ORIGINAL ARTICLE

Associated Factors of Ocular Surface Squamous Neoplasia (OSSN) Recurrency After Excision In Dr. Soetomo Hospital Surabaya

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ABSTRACT

Introduction: Recurrence after surgical excision of ocular surface squamous neoplasia (OSSN) remains a significant clinical challenge. This study examined the demographic and clinical characteristics associated with OSSN recurrence. **Methods**: A retrospective review was performed on medical records from January 2016 to December 2020 for 30 OSSN patients. Data collected included age, gender, and the presence of xeroderma pigmentosum (XP) and HIV, as well as clinical parameters such as laterality, tumour location, tumour type, and tumour size. **Results:** The overall recurrence rate was 10%. Recurrence was more common in men (70%) than in women, with the highest proportion of patients aged 41–60 years (36.7%). Forty per cent of lesions were nodular, and 56.7% were classified as T2. The left and right eyes (36.7% each) and the temporal region (46.7%) were the most common tumour locations. **Discussion:** OSSN incidence correlates strongly with its clinical presentation. Significant associations were found between recurrence and both eye laterality and tumour location, while sex, age, lesion type, and tumour size showed no significant association. These findings may improve clinical evaluation and management of OSSN. **Conclusion:** Demographic and clinical factors, particularly the laterality of the affected eye and tumour location, are key influences on OSSN recurrence post-excision. Further prospective, multi-centre research with larger sample sizes is needed to confirm these associations.

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Keywords: Ocular surface squamous neoplasia, excision, recurrence, demographics, and clinical presentation

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INTRODUCTION

Ocular surface squamous neoplasia (OSSN) is the most common non-pigmented ocular surface tumour. Although OSSN is a rare condition, it can lead to significant ocular and systemic complications. The disease comprises a spectrum of lesions ranging from pre-cancerous dysplasia to malignant tumours, which are characterised by the aberrant proliferation of squamous cells in the conjunctiva, limbus, and cornea. OSSN is also known as conjunctival epithelial neoplasia or squamous cell neoplasia, with its pathology spanning from conjunctival intraepithelial neoplasia (CIN) through carcinoma in situ to invasive squamous cell carcinoma (SCC) (1,2).

In Indonesia, detailed reports of ocular cancer cases are infrequent and tend to be limited to specific regions. Reported incidence rates for OSSN vary between 0.03 and 1.9 per 100,000 people per year in the United States and Australia, and can be as high as 3.5 per 100,000 in Uganda [3]. According to the International Agency for Research on Cancer (IARC), OSSN is slightly more prevalent in men than in women, although the difference is minimal. The rising incidence of OSSN has been linked to risk factors such as ultraviolet-B (UV-B)

exposure, immunocompromised conditions (e.g. HIV and HPV infections), xeroderma pigmentosum (XP), smoking, petroleum exposure, and xerophthalmia (2,4). The principal treatment strategies for OSSN involve surgical excision and the use of adjuvant medication to remove tumours and reduce recurrence. Despite the recognition of no-touch surgery combined with cryotherapy as the gold standard, postoperative recurrence rates persist, ranging from 43% to 51%. Consequently, topical chemotherapy has been adopted as an alternative therapeutic modality. Factors that may contribute to tumour recurrence include patient age, gender, tumour margins, histological grade, lesion location and size, and the availability of adjuvant therapy (1,2,5–8).

The present investigation aims to heighten clinical awareness and enhance evaluation protocols by identifying risk factors for postoperative OSSN recurrence. The analysis specifically focuses on patients at Dr. Soetomo General Academic Hospital, assessing both their clinical presentations and demographic characteristics.

METHODS

A retrospective study was carried out at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, between January 2016 and December 2020. Medical record data were extracted from 30 patients diagnosed with ocular surface squamous neoplasia (OSSN) based on the International Classification of Disease (ICD) codes C69 and D31. The inclusion criteria comprised patients with OSSN who underwent tumour excision and possessed complete histopathological data. Patients with incomplete records or those who had undergone orbital surgeries (e.g., enucleation, exenteration) were excluded. Sample selection was achieved through simple random sampling, and tumour recurrence was monitored between 6 and 12 months following surgery. Data collected included demographic variables (age, gender, xeroderma pigmentosum (XP) and HIV status) and clinical details such as tumour size, type, location, laterality, and the surgical procedure performed.

Data analysis was conducted using Microsoft Excel 2019 and SPSS version 26.0. The results are presented in tables and summarised using descriptive statistics, including percentage distributions for both demographic and clinical data. Associations between demographic and clinical factors and tumour recurrence were evaluated using a two-variable association test via the contingency coefficient method, with statistical significance defined by a p-value of ≤ 0.05.

ETHICAL CLEARANCE

Ethical approval for the study was obtained from the Health Research Ethics Committee of Dr. Soetomo General Academic Hospital (approval number: 0968/LOE/301.4.2/VII/2022).

RESULTS

A total of 30 patients diagnosed with ocular surface squamous neoplasia (OSSN) were included in the analysis, comprising 21 men and 9 women. Twenty-nine patients were from East Java and one from West Papua (see Fig. 1). The types of surgical procedures performed are detailed in Table I. The dataset was complete, displaying 100% data validity with no missing cases. Most patients (36.7%) were aged between 41 and 60 years. Tumour recurrence was observed in three patients (two men and one woman; p = 0.894, r = 0.024) across the age groups 0–20, 21–40, and 41–60 years (p = 0.205).

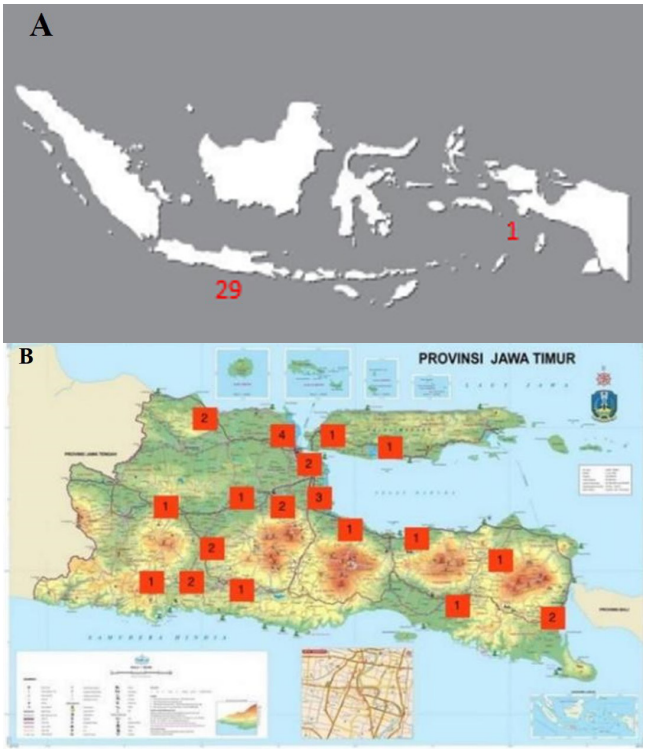

Figure 1: The distribution of OSSN patients in Indonesia was observed in this study. A) 29 patients came from East Java and 1 patient from Fak-Fak, West Papua, B) Distribution of patients' residency in East Java and West Papua areas

Table I: Types of procedures performed in this study

Action	n (%)
Excision + Cryotherapy	20 (66.7)
Excision + Cryotherapy + AMT	4 (13.3)
Excision + Cryotherapy + MMC	2 (6.7)
Excision + Cryotherapy + conjunctival flap	2 (6.7)
Excision + Cryotherapy + AMT + MMC	1 (3.3)
Excision + Cryotherapy + Chemotherapy systemic + MMC	1 (3.3)

Among the 28 patients (93.4%) presenting with unilateral OSSN, 17 cases (56.7%) involved the left eye (p = 0.000, r = 0.628). OSSN was located in the nasal-temporal region for 4 patients (13.3%), in the temporal region for 12 patients (40%), and in the nasal region for

14 patients (46.7%). Recurrence occurred in one patient (3.3%) at the nasal site and in two patients (6.7%) at the nasal-temporal site (p = 0.013, r = 0.474).

The OSSN types identified were nodular (40%), plaque (36.7%), and diffuse (23.3%). Recurrence was detected in one patient regardless of tumour type (p = 0.909). According to the AJCC classification, tumour size was categorised as T1 (<5 mm) and T2 (>5 mm); 13 patients (43.3%) had T1 tumours, while 17 patients (56.7%) had T2 tumours.

All patients underwent surgical excision biopsy and cryotherapy. Among these, 20 patients (66.7%) received additional interventions and adjuvant therapy, including amniotic membrane transplantation (AMT) in 4 (13.3%), AMT with mitomycin C (MMC) in 1 (3.3%), systemic chemotherapy with MMC in 1 (3.3%), a conjunctival flap in 2 (6.7%), and MMC alone in 2 patients (6.7%). Tumour recurrence was documented in two cases with T1 tumours (6.7%) and one case with a T2 tumour (3.3%) (p = 0.390). Table II summarises the factors associated with OSSN recurrence following excision.

Table II: Demographic and Clinical Appearance Characteristics of OSSN

Risk Factors	n (%) n=30	Recurrence		P*	r**
		Yes	No		
Demographic characteristics					
Gender		(n=3; 10%)	(n=27; 90%)		
Male	21 (70)	2 (6.7)	19(63.3)	0.894	0.024
Female	9 (30)	1 (3.3)	8(26.7)		
Age					
0-20 years	2 (6.7)	1(3.3)	1(3.3)		
21-40 years	5 (16.7)	1(3.3)	4(13.3)		
41-60 years	11 (36.7)	1(3.3)	10(33.3)	0.205	0.406
61-80 years	10 (33.3)	0(0)	10(33.3)		
81-100 years	2 (6.7)	0(0)	2(6.7)		
Systemics					
XP	1 (3.3)	1(100)	0(0)		
HIV	1 (3.3)	1(100)	0(0)		
Clinical Appearance					
Laterality					
OD	11 (36.7)	0(0)	11(36.7)		
OS	17 (36.7)	1(3.3)	16()	0.000	0.628
Eye	2 (6.7)	2(6.7)	0(0)		
Tumor Location					
Nasal	12(40)	1(3.3)	11(36.7)		
Temporal	14(46.7)	0(0)	14(46.7)	0.013	0.474
Nasal and Temporal	4(13.3)	2(6.7)	2(6.7)		
Type					
Plaque	11 (36.7)	1(3.3)	10(33.3)		
Nodule	12 (40)	1(3.3)	11(36.7)	0.909	0.079
Diffuse	7 (23.3)	1(3.3)	6(20)		
Size (Classification AJCC)					
T1 (<5mm)	13 (43.3)	2(6.7)	11(36.7)	0.390	0.155
T2 (>5mm)	17 (56.7)	1(3.3)	16(53.3)		

AJCC: American Joint Committee on Cancer

The dataset of OSSN patient samples demonstrated complete data integrity with 100% validity. With regard to gender, relapse was recorded in 2 male patients (6.7%) and 1 female patient (3.3%), a difference that was not statistically significant (P = 0.894, r = 0.024). Analysis by age revealed relapse in one patient from each age group (0–20, 21–40, and 41–60 years), with no significant association found (P = 0.205, r = 0.406). Relapse was observed in 2 patients (6.7%) who exhibited bilateral involvement and in 1 patient (3.3%) with unilateral left eye involvement, yielding a statistically significant association (P = 0.000, r = 0.628). In relation to tumour location, relapses predominantly occurred in the nasal and temporal areas, which was also statistically significant (P = 0.013).

Regarding the OSSN type, relapse occurred with similar frequency across the plaque, nodular, and diffuse forms, demonstrating no significant difference (P = 0.909, r = 0.079). Analysis of tumour size showed that 2 patients (6.7%) with T1 tumours and 1 patient (3.3%) with T2 tumours experienced relapse, although this correlation did not reach statistical significance (P = 0.390, r = 0.155).

Lastly, relapsed cases were reported from Pasuruan, Mojokerto, and Fakfak, with one patient from each region.

DISCUSSION

Ocular surface squamous neoplasia (OSSN) has both genetic and demographic associations. Men appear to be at higher risk—likely due to increased occupational exposure to ultraviolet-B (UV-B) radiation from outdoor work (4,9,10). Sarraf et al. observed a higher, though not statistically significant, recurrence of OSSN in men (11). The present investigation found that 6.7% of male patients experienced tumour recurrence.

Several studies indicate that the average age at OSSN diagnosis is either 63.4 ± 13.0 years (range 23–87 years) or 57.9 years (range 14–90 years), suggesting that age may influence disease progression, particularly during the fifth decade of life (4,12–15).

Our findings also revealed a predilection for left-eye involvement. Seventeen patients (56.7%) exhibited left-sided OSSN, while two (6.7%) had bilateral disease; notably, tumour recurrence was observed in one left-eyed patient (3.3%). Although OSSN is generally unilateral, immunocompromised individuals may develop bilateral lesions. Research by Sarraf et al. and Tanavuvat et al. demonstrated left-eye involvement in 61% and 54.7% of patients, respectively (4,14). In addition, an analysis of control cases indicated a higher recurrence rate in the left eye, although this difference was not statistically

significant (4,16,17).

Ultraviolet exposure accounts for 75% of OSSN cases that manifest in the nasal region. Sarraf et al. reported that the nasal region is affected in 50% of cases, followed by the temporal (28%) and nasal-temporal regions (17%) (4). These findings are in concordance with our results, which identified OSSN in the nasal, temporal, and nasal-temporal areas at rates of 46.7%, 40%, and 13.3%, respectively.

OSSN may manifest as nodular, plaque-like, or diffuse hyperplastic lesions (18). In the current investigation, nodular lesions were the most common (40% of cases), with plaques representing 36.7%. Previous studies have reported that nodular forms can account for up to 57% of cases (9,17). Although all OSSN variants have the potential for recurrence, nodular lesions are associated with a poorer prognosis due to their vertical growth, which increases mitotic activity and tumour aggressiveness (19).

The present analysis found that 56.7% of cases were classified as T2 in size. The extent of tumour excision correlates with the overall spread of OSSN (3,4,20). Over a ten-year period, published data report tumour recurrence rates ranging from 43% to 51%, with mortality between 15% and 30%. Despite treatment with surgical excision, cryotherapy, and Mitomycin-C, recurrence was observed in two patients (6.7%) even when histological margins were clear. Tumour recurrence typically occurs within 3–6 months, with reported rates ranging from 5% to 33%. Incomplete excision and chemotherapy resistance may contribute to multifocal lesion development (15,20). Furthermore, studies suggest that combining surgical excision with postoperative topical Mitomycin-C is more efficacious in preventing recurrence than surgery alone (4,19,20). Table III summarises both recurrence and non-recurrence outcomes, underscoring the limited variability observed in these events.

The present investigation included patients with xeroderma pigmentosum (XP) and HIV, both of whom exhibited tumour recurrence. These conditions increase the risk of OSSN among adolescents; notably, HIV may elevate the risk 8- to 19-fold, especially within the first two years following AIDS onset. OSSN may serve as an indicator of underlying HIV/AIDS in 50% to 86% of cases, and over 90% of OSSN patients may be HIV-positive. Ndlovu et al. reported that HIV-positive OSSN patients commonly present with lesions larger than 5 mm, extending into the fornix, and frequently exhibit leucoplakia along with distinct vascular patterns (15). Moreover, OSSN in HIV-positive patients is associated with a poorer prognosis, a higher likelihood of bilateral involvement, and an 82% recurrence rate within one year post-surgery (3,4,9,15,19,20). In individuals with XP, defective DNA repair mechanisms render them more susceptible to UV-induced cancers in the skin and eyes, with some studies indicating that XP patients may account for approximately 60% of OSSN cases (3,10,16,20).

Table III: Several studies have studied the recurrence in OSSN (Li et al., 2015)

Research	N	Follow-up (Average)	Recurrence rate (%)
This research	30	12 months	10
Li et al, 2015	43	29 months	7.1
Nanji et al, 2014	49	24 months	6.1
Palamar et al, 2014	21	31 months	0
Crim et al, 2013	4	78 months	0
Sturges et al, 2008	14	35.6 months	0
Peksayar et al, 2003	57	31.7 months	12.3
Sudesh et al, 2000	19	37 months	10.5
Tunc et al, 1999	60	56 months	5

Relapse was observed in patients residing in Pasuruan, Mojokerto, and Fakfak, with one case (3.3%) from each region. Although Indonesia's equatorial location—with its high ultraviolet (UV) exposure—is recognised as a contributory factor to the overall incidence of OSSN (as evidenced by Sayed-Ahmed et al.'s findings of higher OSSN prevalence in tropical regions) (21), the uniform distribution of relapse cases across diverse geographical areas in the present investigation suggests that geographical factors alone may not be the primary drivers of recurrence. Instead, patient-specific factors such as immune status, variations in follow-up care, and differences in disease stage at presentation may play more significant roles in influencing relapse outcomes. An increased recurrence rate observed in cases of multifocal OSSN may result from the difficulties encountered in achieving complete surgical excision, as well as the potential resistance of these lesions to chemotherapy. The present investigation observed similar recurrence patterns. Distinguishing between true recurrence, tumour progression, and the emergence of new primary lesions remains challenging when assessing OSSN incidence across various studies.

The limitations of the present study include the small sample size, potential bias inherent in its retrospective design, and inconsistent ICD-10 coding. Furthermore, many patients presented with advanced-stage disease and incomplete follow-up data, which may have reduced the inclusion of certain risk factors and thereby affected the accuracy and generalisability of the findings.

CONCLUSION

Our findings demonstrate that demographic characteristics and clinical conditions play a pivotal role in the post-excision recurrence of ocular surface squamous neoplasia (OSSN), with significant associations observed for tumour laterality and location.

Nevertheless, further prospective research involving larger sample sizes and a multi-centre approach is required to confirm and extend these results.

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