

Outcomes of Management of Sinonasal Malignancies at a Dedicated Cancer Institution: A Retrospective Study

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Abstract

Introduction: Sinonasal malignancies (SNMs) are a rare and heterogeneous group of cancers with an incidence of 3%–5% of all head-and-neck tumours. The aim of the present study was to identify the characteristic features of SNMs and to analyze the treatment outcomes and the prognostic factors affecting it. **Materials and Methods:** A retrospective review of patients with SNM treated at a dedicated cancer center of Pakistan between 2004 and 2018 was carried out. All patients with histologically proven diagnosis of malignancy arising from nasal cavity or paranasal sinuses and being treated with curative intent were included. The medical records of 184 cases were utilized for final analysis. Chi-square test was applied to identify significant differences. Five-year disease-specific survival (DSS) was calculated using Kaplan–Meier curve via log-rank test and comparison was made between squamous and nonsquamous histologies. $P \leq 0.05$ was considered statistically significant. **Results:** Squamous cell carcinoma was the most common histopathology ($n = 62, 33.7\%$). 130 (70.7%) patients presented with stage IV disease. Nodal metastasis was seen in 24 (13%) patients. Treatment failure was seen in 96 (52.2%) patients and was significantly associated with tumour size and the overall stage. DSS of patients with squamous cell carcinoma was 29% as compared to 52% for patients with nonsquamous histologies ($P = 0.001$). **Discussion:** SNM is a diverse group of cancers presenting in late stages. A higher rate of treatment failure associated significantly with stage of the disease was identified in our study.

Keywords: Nasal cavity, paranasal sinus neoplasm, paranasal sinuses, squamous cell carcinoma, treatment outcome

INTRODUCTION

Malignancies of sinonasal region are a rare group of tumors with a reported incidence of 1 in 100,000 people annually.^[1,2] The incidence of these tumours ranges from 0.2% to 0.8% in all cancers and up to 3%–5% of all head-and-neck malignancies.^[3,4] The incidence is higher in Asian and African countries as compared to the United States and European countries. It is the second most common malignancy of the subgroup of head-and-neck cancers in Asian countries whereas the most common malignancy is nasopharyngeal cancer.^[5,6]

The most common site of origin of sinonasal malignancies (SNMs) is maxillary sinus followed by ethmoid sinus. Frontal and sphenoid sinuses rarely present as primary site of origin of SNM.^[1,7] Management of SNM is difficult as they are usually in close relation or adherent to surrounding structures such as skull base and orbit.^[5,8,9]

SNMs are more commonly seen in males with a male-to-female ratio of 2.3:1.^[10] Patients with SNM are

usually more than 40 years of age. In the initial stages, these tumours are usually misdiagnosed due to their nonspecific features and late presentation.^[11,12] Due to delayed presentation of these tumours, it becomes extremely difficult to determine the exact site of origin because of extensive involvement of surrounding structures.^[13,14] Unlike squamous cell carcinoma of other sites in head-and-neck region, lymph node metastasis in SNM is not commonly seen, with incidence ranging from 3.3% to 26%.^[1] The most common histologies are squamous cell carcinoma followed

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Received: 17-01-2021

Last Revised: 13-05-2021

Accepted: 20-05-2021

Published: 24-07-2021

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How to cite this article: Dhanani R, Faisal M, Shahid H, Malik KI, Jamshed A, Hussain R. Outcomes of management of sinonasal malignancies at a dedicated cancer institution: A retrospective study. *Ann Maxillofac Surg* 2021;11:115-20.

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10.4103/ams.ams_16_21

by adenocarcinoma and adenoid cystic carcinoma etc.^[15-21] Early staged tumours can be managed endoscopically^[22,23] whereas open surgical approaches such as craniofacial resection, maxillectomy, midface degloving, lateral rhinotomy, and orbital exenteration deemed necessary for advanced tumours. It is quite challenging to perform surgery with clear margins due to complex anatomy of the region,^[24-27] and hence, adjuvant radiotherapy becomes a very useful treatment modality in such cases. Figures 1-5 shows radiological and clinical images of a case of a 52-year-old male with sinonasal undifferentiated carcinoma of right nasal cavity undergoing wide local excision by Weber Ferguson approach.

Despite high incidence of SNM in Asian countries, there is not much data available in the literature on the treatment outcomes of SNM. Therefore, we wanted to record the treatment outcomes of SNM at our center and add to the scarce local and regional data available in the literature. The primary objective of the study was to identify the characteristic features of SNMs. The secondary objective of the study was to see

the treatment outcomes and prognostic factors affecting the treatment outcomes.

MATERIALS AND METHODS

A retrospective review of all patients with SNM treated at a dedicated cancer center between January 2004 to December 2018 was carried out after taking exemption from the Institutional Review Board (IRB) of and (IRB number: EX-28-04-20-04, date of IRB: June 5, 2020). The study was conducted in accordance with the guidelines of the Declaration of Helsinki (1964). All ethical guidelines were followed with respect to anonymity of the patients.

The criteria of inclusion were all the patients with histologically proven diagnosis of malignancy arising from nasal cavity or paranasal sinuses and being treated with curative intent. Whereas, patients with malignancies arising from nasopharynx, distant metastasis, prior history of treatment from other hospitals, missing data, and lost to follow-up were excluded to eliminate the element of selection bias and confounders. After meeting the criteria of inclusion and exclusion, 184 patients



Figure 1: Computed tomography paranasal sinus coronal view showing large heterogeneously enhancing mass, arising at the floor of the nasal cavity



Figure 2: CT Paranasal sinus axial view showing enhancing mass in the right nasal cavity inseparable from ipsilateral inferior nasal turbinate



Figure 3: Preoperative image showing incision marking of Weber Ferguson approach to access the tumour in nasal cavity

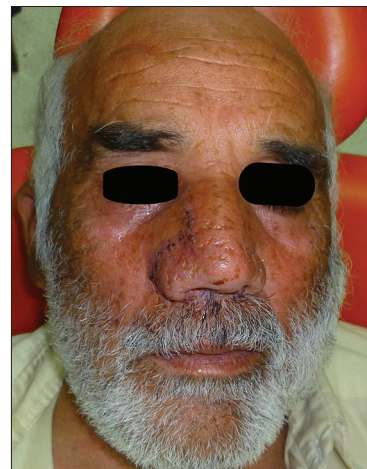


Figure 4: Postoperative image showing the wound closure.

were included in the study and their medical records were reviewed.

Primary variables included were age, gender, risk factors, tumour histology, site, size, neck nodal status, staging, and treatment failure in terms of locoregional recurrence and distant metastasis was collected. The data were analyzed using SPSS software (version 25.0; SPSS, Chicago, IL, USA). Chi-square test was applied to identify significant differences where relevant. Five-year disease-specific survival (DSS) was calculated using Kaplan–Meier curve via log-rank test and comparison was made between squamous cell carcinoma and nonsquamous histologies. $P \leq 0.05$ was considered statistically significant.

RESULTS

A total of 329 patients were identified with the diagnosis of SNMs who were treated at our center during the period of 15 years from 2004 to 2018. After exclusion of 145 patients due to multiple reasons such as outside surgery ($n = 45$), palliative intent of treatment ($n = 90$), and missing data ($n = 10$), 184 patients were included for formal analysis.

The mean age of the patients was 47.8 years (standard deviation [SD] ± 14) with a range of 18–82 years (interquartile range [IQR] = 21). 117 (63.6%) patients were male as compared to 67 (36.4%) females. Squamous cell carcinoma was the most common histopathology ($n = 62$, 33.7%) followed by adenoid cystic carcinoma, sinonasal carcinoma and adenocarcinoma. Maxillary sinus was the primary site in majority of our patients ($n = 88$, 47.8%). Smoking ($n = 40$, 21%) and tobacco chewing ($n = 28$, 15.2%) were the common risk factors present in our patients while majority of them presented with complaints of nasal blockage ($n = 70$, 38%) and epistaxis ($n = 35$, 19%). Details of demographics and patient characteristic features are discussed in Table 1.

The American Joint Committee on Cancer (AJCC) staging 8th edition was used for pretreatment staging.^[28] 130 (70.7%) patients presented with stage IV disease. Regional nodal metastasis was seen in 24 (13%) patients [Table 1].



Figure 5: Intraoperative image showing the tumour in the right nasal cavity

Surgery was performed in 87 (47.3%) patients whereas the remaining 97 (52.7%) patients were treated by radiation and chemotherapy. Out of 87 patients undergoing surgery, 36 (41.4%) patients underwent partial maxillectomy whereas 24 (27.6%) patients underwent total maxillectomy. Neck dissection was carried out in 6 (6.9%) patients diagnosed with squamous cell carcinoma of maxilla.

All patients were followed up to 5 years. The mean follow-up period was 49.4 months (SD ± 12) with a range of 9 months to 66 months (IQR = 38). Treatment failure was seen in 96 (52.2%) patients with locoregional recurrence occurring in 64 (66.7%) patients and distant metastasis in 32 (33.3%) patients. Treatment failure was significantly associated with tumour size ($P = 0.02$) and the overall stage of the disease ($P = 0.04$). Node positivity, histopathology types, and nonsurgical treatment were not significantly associated with treatment failure [Table 2].

A significant difference was seen ($P = 0.001$) between nonsquamous and squamous cell carcinoma groups with 5-year DSS of 52% in patients with nonsquamous histology as compared to 29% in patients with squamous cell carcinoma [Figure 6].

DISCUSSION

SNMs are rare, diverse in histology, and comprise cancers involving nasal cavity as well as paranasal sinuses.^[29] These tumours tend to arise from different tissues within the sinonasal region including minor salivary gland, Schneiderian mucosa, neural tissue, and lymphatics which make them a heterogeneous group of malignant tumours.^[30] As these tumours are relatively uncommon, majority of the data reported in the literature is based on single-institution experiences and retrospective reviews reporting wide range of management outcomes.^[31,32]

Although the varying disease patterns have been reported in the literature,^[33] maxillary sinus is the most common site of origin of these tumours (60%) followed by nasal cavity (20%),

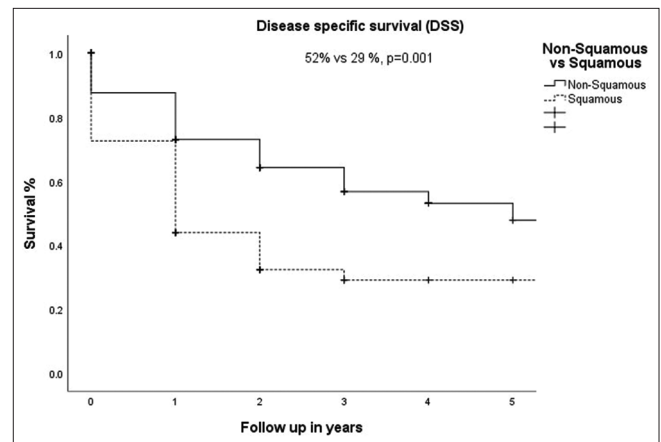


Figure 6: Disease specific survival (DSS) of Squamous cell carcinoma and Non-squamous histologies

Table 1: Demographic and patient characteristic features

Patient characteristics	Frequency, n (%)
Gender	
Male	117 (63.6)
Female	67 (36.4)
Histopathology	
Adenoid cystic carcinoma	32 (17.4)
Adenocarcinoma	16 (8.7)
Melanoma	9 (4.9)
Olfactory neuroblastoma	10 (5.4)
Sinonasal carcinoma	20 (10.9)
Squamous cell carcinoma	62 (33.7)
Others	35 (19)
Primary tumour site	
Maxillary sinus	88 (47.8)
Nasal cavity	65 (35.3)
Ethmoid sinus	30 (16.3)
Sphenoid sinus	1 (0.6)
T Stage	
1	3 (1.6)
2	26 (14.1)
3	24 (13)
4	129 (70.1)
X	2 (1.1)
N Stage	
N0	160 (87)
N1	15 (8.1)
N2	9 (4.9)
Overall stage	
I	4 (2.2)
II	24 (13)
III	24 (13)
IV	130 (70.7)
X	2 (1.1)
Presenting symptoms	
Facial swelling	30 (16.3)
Nasal obstruction	70 (38)
Epistaxis	35 (19)
Visual disturbance	6 (3.3)
Neurological deficit	4 (2.2)
Others	39 (21.2)
Risk factors	
Smoking	40 (21.7)
Tobacco chewing	28 (15.2)
Betel nuts	8 (4.3)
Alcohol	4 (2.2)
Occupational	6 (3.3)

ethmoid sinuses (5%), and rarely from frontal and sphenoid sinuses (3%).^[34] In our series, similar results are seen with respect to the site of origin.

The most common malignant neoplasms arising in this region are squamous cell carcinoma and salivary gland tumours accounting for up to 55% followed by nonepithelial tumours (20%) and glandular tumours (15%).^[35] A similar distribution of histology has been reported in our study.

AJCC staging 8th edition was used to stage these tumours in our series which is being widely used throughout the world.^[28] Eighty-four percent of our cases have presented to us with advanced stage (III and IV) of the disease. It has been reported in the literature that majority of the cases presented at an advanced stage with bulky tumours invading through the bone, sinuses, and other important surrounding structures like orbit.^[36] Considerable variation in the symptoms of these tumours is one of the major factors in delayed presentation and diagnosis. Symptoms such as facial pain, nasal obstruction, nasal discharge, and epistaxis can be misleading. Also, these features can be confused with upper respiratory tract infections and sinusitis. In cases where disease has progressed to advanced stages, the patient usually presents with more serious symptoms including proptosis, diplopia, cerebrospinal fluid rhinorrhea, and epiphora due to intracranial or orbital invasion and similar presenting symptoms were identified in our study.^[37]

Unlike other head-and-neck malignancies in which incidence of cervical lymph node metastasis is high, 87% of our cases were node negative which is consistent with data in the literature stating that cervical nodal metastasis is a rare feature in SNMs.^[1,37,38] Despite that, studies have supported the idea of performing elective neck dissection in cases with aggressive histology and advanced stages of the disease. The lower incidence of cervical nodal metastasis has led to the conservative management of node-negative disease.^[37] On the other hand, Scurry *et al.* have reported cervical recurrence up to 18% and suggested to perform elective neck dissection in N0 for squamous cell carcinoma.^[39] A higher rate of regional recurrence was seen because only squamous cell carcinoma was studied as compared to other studies which included different histopathologies and multiple subsites.

One of the major causes of treatment failure in SNM is local recurrence as compared to distant metastasis.^[1,40] In our series, treatment failure was seen in 96 (52.2%) patients with locoregional recurrence in 64 (66.7%) patients and distant metastasis in 32 (33.3%) patients.

The 5-year survival rate for squamous cell carcinoma of sinonasal region has been reported 25%–50% in the literature. In comparison, the survival rate of adenocarcinoma and adenoid cystic carcinoma ranges between 40% and 60%.^[41] The most common histology in our study was squamous cell carcinoma. As the frequency histology subsets were too low, we divided our study population into squamous and nonsquamous histologies and compared their 5-year DSS rates. A significant difference ($P = 0.001$) was seen in patients with squamous and nonsquamous histologies. Patients with squamous cell carcinoma showed poor outcomes as compared to patients with other histologies [Figure 6].

Over the period of time, studies have investigated the impact of various prognostic factors including size and nodal stage of the disease, nonsurgical treatment options, and histology

Table 2: Association with treatment failure

Characteristics	Total number	Locoregional recurrence	Distant metastasis	P
T stage				
1	3	1	0	0.02*
2	26	6	1	
3	24	8	6	
4	129	49	23	
X	2	0	2	
Nodal status				
Positive	24	7	5	0.83
Negative	160	57	27	
Overall stage				
I	4	1	0	0.04*
II	24	6	1	
III	24	9	5	
IV	130	48	24	
X	2	0	2	
Histopathology				
Adenoid cystic carcinoma	32	9	10	0.14
Adenocarcinoma	16	6	5	
Melanoma	9	2	3	
Olfactory neuroblastoma	10	5	2	
Sinonasal carcinoma	20	8	3	
Squamous cell carcinoma	62	27	5	
Others	35	7	4	
Treatment modality				
Surgery	87	27	11	0.11
Radiation and chemo	97	37	21	

*P is taken as significant if it is ≤ 0.05

types. Positive neck nodes and histology type are reported to be significantly associated with treatment failures.^[1,37] In our series, tumour size and overall stage were found to be independent factors affecting treatment failure and histology type was not significantly associated with treatment failure.

The limitation of our study includes retrospective study design. Although the study has a large sample size including diverse histopathology, the frequencies of histopathology subsets were too low for survival analysis. Separate studies reporting survival outcomes of each histopathology would be desirable in future studies as it will help to identify prognostic factors and outcomes of each histology separately.

CONCLUSION

We conclude that SNM is a rare and diverse group of cancers usually presenting with a variety of symptoms in late stages of the disease. Maxillary sinus is the most commonly involved site. It was more commonly seen in males and was found to be associated with smoking and tobacco chewing. These tumours have a higher rate of treatment failure with poor prognosis and it was found to be significantly associated with T stage and overall stage of the disease. Squamous cell carcinoma was seen as the most common and aggressive pathology as compared to other pathologies.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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