		
Male	87	68.0
Female	41	32.0
Education		
Elementary school	67	52.3
Junior high school	24	18.8
Senior high school	29	22.7
D3/S1/S2	8	6.3
Occupation		
Outdoor	76	59.4
Indoor	52	40.6
Laterality		
Right	59	46.1
Left	69	53.9
Location Tumour		
Nasal	100	78.1
Limbus	18	14.1
Temporal	10	7.8
Clinical Features		
Papiliform	82	64.1
Gelatinous	25	19.5
Leukoplakia	11	8.6
Ulcerative	10	7.8
Recurrent		
Yes	17	13.3
No	111	86.7
Pathological Grading		
CSIN with mild dysplasia	15	11.7
CSIN with moderate dysplasia	19	14.8
CSIN with severe dysplasia	32	25.0
SCC	62	48.4

CSIN Conjunctival squamous intraepithelial neoplasia, SCC Squamous cell carcinoma.

Maj Patol Indones 2025; 34(2): 939-944
DOI: 10.55816/mpi.v34i2.649

P-ISSN 0215-7284
e-ISSN 25279106
Accredited by KEMENRISTEKDIKTI/Sinta-3

Table 2. Relationship between pathological grading and patient's characteristics.

Characteristics	Pathological Grading				Statistics Test
	CSIN with mild dysplasia	CSIN with moderate dyspalsia	CSIN with severe dysplasia	SCC	
	n=15	n=19	n=32	N=62	
Age (in years old)					
Mean (SD)	41.5 (4.1)	43.6 (3.6)	54.8 (2.8)	57.8 (2.1)	F (3, 124)=6.96, p<0.05[1]
Gender					
Males	9 (60%)	13 (68.4%)	22 (68.8%)	43 (69.4%)	p=0.91[2]
Females	6 (40%)	6 (31.6%)	10 (31.3%)	19 (30.6%)	
Education					
Elementary school	3 (20%)	7 (36.8%)	13 (40.6%)	44 (71%)	p<0.05[2]
Junior high school	6 (40%)	6 (31.6%)	5 (15.6%)	7 (11.3%)	
Senior high school	6 (40%)	5 (26.3%)	9 (28.1%)	9 (14.5%)	
D3/S1/S2	0 (0%)	1 (5.3%)	5 (15.6%)	2 (3.2%)	
Occupation					
Outdoor	5 (33.3%)	13 (68.4%)	18 (56.3%)	40 (64.5%)	p=0.14[2]
Indoor	10 (66.7%)	6 (31.6%)	14 (43.8%)	22 (35.5%)	
Laterality					
Right	7 (46.7%)	8 (42.1%)	19 (59.4%)	25 (40.3%)	$\chi^2(3)$=3.23, p=0.36[3]
Left	8 (53.3%)	11 (57.9%)	13 (40.6%)	37 (59.7%)	
Location Tumour					
Nasal	11 (73.3%)	16 (84.2%)	26 (81.3%)	47 (75.8%)	p=0.55[2]
Limbus	2 (13.3%)	1 (5.3%)	3 (9.4%)	12 (19.4%)	
Temporal	2 (13.3%)	2 (10.5%)	3 (9.4%)	3 (4.8%)	
Clinical Features					
Papiliform	9 (60%)	16 (84.2%)	20 (62.5%)	37 (59.7%)	p=0.05[2]
Gelatinous	3 (20%)	2 (10.5%)	10 (31.3%)	10 (16.1%)	
Leukoplakia	3 (20%)	1 (5.3%)	2 (6.3%)	5 (8.1%)	
Ulcerative	0 (0%)	0 (0%)	0 (0%)	10 (16.1%)	
Recurrent					
Yes	2 (13.3%)	1 (5.3%)	2 (6.3%)	12 (19.4%)	p = 0.26[2]
No	13 (86.7%)	18 (94.7%)	30 (93.8%)	50 (80.6%)	

[1]One-way Anova Test, [2] Fisher-Exact Test, [3]Chi-square Test.

Relationship between pathological grading and the patient's characteristics

A one-way ANOVA test was performed to evaluate whether the age of the patients had a relationship with the pathological grading. The outcome indicated that there was a significant difference in average age between grades, F (3, 124) =6.96, p<0.05. This finding suggested that the pathological grade of an older patient would be more severe.

Furthermore, there was no significant association between gender and the pathological grade, according to the Fisher's exact test results (p=0.91). Likewise, there was no significant association between the pathological grade and the patient's occupation (p=0.14). In contrast, the result showed that there was a significant association between level of education and the pathological grade (p<0.05).

In addition, the chi-square test showed that there was no association between laterality and the pathological grade (=3.23, p=0.36). Moreover, the Fisher exact test also suggested that there was no association between tumor location and pathological grade (p=0.55), between clinical symptoms and pathological grade (p=0.05). Similarly, there was also no association between recurrent and pathological grade (p=0.26).

DISCUSSION

Statistics from the International Agency for Research on Cancer (IARC) showed that there is a slightly higher incidence of OSSN in men than in women worldwide, but the difference is not significant.[18] This study found that 128 patients with diagnosed histopathology OSSN, with the majority of male patients (68%). There was no significant association between gender and the pathological grade of OSSN. The average age was 53.04 (16.91) years old, with a range of 16-89 years old. Patients with SCC were slightly older than those with CSIN. Epidemiological studies showed that there had been an increase in the incidence of OSSN in Africa and India, with patients affected by more aggressive tumors at a younger age with an average age of 35 and 38 years old.[13,14] This study was concordant with another study in Thailand, with an average age of 58.8 years old.[7]

Maj Patol Indones 2025; 34(2): 939-944
DOI: 10.55816/mpi.v34i2.649

P-ISSN 0215-7284
e-ISSN 25279106
Accredited by KEMENRISTEKDIKTI/Sinta-3

Indoor or outdoor work determines the amount of UV exposure. In this study, the most common occupations of patients were working outdoors and being exposed to direct sunlight. Several epidemiological studies have identified exposure to ultraviolet-B (UV-B) light as the main cause of OSSN development.[12] The NIH-AARP Diet and Health Study conducted in the United States found that those living at latitudes greater than 35 degrees had a lower risk of OSSN as compared to those living at latitudes below 35 degrees from the equator. According to IARC data, the incidence of OSSN decreased by 49% in areas with a latitude enhancement line of up to 10 degrees as UV radiation was reduced.[1-3] Spending a significant amount of time outdoors, particularly for work, may increase the risk of developing OSSN due to exposure to solar radiation. Spending more than half of the workday outside for six years or more can lead to increased UV-B exposure. In Uganda, individuals who work outdoors have a 74% higher risk of developing OSSN when compared to those who work indoors.[19]

In this study, most subjects (128) presented with unilateral OSSN. The most common eye in this study was the left eye, and the most common location was in the nasal area. This is similar to a study in Northern Taiwan in 2019; the most common site of the eye affected by the tumor was the nasal.[15] OSSN typically affects areas of the eye that are exposed to sunlight, particularly in the nasal or temporal areas.[1-3] The latest education in this study's subjects was elementary school. Higher education may increase awareness and earlier health care–seeking behavior.[16]

OSSN has a varied clinical appearance of papilliform (sessile), gelatinous (clear masses), leukoplakia that looks like whitish masses, or ulcerative. The most common type is gelatinous, or clear mass.[3] In contrast, in this study, papilliform was the most frequent clinical feature (64.1%). We only found clinical features ulcerative in SCC (16.1%).

OSSN is a spectrum of diseases ranging from conjunctival squamous intraepithelial neoplasia (CSIN) to squamous cell carcinoma (SCC) of the conjunctiva, limbus, or cornea.[1-5] According to the World Health Organization (WHO) 2022, CSIN is a precancerous lesion with features of cytological changes, maturation, and architectural changes, with varying degrees of squamous intraepithelial dysplasia, from mild to severe dysplasia.[3] Conjunctival SCC is a malignant tumor of the conjunctival epithelium with squamous differentiation.[3] SCC is characterized by the presence of tumor cells that have crossed the basement membrane and invaded the underlying stroma.[3] In this study, the most pathological grade of OSSN was SCC in 60 subjects (47%). This study aligns with a Korean study reporting that 36.7% of OSSN patients with SCC. This differs from research in New Zealand and the USA, where only 11% have SCC histopathology degrees.[11] This could be due to the bias that patients coming to Cicendo National Eye Hospital with more severe clinical symptoms and histopathology.

The recurrence rate recorded in this study was 17 patients. Recurrence can occur if a residual tumor remains after excision.[3,17] SCC in this study experienced the highest recurrence rate, namely 8 (6.3%) cases. The higher the degree of histopathology, the greater the risk of recurrence. CSIN is usually an indolent tumor but can develop into SCC. The prognosis of OSSN is generally good; the overall risk of tumor death is almost 2%.[3]

CONCLUSION

OSSN at the National Eye Center, Cicendo Eye Hospital from 2019 to 2022 mainly occurred in men aged over 50 years old. The majority of the patients had left laterality and were found in the nasal area. The highest percentage of individuals had completed elementary school and worked in outdoor areas. Moreover, regarding the clinical features, most of them suffered from papilliform. SCC is the most common anatomical pathology grading diagnosed result found in patients with OSSN. Recurrence occurs mainly in 12 SCC cases.

REFERENCES

1. Gurnani B, Kaur K. Ocular surface squamous neoplasia. InStatPearls [Internet] 2022 Jun 6. StatPearls Publishing.
2. Mittal R, Rath S, Vemuganti GK. Ocular surface squamous neoplasia–review of etio-pathogenesis and an update on clinico-pathological diagnosis. Saudi Journal of Ophthalmology. 2013 Jul 1;27(3):177-86.
3. Alkatan, H. A. H. C., Croxatto, J. O., Dubovy, S., Eberhart, C. G., Iacob, C. E., & Li, B. (2023). Conjunctival squamous intraepithelial neoplasia. *WHO classification of tumours of the eye. 5th ed.* ed.; vol. 13

P-ISSN 0215-7284
e-ISSN 25279106
Accredited by KEMENRISTEKDIKTI/Sinta-3

4. Basti S, Macsai MS. Ocular surface squamous neoplasia: a review. Cornea. 2003 Oct 1;22(7):687-704.
5. Holland EJ, Mannis MJ, Lee WB. Ocular surface disease: cornea, conjunctiva and tear film: expert consult-online and print. Elsevier Health Sciences; 2013 May 17.
6. De La Parra-Colin P, Pichardo-Bahena R, Méndez-Martínez R, García-Carrancá A, Santamaría-Olmedo M, Barrientos-Gutiérrez T, Lazcano-Ponce E, Hidalgo-Bravo A. Association of high-risk human papillomavirus with ocular surface squamous neoplasia: a case-control study in Mexico. salud pública de méxico. 2022 May 5;64(2):209-17.
7. Tananuvat N, Niparugs M, Wiwatwongwana D, Lertprasertsuk N, Mahanupap P. Ocular surface squamous neoplasia in Northern Thailand: a 16-year review. BMC ophthalmology. 2022 Dec;22(1):1-0.
8. Kaliki S, Vempuluru VS, Ghose N, Gunda S, Vithalani NM, Sultana S, Ganguly A, Bejjanki KM, Jakati S, Mishra DK. Ocular surface squamous neoplasia in India: a study of 438 patients. International Ophthalmology. 2022 Jun;42(6):1915-26.
9. Patel U, Karp CL, Dubovy SR. Update on the management of ocular surface squamous neoplasia. Current ophthalmology reports. 2021 Mar;9:7-15.
10. Ip MH, Coroneo MT. Treatment of previously refractory ocular surface squamous neoplasia with topical cidofovir. Jama Ophthalmology. 2017 May 1;135(5):500-2.
11. Hossain RR, Oh JA, McLintock C, Murphy C, McKelvie J. Ocular Surface Squamous Neoplasia: A 12-Month Prospective Evaluation of Incidence in Waikato, New Zealand. Vision. 2022 Aug 12;6(3):50.
12. Kiire CA, Stewart RM, Srinivasan S, Heimann H, Kaye SB, Dhillon B. A prospective study of the incidence, associations and outcomes of ocular surface squamous neoplasia in the United Kingdom. Eye. 2019 Feb;33(2):283-94.
13. Pola EC, Masanganise R, Rusakaniko S. The trend of ocular surface squamous neoplasia among ocular surface tumour biopsies submitted for histology from Sekuru Kaguvi Eye Unit, Harare between 1996 and 2000. *Cent Afr J Med.* 2003;49:1–4.
14. Vempuluru VS, Pattnaik M, Ghose N, Kaliki S. Bilateral ocular surface squamous neoplasia: A study of 25 patients and review of literature. European Journal of Ophthalmology. 2022 Jan;32(1):620-7.
15. 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. Journal of the Formosan Medical Association. 2019 Apr 1;118(4):776-82.
16. Gichuhi S, Macharia E, Kabiru J, Zindamoyen AM, Rono H, Ollando E, Wanyonyi L, Wachira J, Munene R, Onyuma T, Sagoo MS. Clinical presentation of ocular surface squamous neoplasia in Kenya. JAMA ophthalmology. 2015 Nov 1;133(11):1305-13.
17. Mirzayev I, Gündüz AK, Ateş FS, Özcan G, Işık MU. Factors affecting recurrence after surgical treatment in cases with ocular surface squamous neoplasia. International journal of ophthalmology. 2019;12(9):1426.
18. Gichuhi S, Sagoo MS, Weiss HA, Burton MJ. Epidemiology of ocular surface squamous neoplasia in Africa. Trop Med Int Health. 2013 Dec;18(12):1424–43.
19. Höllhumer R, Williams S, Michelow PM. Observational study of ocular surface squamous neoplasia: Risk factors, diagnosis, management and outcomes at a tertiary eye hospital in South Africa. PLoS One. 2020;15.
20.

Maj Patol Indones 2025; 34(2): 939-944
DOI: 10.55816/mpi.v34i2.649