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CLINICOPATHOLOGICAL STUDY OF CARCINOMA ORAL CAVITY & PATTERN OF METASTASIS- EXPERIENCE IN A TERTIARY CARE CENTRE

Otorhinolaryngology

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ABSTRACT

Oral cancer (code 145.9, ICD 9) encompasses all malignancies originating in oral tissues & it is a major health problem in many parts of the world. Although incidence is relatively low in the western countries, in the Indian subcontinent & other parts of Asia it remains one of the commonest cancers.

The study was conducted on the patients attending the ENT & HEAD-NECK SURGERY OPD at the INSTITUTE OF OTORHINOLARYNGOLOGY & HEAD-NECK SURGERY, IPGME&R, Kolkata during a period of 1 year from 1st March 2019 to 29th February 2020.

Buccal mucosa was the commonest site & most cases presented in late stage with cervical lymph node metastases entailing poorer prognosis. People should be made aware of the warning symptoms, need for early diagnosis & treatment options available through IEC (information, education & communication programmes) in order to provide better treatment outcomes, improved long term prognosis & thereby reducing the morbidity & mortality of people at large.

KEYWORDS

Oral cancer, squamous cell carcinoma, cervical lymph node metastasis, depth of invasion, stage of disease

INTRODUCTION:

Oral cancer (code 145.9, ICD 9) encompasses all malignancies originating in oral tissues & it is a major health problem in many parts of the world. Although incidence is relatively low in the western countries, in the Indian subcontinent & other parts of Asia it remains one of the commonest cancers. Histologically over 95% of oral cancers are squamous cell carcinomas,arising from mucosal epithelia of oral cavity. It is the 3rdmost common malignancy in developing countries & 8th most common in developed countries.

In 2012, there were 8.2 million cancer deaths worldwide, of which 0.68 million people died from cancer in India.[1] Available treatment options for oral cancers are surgery, radiation & chemotherapy.[2]High usage of tobacco in different forms and delayed diagnosis related to inability to recognize symptoms in early stage are associated with high mortality rate associated with oral cancers. In India cancer of oral cavity is a major problem[3], age adjusted rates of oral cancer is high, i.e. 20/lakh population & accounts for over 30% of all cancers in the country.[4]It is one of the five leading sites of cancer in either sex & only 15% of patients are diagnosed when the disease is in localized early stage.[5]Early diagnosis & treatment of oral SCC is very important in reducing mortality & morbidity from this devastating disease.Stage 1(early disease) & stage 4(advanced) have 5-yearsurvival rate as 80% & 20% respectively.[6]Tobacco & alcohol are known risk factors which have combined effect on development of oral cancers.[7]Other factors like poor nutrition, sun exposure, coexistent HPV infection are also associated.[8] Approximately 30% cases wait for >3months before consulting a doctor for signs of oral cancer,[9] which is related to slow presentation, delayed symptom recognition, poor knowledge, coping responses on part of the patient.[10]Lack of awareness & mis-judgement of symptoms attributed as the commonest cause of delay in seeking medical attention in oral cancer patients.[11]

Oral cancers are a significant public health problem in India. Only early detection provides best treatment outcome & long-term survival. But unfortunately people from lower socio-economic class are more exposed to the risk factors of oral cancers & have low access to health care services, more so in the rural areas.[12]So mostly cases are diagnosed in later stage leading to poorer treatment outcomes & significant cost of palliative treatment which most of the patients fail to bear leading to increased morbidity & mortality. Hence oral cancers pose a challenge & heavy burden even to tertiary care centers in India. Only emphasis on early detection & primary prevention can address the problem.

With this backdrop we undertook this study at a tertiary care Govt Hospital to collect clinico-epidemiological data & to correlate the pathological status to the prognosis of oral cancers.

MATERIALS & METHODS:

Study location: The study was conducted on the patients attending the ENT & HEAD-NECK SURGERY OPD at the INSTITUTE OF OTORHINOLARYNGOLOGY & HEAD-NECK SURGERY, IPGME&R, Kolkata during a period of 1 year from 1st March 2019 to 29th February 2020.

Study population:

Inclusion criteria: All the patients presenting with oral cancers involving the various subsites like lip, alveolus, buccal mucosa, anterior 2/3rd of tongue, retromolar trigone, hard palate & floor of mouth were included in the study, irrespective of age & sex. The presentation included swelling, ulcer, clinically apparent &sometimes biopsy proven cases of malignancy. The patients primarily presenting with neck lymphadenopathy in whom carcinoma was detected clinically or during the evaluation for primary malignancy were also included in our study.

Exclusion criteria:

Non-malignant swelling/ ulcers of oral cavity, pre-malignant lesions (leukoplakia, erythroplakia, lichen planus), recurrence cases, second primary at some other site of the body, post- treatment (post chemo-radiation or post-operative neck dissection) patients were excluded from the study.

Aims & Objective of the study were

1. To see the incidence of oral cancers in the background of local habits
2. To relate T-stage of the disease with thickness & depth in reference to metastasis

Study design: hospital based prospective study
Ethical committee approval was obtained from institutional ethical committee prior to commencement of the study. A pre-designed pre tested proforma was used to document detailed history&clinical findings of the cases included in the study. Detailed local examination of neck was performed along with evaluation of upper aero-digestive tract, nasopharyngoscopy, barium swallow study & upper GI endoscopy to detect the primary lesion as well as to rule out any second primary lesions. Ultrasonography of neck & FNAC of neck node were undertaken. Imaging like CT scan & MRI were included in the work up. Biopsy of primary lesion was done for histological confirmation, assessment of depth of invasion & to classify primary tumor based on grades of differentiation i.e, well, moderate or poorly differentiated. All the primary malignancies were staged according to American Joint Committee on Cancer (AJCC/UICC) TNM Classification.

RESULT & ANALYSIS:

In the present study 88 patients of carcinoma oral cavity were included during the stipulated time period based on the inclusion & exclusion criteria. Buccal mucosa was found to be the commonest site of oral cancer (29.54% cases) followed by gingivobuccal sulcus & gingival involvement (20.45% cases).

Maximum number of patients were recorded in the age group 51-60 years(27.27%), with the eldest patient being 80 years & youngest being 25 years old. Of the patients included in our study, males were more affected with male: female ratio being 2.6:1.

Most of the patients belonged to the lower socio-economic class. Majority of the cases (86%) had no family history of cancer.

Addiction history of the patients revealed betel quid chewing & tobacco chewing being the commonest forms of addictions in oral cancer cases followed by smoking & alcohol consumption in lesser number of cases.

Ulceration/ swelling in the oral cavity was the commonest presentation (81.8%) followed by neck swelling (75% cases). Pain was present in 54.5% cases, indicating more advanced disease. We found that most of patients presented within 6 months from onset of their symptoms (36% cases).

Majority of the patients (54.5%) presented with ulcerative type of lesions in the oral cavity. Neck node metastasis was present in majority of the cases (82%), most of which were unilateral involvement. On analyzing the pattern of metastasis, level IB was found to be mostly affected in oral cavity carcinomas (66.7% cases).

In our study we found that most of the patients with oral cancers presented in stage III as per TNM staging (77% cases). On histopathological correlation well differentiated squamous cell carcinoma was the commonest variant (70%) of the lesions.

Most of the lesions had thickness of ≤10 mm in our study group (47.7%). On considering the depth of invasion, most of the lesions had depth ≤5mm in the present study (56.8% cases). Pattern of neck metastasis was correlated with thickness & depth of lesions which showed out of 58 cases of level IB metastasis, 36 % cases had lesions with thickness ≤10 mm & depth ≤5mm whereas 41.6% cases had lesions with thickness 11-15 mm & depth >5-≤10 mm. Other lymph node levels were involved in fewer number of cases.

DISCUSSION:

Among the 88 patients of carcinoma of oral cavity included in the present study, various clinical & pathological correlations were found, which were corroborated with data available via review of literature.
Various sites of oral cavity were studied regarding incidence of malignancy. Various studies showed buccal mucosa to be the commonest site of oral cancer.[13-15] Similar results were foundin our study. Gingivobuccal sulcus & gingival involvement were the second commonest site. Carcinoma gum was reported to be the commonest subsite (32.7%) followed by buccal mucosa (28.1%) & tongue (26.9%).[16] In another study tongue was the commonest site (40% cases).[17] Result of the study by Ramachandra et al was similar to our study, reporting buccal mucosa to be the commonest (57.5%) followed by tongue (24.2%).[18] In our study tongue the 3rd commonest subsite (11.36%).

The peak age of incidence of oral cancers again varied between different studies. US National Cancer Database reported mean age for oral cancers being 62 years (2006) whereas LarondeD et al reported persons >60 years to be at risk of oral cancers among Canadian population.[19] In India the peak occurrence of oral cancers appears a decade earlier,common age group being 40-50 years.[20]Age group 50-59 years was the commonest reported by Gangane N et al.[15]In the study by Ramachandra et al, majority (38.5%) patients suffered from oral cancer in 4th decade followed by 35.2% in the 3rd decade,[18] indicating an alarming shift of oral cancer occurrence towards the younger age group. The age incidence of oral cancer found in our study closely corroborated to the data available in literature.

Regarding sex distribution, males are affected more often than females. Cancer Research UK reported oral cancer being the 12th most common carcinoma in males & 16th most common carcinoma in females, with M:F ratio 19:10. M:F ratio of 2.9:1 was reported by Bhattacharjee et al[14]& study in Canadian population reveled M:F ratio 2:1 in patients >60 years.[19]Johnson N reported M:F ratio 2.1: 1 in UK population.[21] Similar results were found in the present study.

In our study majority (65.9%) patients belonged to lower socio-economic class & similar results were also observed by Khanna[16] & Nair.[22] People belonging to upper class seek medical advice more commonly than those in lower class & people of lower class also have diet deficient in various nutrients.

Some authors reported hereditary factors important in oral cancers. Goldsteinstressed on the fact that when smoking is combined with familial incidence, chances of oral cancers is more in male relatives.[23] However, we could not find any correlation of oral cancers with familial incidence.

Out of various substance abuse (tobacco, betel quid & alcohol) associated with oral cancers, tobacco has been most strongly implicated in causation of oral cancers. Ganganefound association of all 3 substances with oral cancers.[15]In another study heat & nicotine as irritant were considered to be causative factors.[24]Both smoking & smokeless tobacco have association with oral cancer causation.[25] Passive smoking has also been implicated. Tobacco smoking & chewing have been reported to have synergistic effect on development of oral cancer.[26] Field JK pointed out in the Annual ICMR reportthat areca nut contains high level of arecholine which is associated with oral cancers.[27] Alcohol if consumed for long time along with tobacco, increases the chances of oral cancers.[14,25]In the present study, we found similar results with 95.5% cases chewed betel quid, 90.9% used smokeless tobacco and lesser % of cases, 59% cases smoked tobacco & 54.5% cases consumed alcohol.

In our study, 81.8% cases presented with ulcer/ swelling in oral cavity followed by neck swelling(75% cases) &pain (54.5% cases). In another study most patients complained ulcer/soreness of mouth & pain was a rare symptom in oral cancer patients.[13] These tumors often ulcerate. But in another study pain was the most frequent presentation.[28]

The time interval between onset of symptoms & diagnosis varies between different studies. Average delay being 4.6-5.7 months. These data closely resemble to that of our study as majority of the cases (36%) presented within 6 months of onset of symptoms. The factors responsible for delay included poor socio-economic status, lack of knowledge, fear, superstitions etc.

In the present study most of the patients presented with ulcerative growth (54.5%) followed by proliferative type of growth (22.7%) cases. Other types like ulcero-proliferative (15.9%) & infiltrative (6.8%) growth were far less common in occurrence. In other studies, 40% lingual cancer patients had painless ulcer & 83% carcinoma cheek cases presented with ulceration.[29]

According to studies, incidence of cervical lymph node metastasis increases with the increase in size of the primary tumor and there has been also direct relation of unilateral as well as bilateral metastasis with the size of primary tumor. Some authors suggested stage of tumor to be an independent prognostic factor[30]whereas some refuted it.[31] Di Troriapointed out that lesser chance of tumor developing in smaller superficial lymphatics in comparison to wider lymphatics in deeper tissues.[32] This was corroborated in our study with late stage tumors like

T3 & T4 lesions having higher rates of metastasis. However sometimes T1 & T2 lesions also show significantmetastasis, related to aggressiveness of the primary lesion.[33]

Grade of the tumor, perineural & perivascular invasion are factors which have been positively correlated with cervical lymph node metastasis independent of T stage. According to Broaderscriteria,[34] tumors have been classified into well, moderate & poorly differentiated (with increasing anaplasia of mesenchymal cells & increasing number of mitosis), indicating increase in aggressiveness & rapidity of tumor growth. There has been increase in rates of metastasis from well differentiated tumor to poorly differentiated ones. In the present study poorly differentiated tumor has been associated with higher chances of neck node metastasis than the well differentiated tumours. Similar result has also been reported by Suzuki M.[35]

Management of cervical nodal metastasis involves surgery ranging from radical neck dissection (RND) to modified radical neck dissection (MRND) encompassing the clinically & radiologically detectable lymph nodes. Each surgery has its own complications e.g. RND has been associated with functional disability & cosmetic deformity and so may not be appropriate in all the cases. Thus MRND & its subtypes are becoming operation of choice & so knowing the pattern of metastasis more commonly associated with oral cancers, is very essential. In our study most of the metastases were present in levels I, II & III with very few cases with other levels of metastases, thus indicating that supra-omohyoid neck dissection would suffice in most of the cases. Similar results were reported by Candela FC et al.[36] In patients withearly stage disease with clinically negative neck(T1/T2, N0) there has been controversy between choice of elective neck dissection vs wait-and-see approach. Elective neck dissection gives the advantages of accurate neck staging, removal of any neck metastasis if present, reducing the morbidity associated with second surgery & determine the need of post-operative radiotherapy although it's disadvantage is the natural tumour barriers are destroyed. Li XM et al advocated selective neck dissection for N0 & N1 neck.[37]Wahietal reported cervical nodal involvement in 70.6% cases of oral cancers with 60.9% cases having unilateral & 9.7% with bilateral involvement.[13] Nayak et al reported level Ib involvement in 74.5% of oral cancer patients.[29] Similar observations were made in the present study.Wahi et al reported majority of the cases in stage III[38], closely comparable to data obtained in our study.

Squamous cell carcinoma (SCC) was reported to be the commonest histological type of oral carcinoma.[14,39] National Cancer Registry Project (ICMR), 2010 also reported SCC, well differentiated to be the commonest oral cancer.[5] Similar result was obtained in the present study.

Depth of invasion is defined as extension of tumor beneath epithelial surface, where epithelium is destroyed. Tumor thickness is the measurement of tumor's vertical bulk, encompassing both exo- & endophytic portions of the tumor. Patients with tumor depth <9mm fared better than those with depth>9mm ($p<0.05$).[40]Hence elective neck dissection being essential in cases with depth>9mm to optimize cure rates whereas in cases with depth <9mm, avoiding surgical morbidity is possible as chances of neck metastasis is minimal. Various authors indicated tumor depth strongly associated with nodal disease[41-44] yet no consensus has been achieved on a definitecut-off point. Yuen et al reported that of all tumor parameters, tumor thickness had statistically significant predictive value for subclinical metastasis, local recurrence & diseases free survival.[44] But tumor depth of invasion being a histopathological parameter, it can be transformed into a deciding factor about treatment of the neck by addressing the primary tumor first during surgery & use of intra-operative frozen section.

CONCLUSION:

From this study we could conclude that oral cancers although commonly seen in the 5th-6th decade but gradually increasing incidence is being noted in younger age group. Substance abuse (tobacco, betel quid & alcohol) have definite role in causation & thus people should be made aware of their deleterious effects through appropriate health education programme at community level that can help in prevention of oral cancers to a large extent. Size, grade & depth of invasion (DOI) of tumour dictate the spread of disease, of which DOI is most important indicator of metastasis, most commonly to level IB. Buccal mucosa was the commonest site & most cases presented in late stage with cervical lymph node metastases entailing poorer prognosis. People should be made aware of the warning symptoms, need for early diagnosis & treatment options available through IEC (information, education & communication programmes) in order to provide better treatment outcomes, improved long term prognosis & thereby reducing the morbidity & mortality of people at large.

CONFLICT OF INTEREST: None declared by the authors.

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