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Pattern of Cervical Lymphnode Metastasis from Oropharyngeal Squamous Cell Carcinoma

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Abstract: ***Background:*** Oropharyngeal squamous cell carcinoma (OSCC) is the sixth most common malignancy globally, often presenting with cervical lymph node metastasis. Due to limited local data, this study aimed to assess the pattern of cervical lymph node metastasis in OSCC at the Department of Otolaryngology & Head-Neck Surgery, Sylhet M.A.G Osmani Medical College. ***Methods:*** This hospital-based cross-sectional study was conducted over 6 months with ethical approval. A total of 100 patients with OSCC were enrolled using predefined criteria. Data were collected via structured questionnaires, clinical evaluations, imaging (CT/MRI), FNAC, biopsy, histopathology, and operative findings, then analyzed using SPSS 26. ***Results:*** The mean age was 53.09±9.35 years; 65% were male and 80% belonged to the lower-middle socioeconomic class. Lymph node involvement was ipsilateral in 75%, contralateral in 20%, and bilateral in 5%. Multiple nodal involvement was seen in 70%. Nodes were hard (52%), firm to hard (35%), and cystic (2%), with 70% being mobile. Node size exceeded 6 cm in 45% of cases. Primary tumor sites were tonsil (55%), base of tongue (25%), soft palate (15%), and posterior pharyngeal wall (5%). Tumor staging showed T2 (54%), T1 (24%), T3 (13%), and T4 (9%), while nodal stages were N3 (45%), N2 (35%), and N1 (20%). Ipsilateral nodal involvement was highest at level II (52%) and III (24%). ***Conclusion:*** Tonsil was the most common primary site. Most metastases were ipsilateral, with level II and III lymph nodes most frequently involved. Further research is warranted for broader validation.

Keywords: Oropharyngeal Carcinoma, Cervical Lymph Nodes, Metastasis Pattern, Nodal Staging, Tumor Site Involvement.

Original Research Article

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Article at a glance:

Study Purpose: *This study aims to assess the pattern of cervical lymph node metastasis in patients with oropharyngeal squamous cell carcinoma at a tertiary care center.*

Key findings: *Most cervical metastases were ipsilateral, with level II and III lymph nodes most frequently involved, and tonsil being the most common primary site.*

Newer findings: *Ipsilateral involvement was seen in 75% of cases, and 70% of the patients had multiple nodal metastases, highlighting aggressive spread in OSCC.*

Abbreviations: *OSCC - Oropharyngeal Squamous Cell Carcinoma, FNAC - Fine Needle Aspiration Cytology, CT - Computed Tomography.*

INTRODUCTION

Oropharyngeal squamous cell carcinoma (OPSCC) falls under the broad category of head and neck squamous cell carcinoma (HNSCC). Other sub-sites of HNSCC include oral cavity, hypopharynx, larynx, and nasopharynx.[1] The Oropharynx is classically divided into four distinct subsites: Base of tongue (BOT), Soft palate, Palatine tonsil (both) and Posterior pharyngeal wall. In 2018, oropharyngeal cancer attributed to 0.5% of incidence and mortality of all cancer Among the 18.1 million new cases of all caner worldwide oropharyngeal cancer shared 92,887 new cases.[2] The incidence of OPSCC has decreased in most developed countries over the past decades. But, it

remains a common cancer for both male and female individuals in south–central Asia and in central and Eastern Europe. In Bangladesh oropharyngeal cancer is very common and one of the top 5 most frequent cancer. It contributed to 2.4% of incidence, 3% death of all cancers in 2018. Cervical region is the most common site for lymphadenopathy for OPSCC. Lymph node metastases in this region are a strong factor in terms of increased recurrence and disease-specific and overall death.[3] Determining lymph node metastases in OPSCC is important for staging, prognosis, and defining the appropriate treatment.[4,5] The lack of a well-developed basement membrane in the lymphoepithelium of the oropharynx results in a high incidence of lympho-vascular invasion and early lymph node metastasis .[6] Therefore, an understanding of the anatomical sub sites and lymphatic drainage is essential. The Lining Epithelium of oropharynx is Nonkeratinised Stratified squamous epithelium. The American Academy of Otolaryngology & Head- Neck Surgery modification of system used to assign levels for cervical lymph nodes. (Courtesy: Memorial Sloan-Kettering Cancer Center in order to establish a consistent and easily reproducible, user friendly method for description of regional cervical lymph nodes which establishes a common language between the clinician and the pathologists. Lymphatic drainage of the head-neck tissue is divided into a superficial & a deep system & usually the passage of lymph is lateralized & sequential & follows a predefined route from superficial to deep. Submental and sub-mandibular lymph nodes (level Ia and Ib) might be involved by malignant tumors of oral cavity, tongue, lips, oropharynx, nasopharynx, and scalp. Jugulodiagastric lymph nodes (level II) can harbor malignant cells from tonsils, pharynx, larynx, nasal sinuses as well as salivary glands. Level III, IV and V lymph nodes drains malignancy from pharynx, larynx, skin, as well as thyroid.

The study of Vartanian *et al*., aimed at describing the distribution of lymph node metastases in patients with OPSCC, included 81 patients.[7] There were 5 cases of clinically detected ipsilateral neck lymph nodes at level I, 55 at level II, 14 at level III, 2 at level IV, and none at level V. On clinical examination there were 2 cases of single neck level involvement at level I, 40 at level II, 2 at level III, and none at levels IV and V. Contralateral nodes were detected in 4 patients [7]. In more than 60% of metastatic neck node, primary sites can be identified by taking comprehensive history and initial physical examination. However, further evaluation by fibre optic laryngoscopy and biopsy and histopathological examination & imaging is required for confirmatory diagnosis and effective management. Fine needle aspiration cytology is most important diagnostic tool in demonstrating metastatic carcinoma in lymph node. The treatment options for metastatic neck disease are surgery, radiotherapy, chemotherapy or a combination of these.[8] Metastatic Neck node may be ipsilateral, contralateral or bilateral, may be single or multiple, may be solid or cystic in a repeated decorative design known as pattern. The 5 years survival rate of the metastatic neck is by approximately 50%. The survival rate reduced further when multiple nodes are involved as extra nodal spread. With further progression the incidence of distant metastasis also increases dramatically making the disease incurable.[8] It being of the common cancer in Bangladesh, early treatment of the tumour and better prognosis is warranted with good loco-regional control, reduction of distant metastasis and so improved survival. Therefore, this study was designed to evaluate pattern of cervical lymphnode metastasis from oropharyngeal squamous cell carcinoma.

OBJECTIVE

General Objective

To observe the metastatic cervical lymph nodes from oropharyngeal squamous cell carcinoma.

Specific objectives

To observe the site, size, histological type of primary lesion and metastatic cervical lymph nodes

To observe whether it is unilateral, bilateral or contralateral.

To observe the characteristics of oropharyngeal squamous cell carcinoma.

METHODOLOGY

Study design: Cross Sectional Study.

Study place: Department of Otolaryngology & Head-Neck Surgery, Sylhet M.A.G Osmani Medical College Hospital.

Study period: The study was conducted during the period from 1st September 2018 to 31st August 2020.

Study population

Among the target population, all adult patients with metastatic cervical lymphadenopathy from oropharyngeal squamous cell carcinoma who fulfilled the inclusion criteria were considered as study population.

Sampling Technique

Purposive sampling technique was applied

Sample size

The Sample size of this study was determined by following question Formula of sample size calculation: (Guilford's and Frucher's formula)

Here,

$$n = \frac{Z^2 pq}{d^2}$$

n = sample size
z = 1.96 (in 95% Cl)
p = Prevalence: 0.5 (as exact population prevalence is unknown)
q = 100- p
d = allowable error: 10% (0.1)
n (total study subjects) = 96.04
Total 100 patients were included in the study.

Inclusion criteria for Case:

All patients with primary oropharyngeal squamous cell carcinoma and neck node metastasis evidenced by FNAC and histopathology.
Aged more than 18 years of both sex.

Exclusion criteria for Case:

Patient with metastatic lymphnodes with previous history of chemoradiation.
Patient with metastatic lymphnodes with previous history of surgery in neck.
Patient with advanced stage of diseases.

Data collection technique

This Cross-Sectional Study was done in the Department of Otolaryngology & Head-Neck Surgery, Sylhet M.A.G Osmani Medical College Hospital. Formal ethical clearance was taken from the ethical review committee of SOMC before starting the study. The patients attended the indoor and the outdoor of the respective department during the study period were approached for this study. Total 100 patients were selected according to inclusion and exclusion criteria. A structured questionnaire was used for data collection, pre-tested before final implementation. Patients admitted to the Otolaryngology & Head-Neck Surgery department underwent detailed history-taking and thorough clinical examination, focusing on the ear, nose, throat, and neck. Indirect and Fibre Optic Laryngoscopy (FOL) with photographs were performed for every patient to assess lymph node involvement. General investigations and specific imaging, including CT scan/MRI of the neck, were conducted. Punch biopsy from oropharyngeal lesions was performed, while FNAC and histopathology of enlarged lymph nodes were handled consistently by the pathology department. Peroperative findings in metastatic lymph nodes were recorded for patients undergoing surgery by senior faculty members. Histopathological reports were collected, and patients were discharged with post-operative management advice. All information was recorded in separate case record form. Collected data was checked for error and analysed using SPSS 26.

Data Collection Tools

A semi-structured questionnaire
Tools for physical (ENT) exam
Informed written consent form in Bangla
Informed written consent form in English

Data processing and analysis

Data were processed and analyzed manually and using SPSS (Statistical Package for Social Sciences) Version 26. Quantitative data were expressed as mean and standard deviation, while qualitative data were presented as frequency and percentage. Statistical significance was determined with a probability (p) value, where p 0.05 was considered insignificant.

RESULTS

Table 1: Distribution of the patients by Age (n=100)

Age group in year	No. of patient	Percentage	mean±SD (yrs)
20 to 30 years	1	1	**53.09±9.35**

31 to 40 years	14	14
41 to 50 years	20	20
51 to 60 years	40	40
> 60 years	25	25
Total	100	100

40% patients were aged between 51 to 60 years and 25% were more than 60 years. Beside 20% patients were aged between 41 to 50 years, 14% were 31 to 40 years and only 1% were aged between 20 to 30 years. Mean age of the patients was 53.09±9.35 years. Most of the scc appear in people over 50 years in our study.

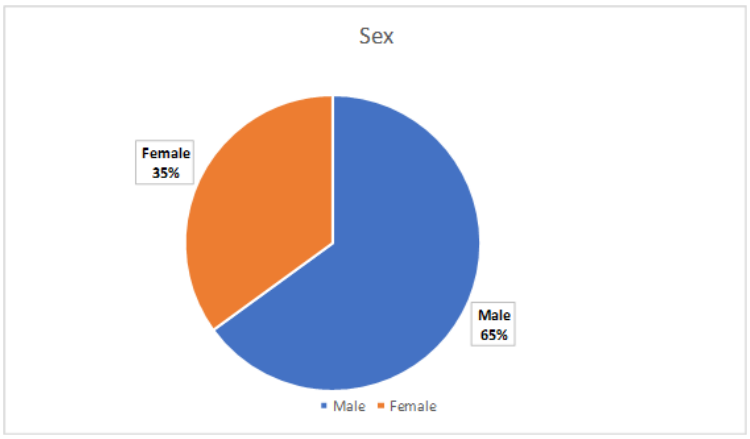

Figure 1: Gender Distribution of the Study Patients

Pie chart shows that among the patients 65% were male and 35% were Female. Male are predominance in the current study.

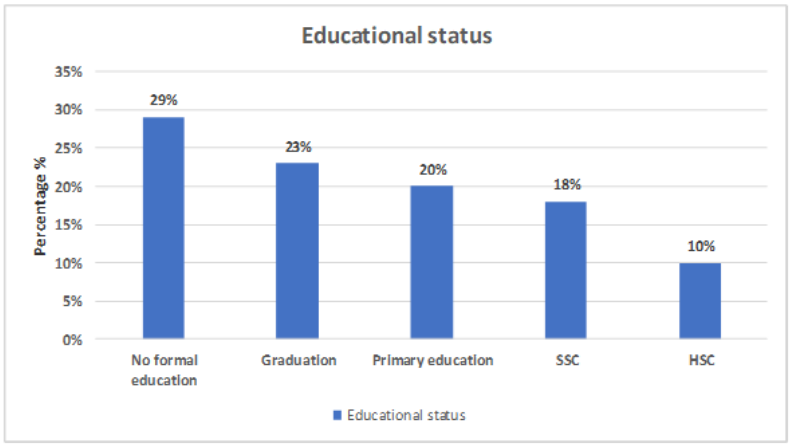

Figure 2: Distribution of the patients by Educational Status (n=100)

Bar chart shows that 29% patients had no formal education, 20% had primary education, 18% had S.S.C and 10% had H.S.C. Whereas 23% had completed Graduation. Here majority patients had no formal education.

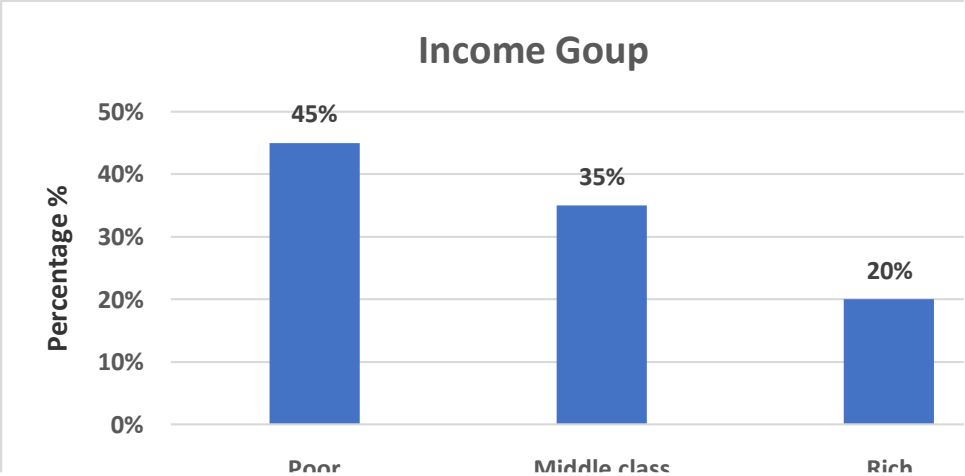

Figure 3: Distribution of the patients by Income group (n=100)

Bar chart shows that 45% patients were poor and 35% were middle class beside only 20% were rich.

Table 2: Distribution of the patients by T staging of Disease (n=100)

Staging of disease	Number of Patients (n)	Percentage (%)
T_1	24	24
T_2	54	54
T_3	13	13
T_4	9	9
Total	**100**	**100**

54% patients had Stage T_2, 24% patients had Stage T_1, 13% patients had Stage T_3 and 9% patients had Stage T_4. Most common patients had T_2 stage.

Table 3: Staging of Lymph node metastasis (n=100)

Staging of lymph node	Number of Patients (n)	Percentage (%)
Stage N_1	20	20
Stage N_2	35	35
Stage N_3	45	45
Total	100	100

45% patients had Stage N_3, 35% patients had Stage N_2 and 20% had Stage N_1. Most common lymph node stage was N_3.

Table 4: MRI Findings of Nodal involvement (n=100)

MRI Findings	Number of Patients (n)	Percentage (%)
Ipsilateral	75	75
Contralateral	20	20
Bilateral	5	5
Total	100	100

Cervical metastasis 75% was ipsilateral, 20% was contralateral and 5% was bilateral in case of MRI findings. Majority was ipsilateral.

Table 5 Per-operative findings of nodal involvement (n=100)

Per-operative Findings	Number of Patients (n)	Percentage (%)
Ipsilateral	75	75
Contralateral	20	20
Bilateral	5	5
Total	100	100

Per-operative findings that 75% was ipsilateral, 20% was contralateral and 5% was bilateral in per-operative findings.

Table 6: Site of the Primary OPSCC according to level of metastasis

		Level of Metastasis				Total
		Level I	Level II	Level III	Level IV	
Site	Palatine tonsil	15	23	7	10	55
	Base of the tongue	0	15	10	0	25
	Soft palate	0	12	3	0	15
	Post-pharyngeal wall	0	0	5	0	5
Total		15	50	25	10	100

Level of metastasis based on primary OPSCC site. Only palatine tonsil group (n=10) shows level IV metastasis. Among 100 patients 50 patients shows level II metastasis. This difference was statistically significant (χ 2= 43.85; P < .002).

Table 7: Tumor site distribution according to staging

		Stage of tumor				Total
		T_1	T_2	T_3	T_4	
Site	Palatine tonsil	5	38	6	6	55
	Base of the tongue	10	10	3	2	25
	Soft palate	9	1	4	1	15
	Post-pharyngeal wall	0	5	0	0	5
Total		24	54	13	9	100

Staging of primary head neck tumor based on site of tumor. 54 patients belong to T_2 stage, among them highest frequency (n=38) is seen in palatine tonsil group. Only 9 patients belong to T_4 stage, and again most of them (n=6) are from palatine tonsil group. This difference is statistically significant (χ 2= 32.27; P < .001).

DISCUSSION

This study was to observe the metastatic cervical lymph nodes in oropharyngeal squamous cell carcinoma. It was a cross-sectional study. In this current study total number of the patients were 100. Sample size was calculated by using (Guilford's and Frucher's formula) and fixing prevalence value 50 as there is no prevalence value in our country. In this study Majority (40%) of the patients were aged between 51 to 60 years and 25% were more than 60 years. Mean age of the patients was 53.09±9.35 years of SD. Most SCCs appear in people over 50 years in our study, it was found that chance of occurring SCC increases with ages. Similar findings was observed in a previous study by Lim *et al.,* observed mean age of 55 years and age range was 22 to 78 years.[9] Hassan *et al.,* observed age range from 20 to 68 years with a mean age 53.6 years and the highest age group was the sixth decade with 32 (53.3%) patients.[10] This study showed that among the patients 65% were male and 35% were Female. Man are thought to be more exposed to the risk factor and come hospital more. It can be the reason of male predominance in the current study.

Rahman *et al*., also observed the similar findings with 78.33% male and 21.67% female.[8] In the study of Hassan *et al*., among 60 patients 28 patients were males and 32 were females.[10] Another study of Shah *et al*., there were 139 males and 68 females in the oropharyngeal SCC patients.[11]

TNM staging is used to describe the amount and spread of cancer in a patient's body. It depends on patients' condition so it can be varied study to study. According to this study 54% patients had Stage T_2, 24% patients had Stage T_1, 13% patients had Stage T_3 and 9% had Stage T_4. Majority of the patient was stage T_2.The primary tumor does not have readily discernible sign or symptoms as they grow within the tonsillar capsule and crypts. It is difficult to noticed anything suspicious on examination of the tonsil other than slight enlargement or the development of firmness around area. In the study of Lim *et al*., according to clinical T stages 18 was T_1, 50 was T_2, 17 was T_3 and T_4 was in 19 cases. Vartanian *et al*., observed T_1 in 2 patients (2%), T_2 in 21 patients (26%), T_3 in 36 patients (44%), and T_4 in 21 patients (26%).[7]

In this study 45% patients had Stage N_3, 35% patients had Stage N_2 and 20% patients had Stage N_1. Most common lymph node stage was N_3. Because most of the patient come to hospital with late presentation. Initially they are asymptomatic and painless cervical lymphadenopathy treated by village doctor. When primary tumor and cervical lymphnodes are gradually enlarge in size they come to the hospital. Rahman *et al*., observed highest involvement (40%) in stage N_2 beside 33.33% had Stage N_1 and 26.67% had Stage N_3 .[8] Among all the enrolled patients in this study it was found that 39 patients had involved neck lymph node level II, 18 had Level III, 8 had Level I and 10 had Level IV involvement in case of ipsilateral nodal involvement. In case of contralateral nodal involvement 10 had involved level II, 5 had Level I and 5 had Level III involvement. Beside in Bilateral nodal involvement, 2 involved level I, 2 had Level III and 1 had Level II involvement. In this study most common involvement in neck lymph node level II Jugulodiagastric lymph nodes (level II) can harbor malignant cells from tonsils, pharynx, larynx, nasal sinuses as well as salivary glands. Rahman *et al*., also observed highest involvement in neck lymph node level II & III [8].

In the study of Vartanian *et al*., observed that most common sites for the metastases detected clinically as well as histopathologically were at levels II and III. There were 5 cases of clinically detected ipsilateral neck lymph nodes at level I, 55 at level II, 14 at level III, 2 at level IV, and none at level V. Cervical region is the most common site for lymphadenopathy. Metastasis to regional lymphnodes as the oropharynx has a rich supply of lymphatics giving way to the tumor cells to metastasis to other lymphnodes.[12] The presence of a cervical lymph node metastasis is one of the most important prognostic factors in treating patients for oropharyngeal squamous cell carcinoma (SCC). This study has provided further knowledge on the pattern of cervical lympnode metastasis from orophanyngeal squamous cell carcinoma.

CONCLUSION

In this study, most common involved primary site of lymph node metastasis in oropharyngeal squamous cell carcinoma was tonsil. Around three-fourth of study population had the disease ipsilaterally, a little less than one-fourth had contralaterally and 5% had the involvement bilaterally. The most common stage of carcinoma and lymph node metastasis was T_2, T_1 and N_3 respectively. The pattern of cervical lymphnode metastasis observed in this study will help for management planning for them specialy wheather primary surgery, surgery after chemoradiation extent of neck dissection or only chemoradiation for a particular patient of oropharyngeal squamous cell carcinoma with cervical neck node metastasis. However further study with large number of patients for a wide period recommended to get the exact scenario in this context.

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