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Demographic Profile, Risk Factors and Histopathological Characteristics of Ocular Surface Squamous Neoplasia

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Abstract **Original Research Article**

Background: Ocular Surface Squamous Neoplasia (OSSN) is a spectrum of ocular surface epithelial lesions ranging from dysplasia to invasive squamous cell carcinoma. Risk factors include Ultraviolet (UV) radiation, human immunodeficiency virus (HIV) infection and other forms of immunosuppression, human papillomavirus (HPV) infection, chronic ocular surface inflammation, smoking and exposure to certain occupational or environmental irritants. Early treatment and histopathological assessment of the excised specimen is important to reduce morbidity. ***Methods:*** This cross-sectional study was conducted in the Department of Oculoplasty and Ocular Oncology, Ispahani Islamia Eye Institute and Hospital from 1st September 2021 to 28th February 2022. A total of 32 patients with OSSN were included using purposive convenient sampling. Patients were clinically evaluated and underwent surgical excision, followed by histopathological examination. Postoperative follow-up was performed at the 1st, 14th postoperative days, 4th, 6th weeks and at 6 months. ***Results:*** Among 32 patients, 13 (40.6%) were above 60 years, 7 (21.9%) were aged 51–60 years, 8 (25%) were aged 41–50 years, and 4 (12.5%) were aged 31–40 years. Males predominated, with 21 (65.6%) cases compared with 11 (34.4%) females. Sunlight exposure was reported in 43.75%, smoking in 37.5%, exposure to chemical agents 3.13% and 15.63% were suffered from malnutrition. Leukoplakic type of OSSN was most predominant 22 (68.75%) and 26 (81.25%) patients presenting with cornea, limbus, and conjunctival surface involvement. Histopathology showed mild dysplasia in 12 (37.5%), moderate dysplasia in 10 (31.3%), severe dysplasia in 4 (12.5%) and invasive squamous cell carcinoma in 6 (18.8%). ***Conclusion:*** OSSN predominantly affected older males, with sunlight exposure and smoking being the common reported risk factors. Histopathology demonstrated a spectrum from mild dysplasia to invasive carcinoma.

Keywords: Ocular Surface Squamous Neoplasia; dysplasia; squamous cell carcinoma; histopathology.

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INTRODUCTION

Ocular Surface Squamous Neoplasia (OSSN) is a category of epithelial lesions affecting the conjunctiva and cornea. It ranges from low grade dysplasia to high grade dysplasia and carcinoma in situ and can also progress into invasive squamous cell carcinomas [1]. This is the most common primary epithelial tumour of the ocular surface. OSSN can occur at any age however it is more common in older patients [2]. There can be a large variation in presentation including gelatinous, papillary, leukoplakic, nodular or raised lesions. It can therefore often be difficult to clinically differentiate from other ocular surface lesions [3].

There are numerous risk factors which have been associated with the development of OSSN [4]. An important environmental risk factor is UV light. Patients who have long term exposure to UV light are at greater risk [5]. Other risk factors include HIV infection, immunosuppression, HPV infection, chronic inflammatory disease, smoking and exposure to various irritants [6]. These risk factors can vary between different populations depending on their geographical, occupational, socio-economic and lifestyle factors [7].

The most common areas affected by OSSN are the interpalpebral ocular surface with the limbus and conjunctiva being the main areas of involvement [8]. Presentation can include a mass on the ocular surface,

redness, irritation, foreign body sensation, watering, photophobia or decreased vision [9]. Some lesions can be asymptomatic and found on routine examination. Detailed slit lamp examination is required to identify any suspicious lesions and to assess the extent of the lesion [10].

Histopathology is an important investigation in diagnosing OSSN [11]. Histologically it can range from low to high grade dysplasia, intraepithelial carcinoma or invasive squamous cell carcinomas [12]. Histopathology can provide information on the degree of epithelial atypia, maturation, organisation, basement membrane and any infiltration. It can help to determine if the lesion is pre-malignant or malignant [13].

It is important to identify OSSN early to ensure it is treated appropriately. If left untreated or at a late stage it can infiltrate surrounding ocular structures causing significant morbidity [14]. Surgical excision with wide margins often combined with adjuvant therapy such as cryotherapy [15]. Histopathology should be carried out on the lesion to make a definitive diagnosis [16,17].

Despite increasing recognition of OSSN, variations in demographic characteristics, associated risk factors, clinical presentation, anatomical distribution and histopathological patterns can occur between different patient populations. Therefore, evaluating these characteristics in patients presenting to specialized ocular oncology services may contribute to better understanding of the disease pattern and facilitate early diagnosis and appropriate management. This study was undertaken to assess the demographic profile, associated risk factors and histopathological characteristics of Ocular Surface Squamous Neoplasia among patients attending a specialized ophthalmic service.

METHODOLOGY & MATERIALS

This cross-sectional study was conducted in the Department of Oculoplasty and Ocular Oncology, Ispahani Islamia Eye Institute and Hospital (IIEI&H), from 1st September 2021 to 28th February 2022. The study population comprised all patients with Ocular Surface Squamous Neoplasia (OSSN) who attended the department during the six-month study period. Purposive convenient sampling was used and a total of 32 patients were included. Patients with OSSN diagnosed clinically, who underwent surgery and provided appropriate consent were included, while patients with recurrent OSSN, lesions extending toward the orbit, invasive squamous cell carcinoma with intraocular extension, xeroderma pigmentosa and those whose histopathology showed squamous hyperplasia were excluded. Data were collected using a semi-structured research questionnaire, checklist and informed written consent form through face-to-face interviews, counseling, clinical examination and meticulous slit-lamp evaluation. Clinically suspected OSSN lesions were documented and eligible patients underwent pre-operative investigations followed by surgical excision with a 4 mm healthy margin using a non-touch technique. The excised specimens were sent for histopathological examination. Cryotherapy was applied to the conjunctival cut margin and the wound was covered with an amniotic membrane graft secured with tissue glue and 8-0 Vicryl sutures. Patients were followed up at the 1st, 14th postoperative (POD) days, 4th, 6th weeks and at 6 months, with postoperative outcomes documented. The study protocol adhered to the tenets of the Helsinki Declaration and was approved by the Institutional Ethical Review Committee of IIEI&H. Written informed consent was obtained from all participants and confidentiality and privacy were maintained. Data were analyzed using SPSS version 24. Descriptive statistics were presented as frequencies, cross tables and text. Student's t test and one-way ANOVA were used for quantitative variables, while the Chi-square test was used for qualitative variables. A P value less than 0.05 at the 95% confidence level was considered statistically significant.

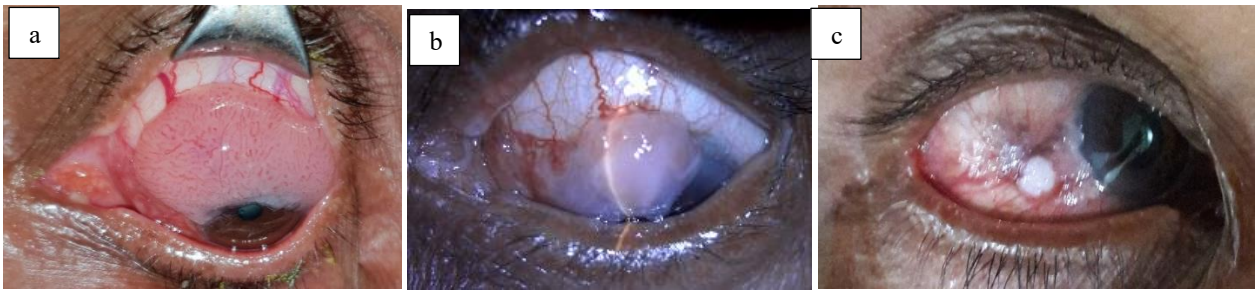


Figure 1: Morphological type of OSSN a) Papillomatous type b) Gelatinous type c) Leucoplakic type

RESULTS

This study was performed in Oculoplasty and Ocular Oncology Department at Ispahani Islamia Eye Institute and Hospital from1st September 2021 to 28th February 2022. During 6 months of period of time all patients come with OSSN are included for the study. A

total 32 patients were included. Every patient was meticulously evaluated and went for surgery. The post-surgical outcome was noted with proper documentation. Follow up was taken at 1st, 14th POD, 4th, 6th weeks and at 6 months.

Table 1: Demographic Distribution of Patients (n = 32)

Demographic Variable	Category	Frequency (n)	Percentage (%)
Gender	Male	21	65.6
	Female	11	34.4
Age (Years)	31–40	4	12.5
	41–50	8	25
	51–60	7	21.9
	>60	13	40.6
Total		32	100

Table 1 presents the demographic distribution of the 32 patients included in the study. The data reveals a male predominance, with males accounting for nearly two-thirds of the cohort (n=21, 65.6%), compared to females (n=11, 34.4%). In terms of age distribution, the majority of patients fall into the older age brackets. The highest proportion of patients is over 60 years of age (n=13, 40.6%), followed by those in the 41–50 age group (n=8, 25%). Patients aged 51–60 (n=7, 21.9%) and 31–40 (n=4, 12.5%) make up the remainder of the cohort. Overall, this indicates that the patient population is predominantly older adults, with the vast majority (87.5%) being over the age of 40.

Table 2: Distribution of Patients According to Exposure to Risk Factors (n = 32)

Risk Factor	Frequency (n)	Percentage (%)
Exposure to Sunlight	14	43.75
Smoker	12	37.50
Exposure to Chemical Agents	1	3.13
Malnutrition	5	15.63
Total	32	100

Table 2 outlines the distribution of the 32 patients based on their exposure to various risk factors. The most prevalent risk factor reported was exposure to sunlight (43.75%, n=14), closely followed by smoking (37.50%, n=12). Malnutrition accounted for 15.63% (n=5) of the cases, while exposure to chemical agents was reported in only one patient (3.13%).

Table 3: Involvement of OSSN to Ocular Surface (n = 32)

Anatomical Involvement	Frequency (n)	Percentage (%)
Cornea, Limbal, and Conjunctival Surface	26	81.25
Conjunctival Involvement Only	6	18.75
Total	32	100

As shown in Table 3, the anatomical distribution of Ocular Surface Squamous Neoplasia (OSSN) was analyzed among the 32 patients. The vast majority of cases demonstrated extensive multi-surface involvement, with 26 patients (81.25%) presenting with lesions affecting the cornea, limbus, and conjunctival surface simultaneously. In contrast, a smaller subset of 6 patients (18.75%) presented with disease that was confined exclusively to the conjunctiva.

Table 4: Morphological Type of OSSN (n = 32)

Morphological Type	Frequency (n)*	Percentage (%)
Leukoplakic	22	68.75
Papillomatous	7	21.88
Gelatinous	3	9.38

Table 4 outlines the clinical morphological characteristics of the OSSN lesions within the study cohort. The leukoplakic type was the most predominant presentation, accounting for over two-thirds of the cases at 68.75% (n=22). This was followed by the papillomatous morphology, which was observed in 7 patients (21.88%), while the gelatinous type was the least common, representing only 9.38% (n=3) of the total lesions.

Table 5: Distribution of patients according to Histological Type of OSSN (n=32)

Grading	Frequency (n)	Percentage (%)
Mild Dysplasia	12	37.5
Moderate Dysplasia	10	31.3
Severe Dysplasia	4	12.5
Invasive SCC	6	18.8

Table 5 shows total 12 (37.5%) patients are found mild dysplastic changes in their histological findings, 10 (31.3%) patients were found moderately dysplasia, 4 (12.5%) were found severely dysplastic changes and 6 (18.8%) patients were suffered from invasive squamous cell carcinoma.

DISCUSSION

Introduction Ocular Surface Squamous Neoplasia (OSSN) encompasses a range of ocular surface epithelial tumors from dysplasia to invasive squamous cell carcinoma. This study aimed to identify the demographics, risk factors, clinical features and histopathological findings in 32 patients diagnosed with OSSN and surgically treated at the ocular oncology service.

The results of this study showed that OSSN occurs mainly in elderly patients (13 patients, 40.6%). 8 patients were aged between 41-50 years (25%), 7 patients were aged between 51-60 years (21.9%) and 4 patients were aged between 31-40 years (12.5%). This is in line with previous studies which found the mean age of patients with OSSN diagnosed histopathologically to be 72 years (n=153) [17]. Schuh et al. also found that OSSN can occur at many ages throughout adulthood, therefore demonstrating age to be an important demographic factor. Goto et al. found that the mean age of patients with conjunctival squamous cell carcinoma was 60.2 years [18]. The age range seen in this study demonstrates that OSSN occurs mainly in elderly patients due to the accumulation of risk factors.

It was found that there was a clear male predominance in this study, 21 patients were male (65.6%) compared to 11 female patients (34.4%) giving a male to female ratio of 1.9:1. Similar findings were found by Schuh et al. with a slight predominance of males (66%) [17]. Male predominance may be due to increased occupation/exposure to risk factors in some populations. Alkatan et al. emphasised the importance of demographic and environmental factors when assessing conjunctival lesions in a tertiary setting [19].

Risk factors were identified with the most common being exposure to sunlight (43.75%). Smoking was the second most common risk factor (37.5%), followed by malnutrition (15.63%) and exposure to chemical agents (3.13%). It makes sense that exposure to sunlight was the most common risk factor as chronic UV exposure is an important environmental risk factor. Pe'er et al. describe OSSN as having associations such as UV exposure, immunosuppression, HPV infection and other environmental factors [20]. Tananuvat et al. also highlight the importance of environmental and demographic factors [21]. There was a relatively high number of smokers in our study, showing that lifestyle factors should be considered [14]. 26 patients (81.25%) suffered from combined corneal, limbal and conjunctival involvement. Whereas 6 patients (18.75%) had purely conjunctival lesions. It is important to identify the anatomical extent of OSSN to ensure accurate diagnosis. Höllhumer et al. highlight the importance of identifying anatomical extension [22]. Lan et al. also identified that OSSN can affect different parts of the ocular surface and detailed examination is required to ensure accurate management [12].

The most common presentation of OSSN was leukoplakia (22 cases, 68.75%). Followed by papilloma (7 cases, 21.88%) and gelatinous (3 cases, 9.38%). Pe'er et al. describe OSSN as having many different presentations, therefore it is important to look at the morphology of OSSN [20]. Patel et al. also discuss the varying clinical appearance of OSSN and importance of accurate diagnosis and treatment [23].

Histopathology showed that 12 patients (37.5%) had mild dysplasia. 10 patients (31.3%) had mild dysplasia, 4 patients (12.5%) had severe dysplasia and 6 patients (18.8%) had invasive squamous cell carcinoma. This shows the range of histopathology seen in OSSN. Julius et al. describe how primary ocular surface tumours can have varied histopathological findings, therefore it is important to obtain tissue samples [24]. Gurnani et al. also highlight the molecular and pathological variation [25]. Schuh et al. found that 45.8% had invasive SCC, 37.9% had carcinoma in situ and 16.3% had epithelial dysplasia (n=153) [17]. There was a higher number of invasive cases in this study which may be due to differences in referrals, demographics, disease duration and case selection. Goto et al. found that SCC was an important malignant conjunctival tumour in their tertiary population with 97 cases of SCC (n=359 primary malignant conjunctival tumour) [18]. Accurate clinical examination, wide surgical excision and histopathology are important to ensure accurate diagnosis, appropriate treatment and to prevent progression.

Limitations of the study

This study was conducted at a single specialized eye-care center with a relatively small sample of 32 patients, which may limit the generalizability of the findings. The short six-month study period and purposive convenient sampling may also have introduced selection bias. In addition, the study mainly assessed demographic characteristics, reported risk factors, anatomical distribution and histopathological findings without long-term evaluation of recurrence or disease progression.

CONCLUSION

The study demonstrates that OSSN was more common among older patients and males, with sunlight exposure and smoking being the most frequently reported risk factors. The cornea, limbus, and conjunctival surface was involved predominantly, while histopathology revealed a spectrum from mild dysplasia to invasive squamous cell carcinoma. Early recognition of risk factors and suspicious ocular surface lesions, supported by appropriate histopathological evaluation, is important for timely diagnosis and management of OSSN.

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