IMPACT OF TUMOUR THICKNESS AND DEPTH OF INVASION ON CERVICAL LYMPH NODE METASTASIS IN SQUAMOUS CELL CARCINOMA OF BUCCAL MUCOSA

By

Dr. HARSHITA T R

Dissertation submitted to the

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In partial fulfillment of the requirements for the degree of

MASTER OF SURGERY IN OTORHINOLARYNGOLOGY

Under the guidance of

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DEPARTMENT OF OTORHINOLARYNGOLOGY

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Date:

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LIST OF ABBREVIATIONS

USG	⇨	Ultrasonography
FNAC	⇨	Fine Needle Aspiration Cytology
CT	⇨	Computerized Tomography
MRI	⇨	Magnetic Resonance Imaging
RND	⇨	Radical Neck Dissection
SAN	⇨	Spinal Accessory Nerve
IJV	⇨	Internal Jugular Vein
SND	⇨	Selective Neck Dissection
AJCC	⇨	American Joint Committee on Cancer
SCC	⇨	Squamous Cell Carcinoma
MRND	⇨	Modified Radical Neck Dissection
FND	⇨	Functional Neck Dissection
OSCC	⇨	Squamous Cell Carcinoma Oral Cavity
END	⇨	Elective Neck Dissection
TT	⇨	Tumour Thickness
HPE	⇨	Histopathological Examination
SOND	⇨	Supra Omohyoid Neck Dissection

ABSTRACT

Background:

Prevalence of oral carcinoma is high in Kolar due to the tobacco chewing habits of people. Oral cancer is the most common cancer in males and 3rd most common in females in India. Squamous cell carcinoma of the head and neck grows locally and spreads to the cervical lymph nodes. Lymph node metastasis is considered to be one of the most significant prognostic factors in head and neck cancer. So it is important to know the factors which are likely to predispose the lymph node metastasis as it will a direct impact on the treatment.

In clinical practise a large number of patients undergo neck dissection presuming metastasis in lymph nodes. As a result few patients would have undergone neck dissection unnecessarily. It is therefore important to identify the factors which predispose to early lymph node metastasis.

Tumour thickness (depth of invasion) in areas like tongue, floor of the mouth and lower lip has been used in various studies to predict the outcome of cervical lymph node metastasis. But a proper cut off point has not been established in the case of buccal mucosa. Making use of standard pathological evaluation, this study aims to establish the importance of tumour thickness and depth of invasion as a factor affecting cervical node metastasis in early squamous carcinomas of the buccal mucosa. This way it would be helpful to identify those patients who are more likely to have metastasis of lymph nodes and could be the ones for elective node dissection at the time of first surgery.

Objectives:

1) To document the thickness of primary tumours in the postoperative specimen of carcinoma buccal mucosa.

2) To document the depth of invasion of the primary tumours in the postoperative specimen of carcinoma buccal mucosa.

3) To find out whether the lymph node in the resected specimen (neck dissection) harbor metastasis.

4) To find out the association between the thickness of the primary tumour and depth of invasion of primary tumour with the incidence of lymph node metastasis in T2 and T3 buccal mucosa carcinomas.

Methods:

Our study included 53 patients presenting with squamous cell carcinoma of buccal mucosa with T2 and T3 lesions. All the patients were treated with wide excision of primary tumour and simultaneous neck dissection as primary treatment. The excised specimen was evaluated for tumour thickness and tumour depth.

The resected neck dissection specimen was histologically examined to look for metastasis. The results were documented. An attempt was made to correlate thickness of primary tumour and depth of invasion of the primary tumour with cervical lymph node metastasis.

Results:

In our study, out of 53 patients with the age ranging from 35–84 years, females predomination was observed in this region. 39.6% of the patients had cervical lymph node metastasis, recorded on HPE. Tumour thickness and lymph node metastasis was not statistically significant. Tumour depth of more than 4 mm was statistically significant in predicting lymph node metastasis.

Conclusion:

The tumour thickness was not affecting the lymph node metastasis in this study. However, tumour thickness of more than 10mm predicted aggressive lymph node metastasis, though not observed to be statistically significant. There was a statistically significant correlation between tumour depth of more than 4mm and cervical lymph node metastasis. The measurement of tumour thickness and depth of invasion is easy and cheap to perform. Based on this we have come to the conclusion that it is preferable to do an elective neck dissection even for N_0 neck, if tumour depth is more than 4 mm.

KEYWORDS:

Buccal mucosa carcinoma, tumour thickness, depth of invasion, lymph node metastasis

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INTRODUCTION

Squamous cell carcinoma of Head and Neck is common in and around Kolar District.[1] Squamous cell carcinoma of the head and neck grows locally and spreads to the cervical lymph nodes. Lymph node metastasis is considered to be one of the most significant prognostic factors in the head and neck cancer. So it is important to know the factors which are likely to predispose the lymph node metastasis as it will have a direct impact on the treatment.[2]

In spite of various techniques for detection of metastasis, it can be missed. So in clinical practise a large number of patients undergo neck dissection presuming metastasis in lymph nodes. As a result few patients would have undergone neck dissection unnecessarily.[3] It is therefore important to identify the factors which predispose to early lymph node metastasis.

Tumour thickness and depth of invasion in areas like tongue, floor of the mouth and lower lip have been used in various studies to predict the outcome of cervical lymph node metastasis. But a proper cut off point of tumour thickness and depth of invasion has not been established in the case of buccal mucosa.[4] Making use of standard histopathological evaluation, this study aims to establish the importance of tumour thickness and depth of invasion as a factor affecting cervical node metastasis in early squamous carcinoma of the buccal mucosa. This way it would be helpful to identify those patients who are more likely to have metastasis to lymph nodes and they could be the ones for elective node dissection at the time of first surgery.

AIMS AND OBJECTIVES OF THE STUDY

1) To document the thickness of primary tumours in the postoperative specimen of carcinoma buccal mucosa.

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REVIEW OF LITERATURE

HISTORY

Carcinoma is a Greek word meaning a crab. Its latinised form is 'cancer'. Another term for cancer is malignancy from its Latin roots malignus and genus meaning endangering harm. Cancer is a term used to characterize abnormal growth of cells, which may result in the invasion of normal tissue or the spread to organs.

In historical review, buccal mucosa and alveolar malignancies have been dated back to time before Christ; references have been made to such tumours by **Edwin Smith Papyrus** (2300 B.C.) and by **Ekers Papyrus** (1500 B.C.).

Sir Henry T. Batlin, a surgeon from St. Bartholomew's Hospital, London, in 1885 A.D., performed wide excision of head and neck cancers with mandible and lymphatics of the upper neck. He, along with **Kocher,** emphasized the advantage of excising metastatic neck nodes.

EMBRYOLOGY

The stomatodeum bounded by brain above and pericardial sac below becomes apparent at 4^{th} week of intra-uterine life. The breakdown of buccopharyngeal membrane causes mouth to become continuous with developing pharynx.[5]

Mesodermal condensation in lateral wall and floor of pharynx gives rise to branchial arches which differentiate to produce cartilaginous bar, branchial musculature and

branchial arch artery with each arch receiving an afferent and an efferent nerve supply, post and pre-trematic nerve supply.[5]

The mandibular processes arising from lateral aspects of developing head fuse by 6th week in midline and the maxillary processes arising as buds from mandibular processes, grow forwards and meet with lower end of nasal septum and its contralateral side in the midline. Fusion of maxillary processes separates primitive nasal cavity from primitive oral cavity.[5]

Development of Tongue

The anterior (2/3rd) of tongue arises from mandibular arches from paired eminences and tuberculum impar and posterior (1/3rd) part arises from hypobranchial eminence. This grows forward over second arches to become continuous with anterior part. Sulcus terminalis lies posterior to site of union of the two parts. Foramen caecum is the small median pit in dorsum of tongue.[5]

Mucosal cover of body of tongue arises from 1st arch tissue and its sensory innervations from lingual branch of mandibular division of trigeminal nerve. The 3rd arch nerve – glossopharyngeal nerve provides sensory innervations to posterior 1/3rd of tongue. Some amount of tissue between the above two parts are supplied by 7th nerve. Gustatory function is by Chorda tympani branch of Facial nerve.[5]

Figure 1 : EMBRYOLOGY – 4th WEEK OF INTRA-UTERINE LIFE

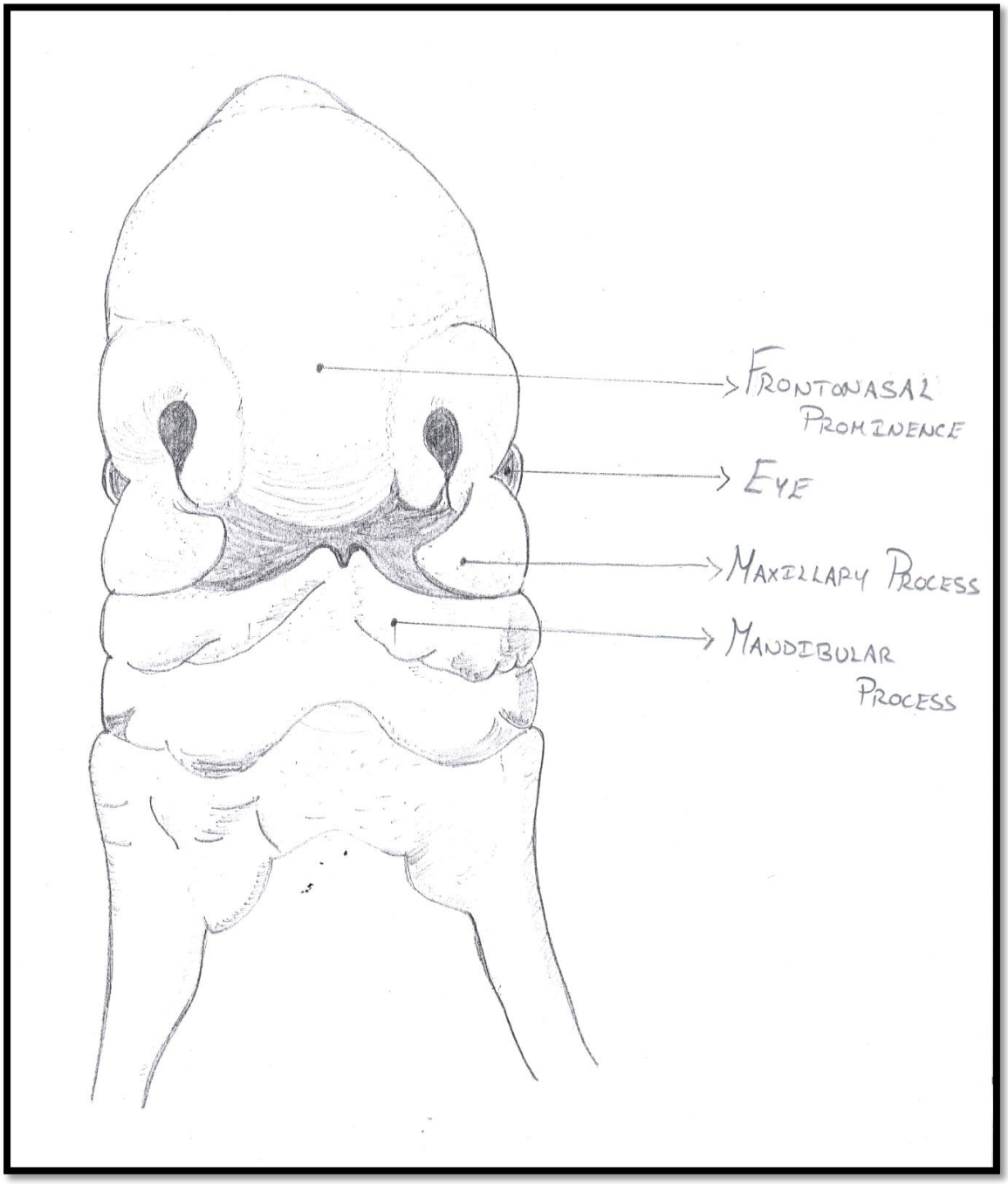


Figure 2 : DEVELOPMENT OF PALATE

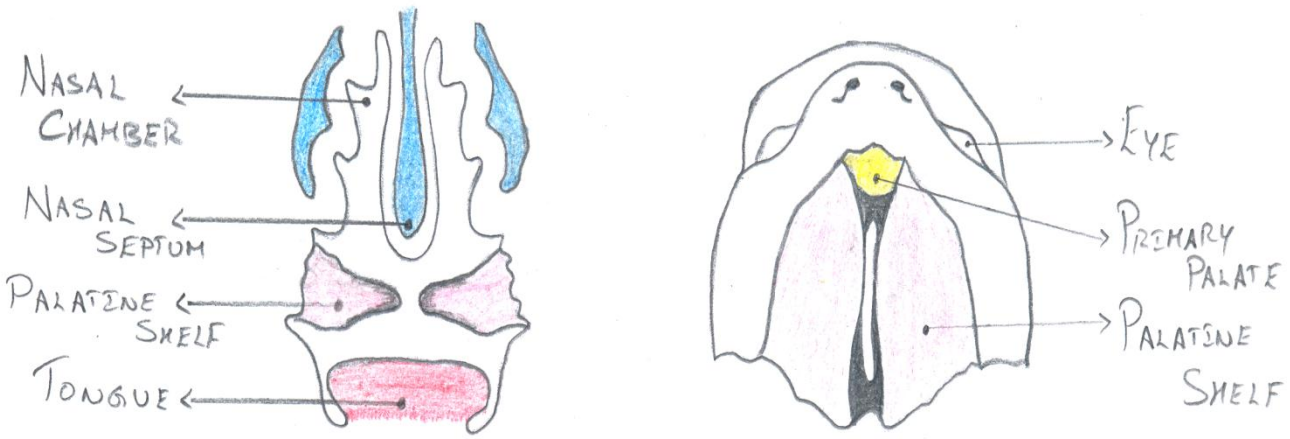


Figure 3: DEVELOPMENT OF TONGUE

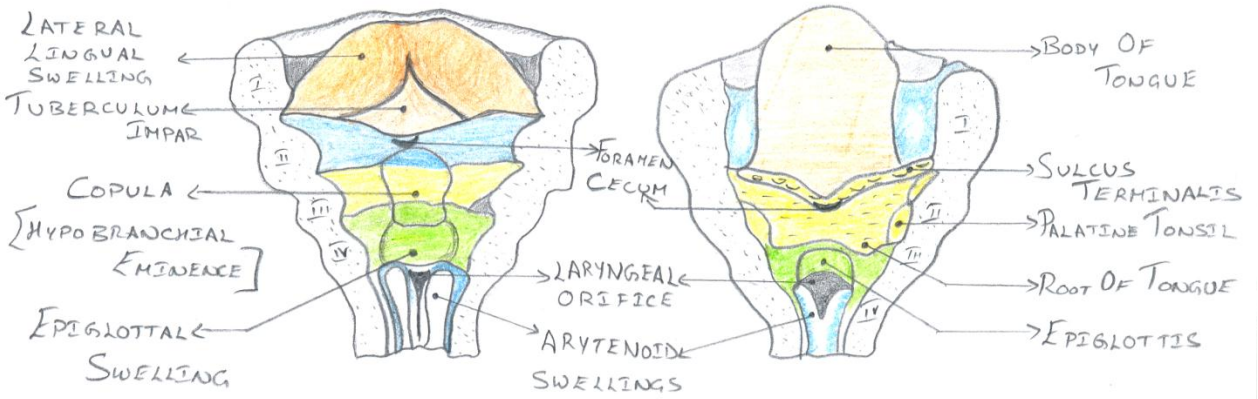
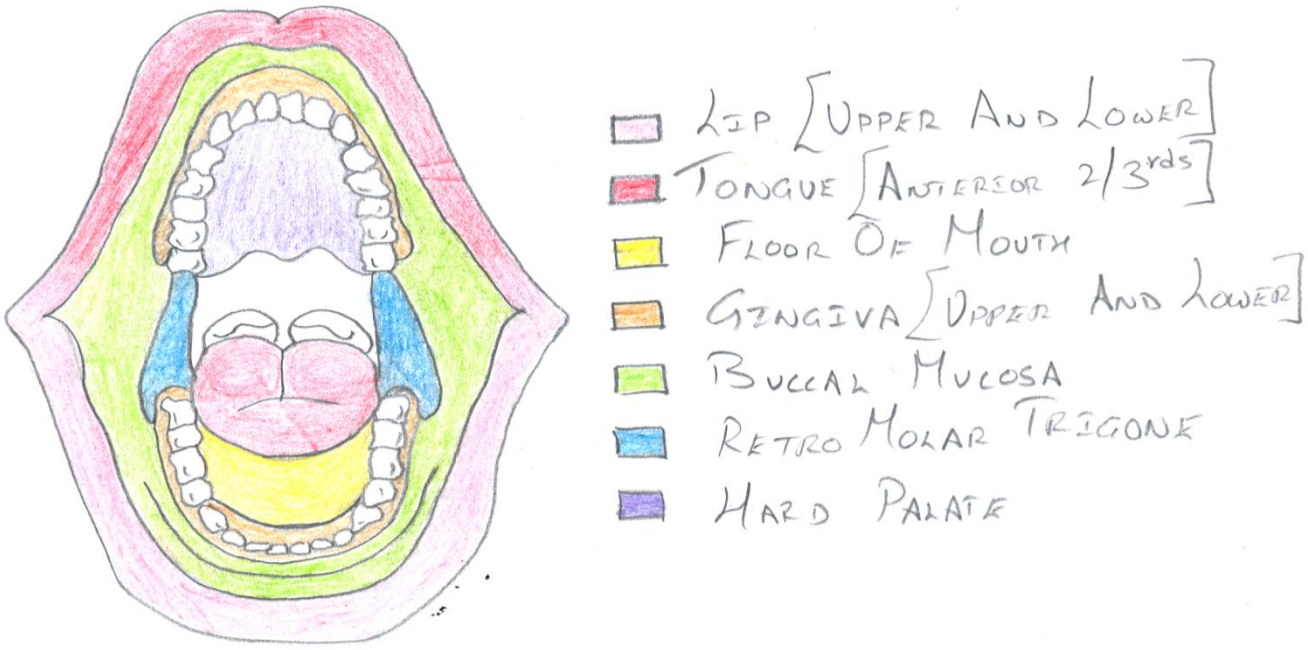


Figure 4: Anatomy of oral cavity



The various anatomical sites within the oral cavity as described by the American Joint Committee for Cancer staging[6] are:

- Lip
- Tongue (Anterior 2/3rd)
- Floor of mouth
- Gingiva - Upper alveolus
  - Lower alveolus
- Buccal mucosa
- Retromolar trigone
- Hard palate

The oral cavity extends from the skin vermilion junction of the lips to the junction of the hard and soft plate above and to the line of circumvallate papillae below and is divided into the following specific areas:

Mucosal lip: The lip begins at the junction of the vermilion border with the skin and includes only the vermilion surface that is the portion of the lip that comes into contact with the opposing lip. It is well defined into an upper and lower lip, which joins at the commissures of the mouth.

Buccal mucosa: This includes all the membrane linings of the inner surface of the cheeks and lips from the line of contact of the opposing lips to the line of attachment of mucosa to the alveolar ridge (upper and lower) and to the pterygomandibular raphe.

Lower alveolar ridge: This refers to the mucosa overlying the alveolar process of the mandible, which extends from the line of attachment of mucosa in the buccal gutter to the line of free mucosa of the floor of the mouth. Posteriorly it extends to the ascending ramus of the mandible.

Upper alveolar ridge: This refers to the mucosa overlying the alveolar process of the maxilla, which extends from the line of attachment of mucosa in the upper gingival buccal gutter to the junction of the hard palate. Its posterior margin is the upper end of the pterygopalatine arch.

Retromolar gingiva (Retromolar trigone): This is the area of the attached mucosa overlying the ascending ramus of the mandible from the level of the posterior surface of the last lower molar tooth to the apex superiorly, which is adjacent to the tuberosity of the maxilla.

Floor of the mouth: This is a semilunar space over the mylohyoid and hyoglossus muscles, extending from the inner surface of the lower alveolar ridge to the undersurface of the tongue. Its posterior boundary is the base of the anterior pillar of the tonsil. It is divided into two sides by the fraenulum of the tongue and contains the ostia of the submandibular and sublingual salivary glands.

Hard palate: This is the semilunar area between the upper alveolar ridge and mucous membrane covering the palatine process of the maxillary palatine bones. It extends from the inner surface of the superior alveolar ridge to the posterior edge of the palatine bone.

Anterior two –thirds of the tongue (Oral tongue): This is the freely mobile portion of the tongue that extends anteriorly from the line of circumvallate papillae to the under surface of the tongue at the junction of the floor of the mouth. It is composed of four areas: the tip, the lateral borders, dorsum and the under surface (non-villous ventral surface of the tongue).[6]

THE BLOOD SUPPLY OF THE ORAL CAVITY:

Branches of the external carotid artery provide blood supply to the oral cavity. Lingual arteries provide blood supply to the tongue. Blood supply to the lips and the cheek mucosa is provided through the facial arteries and the internal maxillary and inferior alveolar arteries provide blood supply to the alveolar ridges.[7]

THE NERVE SUPPLY OF THE ORAL CAVITY:

The sensory nerve supply to oral cavity is provided by sensory component of second and third division of trigeminal nerve, through superior and inferior alveolar and lingual nerves. Special senses of taste and secretomotor fibres to the salivary glands are provided through chorda tympani nerve traversing along the lingual nerve. Motor control of the lips and cheek is provided by the facial nerve. The hypoglossal nerve is the motor nerve for the intrinsic and extrinsic muscles of the tongue and for the movements of the medial and lateral pterygoid muscles, and their actions are

controlled by the motor components of the second and third divisions of the trigeminal nerve.[7]

LYMPH NODE GROUPS[8]

The lymph nodes may be subdivided into specific anatomic subsites and grouped into seven levels:

Level I: Submental IA

Submandibular IB

Level II: Upper jugular sublevels IIA and IIB (anterior and posterior to the spinal accessory nerve respectively)

Level III: Mid-jugular

Level IV: Lower jugular

Level V: Posterior triangle

Level VI: Prelaryngeal (Delphian)

Pretracheal

Paratracheal

Level VII: Upper mediastinal

Other groups: Sub-occipital

Retropharyngeal

Parapharyngeal

Buccinator (facial)

Preauricular

Periparotid and intraparotid.

The location of the lymph node levels is as follows:

Level I: Contains the submental and submandibular triangles bounded by the anterior belly and the posterior belly of the digastric muscle, and the hyoid bone inferiorly, and the body of the mandible superiorly.

Level II: Contains the upper jugular lymph nodes and extends from the level of the skull base superiorly to the hyoid bone inferiorly.

Level III: Contains the middle jugular lymph nodes from the hyoid bone superiorly to the level of the lower border of the cricoid cartilage inferiorly.

Level IV: Contains the lower jugular lymph nodes from the level of the cricoid cartilage superiorly to the clavicle inferiorly.

Level V: Contains the lymph nodes in the posterior triangle, which are bounded by the anterior border of the trapezius muscle posteriorly, by the posterior border of the sternocleidomastoid muscle anteriorly, and by the clavicle inferiorly.

For descriptive purposes Level V may be further subdivided into upper and lower levels corresponding to the inferior belly of omohyoid.

Level VI: Contains the lymph nodes of the anterior central compartment from the hyoid bone superiorly to the suprasternal notch inferiorly. On each side, the medial border of the carotid sheath forms the lateral boundary.

Level VII: Contains the lymph nodes inferior to the suprasternal notch in the superior mediastinum.

ORAL CAVITY CANCER

EPIDEMIOLOGY

Right down the history, man has been trying to conquer the malignant diseases. However malignancies remain a major cause for death and morbidity. It is estimated that about nine million new cancers are diagnosed every year in the world. Worldwide estimate of oral cancer detection each year is 4,05,000 cases with 2/3rd occurring in developing countries. India, Sri Lanka, Pakistan, Bangladesh, Hungary & France have the highest rates with the former 4 accounting for 30% of newly detected cases and seen more commonly in men.[9] And the estimated number of new cancers in India is about seven lakhs, and about 3.5 lakhs people die of cancer every year.[10] According to the cancer registry of Kidwai Memorial Institute Of Oncology, Bangalore, Karnataka, on an average, about 5000 new cancers are registered per year[11]. Oral cancer ranks among the top three types of cancers in India. Age adjusted rates of oral cancers in India is 20 per 100,1000 population and accounts for over 30% of all cancers in the country.[12]

In the western world the tongue and floor of the mouth are the most common sites of origin for primary squamous cell carcinoma in the oral cavity.

However, in India the buccal mucosa and retromolar trigone are the most frequently encountered primary sites.[13] Carcinoma of buccal mucosa accounts for 40% of oral cancers in South East Asia.[14] 85% cases occur >50 years of age, except in developing countries where onset is earlier due to tobacco/ pan chewing habits. In India, the male: female ratio is said to be 4:1. Floor of mouth accounts for 18-33% of oral cancers and

seen more frequently in men in 6^{th}-7^{th} decade. 22-39% of oral carcinomas arise in the tongue, most commonly in middle $1/3^{rd}$ and in lateral aspect preceding ventral aspect. 90% are >40 yrs of age & male: female ratio decreasing.[14]

Retromolar trigone incidence in oral cancers is 6 - 7% and is more common in males. Incidence of carcinoma in Maxillary alveolus is 3.5 – 6.5% & hard palate is 1 – 3%. Oral cancers are more common in males except in hard palate carcinomas where precedence in females is more due to reverse smoking. Mandibular cancers account for 7.5 – 17.5 % of oral cancers. Ratio for mandibular: maxillary alveolus cancers is 3:1 & is more common in males.[14]

ETIOLOGY:

The cause of oral cancer is yet to be completely understood. Several risk factors have been implicated.

1] Smoking:

Tobacco is smoked more commonly in the form of cigarette and bidi. Some smoke a chutta (a cigar) with the burning end inside the mouth. Chemical carcinogens in the burning tobacco or repeated thermal injury are agents, which are risk factors for oral cancer. Risk increases with the amount smoked and with the total cumulative lifetime smoking years. Tobacco is smoked commonly in the form of bidi, a type of cheap cigarette made by rolling a rectangular dried piece of tendu leaf (Diospyros melanoxylon) with 0.30-0.36 gm of Saurashtra or Nipani tobacco and securing the roll with thread. The length varies from 4 cms to 7.5 cms. As compared with cigarette smoke, bidi smoke has high content of several toxic agents such as carbon monoxide, ammonia, hydrogen cyanide, phenol and carcinogenic hydrocarbons.

The other ways of smoking tobacco are clove-flavoured cigarette, various forms of pipes (wooden, clay, metal), the hookah (the Hubble bubble or water pipe), cheroots (or chuttas) and dhumtis. Tobacco may be used in raw or as processed mixtures and as a pyrolised form. The raw forms are used with lime and with areca nut (Mawa-smokeless tobacco). Khaini is a mixture of freshly powdered tobacco and slaked lime; a quid of the mixture is kept for hours in the lower gingivolabial sulcus and sucked, which is risk factor for khaini cancer (squamous cell carcinoma of the lower lip). The processed forms, for example zarda, gutkha, and Manipuri tobacco are industrial products. The pyrolised (roasted) forms of tobacco (mishri, bajjar, etc) are used as dentifrice. Oral use of snuff is also practised in specific areas.[15]

Photo 1 : DIFFERENT FORMS OF TOBACCO

2] Spirits: - Consumption of calvados {a pot distilled spirit}

3] Sepsis: - Septic and decayed teeth.

4] Sharp teeth: - Poor oral hygiene, faulty restorations, and ill-fitting dentures.

5] Spices

6] Syphilis

7] Betel quid chewing habit: - The quid consists of a betel leaf wrapped around an areca nut, which is high in tannin, quick lime and tobacco. Oral cancer develops at the site where quid is habitually kept. Smoking along with betel quid chewing enhances the risk of oral cancer by 20 to 30 times.

8] Snuff dipping and other tobacco products

9] Alcohol: Alcohol consumption has a synergistic local effect of dissolving the carcinogen in the sump area of the mouth and a systemic downward effect on the immune system. Alcoholics often have nutritional problems.[16]

10] Industrial chemicals

11] Viruses: Herpes simplex virus and the Human papilloma virus (subtype 16)

12] Immune status: - Immune deficient due to low cell mediated immunity.

13] Genetic factors: - Most sporadic tumours are the result of a multi-step process of accumulated genetic alterations. These alterations affect epithelial cell behaviour by loss of chromosomal heterozygosity, leading to a series of events which progresses to the stage of invasive squamous cell carcinoma. These genetic alterations are seen in the clinical and microscopic pathology from hyperplasia to invasiveness of the tumour. Overexpression or underexpression of p53and other genes may predispose to development of cancer and recurrence following treatment. Mutation of p16 causes cancer however overexpression shows favourable prognosis. Overexpression of c-erbB-2 has shown correlation with nodal disease and metastasis and worsened survival.

The syndromes that are characterized by mutagen sensitivity, includes Xeroderma pigmentosum, Fanconi's anaemia and Ataxic telangiectasia, have all been associated with oral cavity cancers.[17] Other relevant genetic markers may include inducibility of cytochrome p450 enzyme system.[18]

14] Social status: - Related to social habits and to low socio-economic status

15] Diet

16] Occupation: Employment in textile industries

TUMOUR BIOLOGY[19]

The development of a tumour involves three phases:

a) Initiation

b) Promotion

c) Progression

The initiation phase is characterized by the series of mutations that occur in sequence. For initiated cells to become tumour cells, exposures to promoting agents or conditions are required (promotion phase). The end of the promotion phase is characterized by the appearance of the first neoplastic cells. Before the appearance of neoplastic cells, the abnormal cells are called preneoplastic or premalignant cells. The progression phase is characterized by invasive growth of the transformed cells and progression of the tumour lesion into a highly metastatic tumour that may ultimately kill the host.

TUMOUR ESCAPE MECHANISMS[19]

A) Tumour related:

a) Tumour is not immunosensitive

1) No expression of tumour-specific antigens

2) No or low expression of major histocompatibility complex molecules correlated with tumour aggressiveness and metastatic potential

3) No antigen processing or presentation (masked/modulated)

4) Resistance to immune cell-mediated killing, such as induction of apoptosis through the apoptosis-inducing molecule F_{as}

b) Tumour is not immunogenic

1) Lack of co-stimulatory molecules, therefore does not induce an immune response

2) Secretion of immunosuppressive factors that inhibit T-cell functions or defects in T cells

3) Shedding of tumour antigens that down regulate T-cell molecules

4) Induction of T-cell tolerance

5) Failure of T-cell apoptosis (programmed cell death)

B) Host related:

1) Tumour grows too fast for the immune system

2) Inherited or acquired immunodeficiency

3) Treatment (radiation, chemotherapeutic drugs) or chemical or physical carcinogens related immunosuppression

4) Deficiency in antigen presentation by antigen-presenting cells

5) Lack of access of effector cells to the tumour

6) Expression of immunodominant antigens on parental tumour that prevents stimulation with other tumour antigens

7) Age- long latent period of carcinogens Failure of an antitumour immune response related to age

CARCINOGENESIS[20]

Tumour development represents the loss of the normal signalling mechanisms involved in controlled cell growth.

Loss of cancer cell ability to undergo apoptosis (programmed cell death) allows the accumulation and clonal expansion of cells that otherwise might have died if their cell death machinery were preserved and functional. Tumour growth represents the sum of cell proliferation minus cell death. Carcinogensis involves DNA damage and the progression of mutated cells through the cell cycle called as initiation and promotion.

Around 6-10 independent genetic mutations are required for the development of malignancies in head and neck. Overexpression of mitogenic receptors, loss of tumour suppressor proteins and expression of oncogene-derived proteins that inhibits apoptosis and overexpression of proteins that derive the cell cycle, allow the unregulated cell growth.

Genetic mutation occurs as a result of DNA damages especially 9p, 3p, 11q, 8p, and 17p region. Rate of p53, p16 mutation is greater in smokers, which contributes to oral cancer and shows high incidence of recurrence after any treatment.

TNM CLASSIFICATION[21]

Primary Tumour (T)

TX Primary tumour cannot be assessed

T0 No evidence of primary tumour

Tis Carcinoma in situ

T1 Tumour 2 cm or less in greatest dimension

T2 Tumour more than 2 cm but not more than 4 cm in greatest dimension

T3 Tumour more than 4 cm in greatest dimension

T4a Tumour invades adjacent structures (e.g. through cortical bone, into deep {extrinsic} muscles of tongue {genioglossus, hyoglossus, palatoglossus and styloglossus}, maxillary sinus and skin of face)

T4b Tumour invades masticator space, pterygoid plates, or skull base and /or encases internal carotid artery

Regional Lymph Nodes (N)

NX Regional lymph nodes cannot be assessed

N0 No regional lymph node metastasis

N1 Metastasis in a single ipsilateral lymph node, 3cm or less in greatest dimension

N2a Metastasis in a single ipsilateral lymph node more than 3 cm but none more than 6 cm in greatest dimension

N2b Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension

N2c Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension

N3 Metastasis in a lymph node more than 6 cm in greatest dimension

Distant metastasis (M)

MX Distant metastasis cannot be assessed

MO No distant metastasis

M1 Distant metastasis

Stage grouping:

Stage 0	TIS	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1	N1	M0
	T2	N1	M0
	T3	N1	M0
Stage IVA	T4a	N0	M0
	T4a	N1	M0
	T1	N2	M0
	T2	N2	M0
	T3	N2	M0
	T4a	N2	M0
Stage IVB	Any T	N3	M0
	T4b	Any N	M0
Stage IV C	Any T	Any N	M1

Histological Grade (G)

GX Grade cannot be assessed

G1 Well differentiated

G2 Moderately differentiated

G3 Poorly differentiated

Residual tumour(R)

Rx Presence of residual tumour cannot be assessed

Ro No residual tumour

R1 Microscopic residual tumour

R2 Macroscopic residual tumour

PATTERN OF CERVICAL LYMPH NODE METASTASIS

Around 300 lymph nodes are located in the head and neck, and they comprise 30% of the total 800 lymph nodes in the human body. Kocher and Uber reported the detrimental effect of neck metastasis in patients with head and neck cancer in 1880. George Washington Crile reported his experience with 132 neck dissections in *JAMA: The Journal of the American Medical Association* in 1906 .The functional neck dissections was intended to reduce morbidity and maintain function with the better understanding of the lymph node metastasis in the 1960s.

The capacity for metastatic spread can be regarded as the single most characteristic feature of malignant tumour. The first step in the metastatic process is breach of the basement membrane at the site of primary tumour. This occurs through hydrolytic enzymes secreted by tumour like the urokinase type plasminogen activator, collagenase and stereomelysins.[22] The enzymes degrade the

basement membrane proteins such as collagen IV, laminin and proteoglycans, which allow the spread of tumour cells.[23]

The lymphatic spread provides the main mode of spread beyond the primary site of origin for squamous cell carcinoma of head and neck region. The tumour cells disseminate as emboli within the lymphatic system. The tumour emboli are carried to the afferent lymphatic vessels of first level of lymph nodes. The tumour cells localize first in the sub capsular sinus then progressively grow to replace the cortex and medulla. Eventually tumour invades the capsule of the node heralding extra capsular spread.[22] The extra capsular spread may occur in much smaller lymph nodes where tumour emboli first lodge in the capsular lymphatic sinuses and focal destruction of capsular collagen by type I collagenase.

As the first level of lymph nodes is replaced by metastatic tumour, afferent lymph flow is deflected carrying tumour cells to the second and third level of nodes. Increasing obstruction in the lymphatics and intranodal sinuses eventually may lead to reversal of lymphatic flow and retrograde spread of tumour cells to unpredictable nodal groups.

Lympho-hematogenous spread can occur by tumour cells invading blood vessels within the lymph node or by traversing small lymphatico-venous communication. Once the tumour cells arrive at draining lymph node, they can proliferate, die, remain dormant or enter the blood circulation through blood vessels in the node. The pattern of lymphatic spread follows a predictable pattern. In general, well-localized tumours spread to ipsilateral first or second echelon lymph nodes. The tumour at or near midline may spread to both sides of neck.

The patients with clinically positive nodes in the ipsilateral neck are at risk for contralateral lymph node metastasis.[24] This occurs because mainly through the

anastomotic channels decussating in the midline at the submental and submandibular triangles.

The **Lindberg** study defined the nodal groups at most risk for each primary and the pattern of subclinical microscopic metastasis follows a similar distribution. Carcinoma located anteriorly within the oral cavity spreads most commonly to the submental and submandibular lymph nodes, followed by the upper jugular nodes. The posteriorly located oral carcinoma is more likely to spread to the upper jugular nodes and less frequently spread to the submandibular nodes.[25]

Shah reported a comprehensive histopathological study, which confirmed **Lindberg's** clinical findings.[26] The level I, II and III were at highest risk for metastasis from oral cavity cancer. Thus first echelon of lymph nodes for oral cavity lies in level I, II and III.[25]

The incidence of lymph node metastasis that can be detected clinically is about 60%. The incidence of occult metastasis in patients with clinical N_0 is around 30%.[26] Site of the tumour, thickness and histological features including extracapsular invasion, positive margins of the excised tumour influence the lymph node metastasis. [22]

The following table describes the lymph node levels and the nodes that are at greatest risk of harbouring metastases from different primary sites[26].

TABLE 1: Table showing lymph node levels that are at risk for harbouring metastases from different primary sites

Lymph node group	**Primary site**
Level 1A	Floor of mouth, anterior 2/3 tongue, anterior part of mandibular ridge, lower lip.
Level 1B	Oral cavity, anterior nasal cavity, soft tissue of the mid face, submandibular gland.
Level II	Oral cavity, Anterior Nasal cavity, Nasopharynx, Oropharynx, Hypo pharynx, Supra glottic larynx, Parotid.
Level III	Oral cavity especially tongue, Nasopharynx, Oropharynx, Hypo pharynx, Supra glottic larynx, thyroid
Level IV	Hypopharynx, Thyroid, Larynx, Cervical oesophagus.
Level V	Nasopharynx, Oropharynx, Cutaneous structures of the posterior scalp and neck.
Level VI	Thyroid gland, Glottic and subglottic Larynx, apex of Pyriform fossa, Cervical oesophagus.

EVALUVATION OF CERVICAL LYMPH NODES

A proper evaluation of cervical lymph nodes is important as it influences the choice of treatment modality, staging of the disease and functional outcome. The assessment of cervical lymph nodes depends on history, clinical examination and radiology.

History should include symptoms of upper aero digestive dysfunction. Social history should contain a detailed history regarding alcohol and tobacco consumption. Clinical examination remains the most important method of assessing regional lymph nodes. Physical examination should include careful inspection of the mucosal surface of oral cavity, Oropharynx, indirect laryngoscopy, posterior rhinoscopy and palpation of the neck.

The neck palpation should be from behind the patient using both hands for palpation. Each side of the neck should be palpated separately. The sequential examination starts first from submental and submandibular triangles. Then the neck anterior to sternocleidomastoid is palpated from above downward, till clavicle, along the supraclavicular fossa and upwards along the anterior border of Trapezius. In addition the parotid region, the posterior auricular region, the facial nodes should also be examined. Some nodes in the neck are difficult to palpate. The retropharyngeal and Para pharyngeal nodes are almost impossible to detect unless they are very large. The patients with short neck are more difficult to examine for staging. Area deep to sternomastoid should be given special attention and must be palpated by insinuating the fingers below the muscle.

The structures in the neck which may be mistaken for enlarged lymph nodes are the transverse process of the atlas, the carotid bifurcation and the submandibular salivary gland. In addition, the lymph nodes may be enlarged due to infection causing reactive hyperplasia rather than a metastatic deposit.[27]

The clinical examination of the neck has a variable reliability. Ali and co-workers, in their review of 266 specimens from radical neck dissections found a false positive rate of 20% and false negative rate of 21 %.[28]

Clinically the lymph nodes bigger than 1cm in areas like submandibular and submental become palpable whereas lymph nodes in other deeper parts of the neck are palpable when they attain a size of 1.5 cm

Ultrasonography (USG) is more sensitive than clinical examination in detecting metastatic nodes. Malignant nodes show a heterogeneous appearance with a solid and cystic image, round shape, clustering and speckled calcifications on USG. This investigation will also demonstrate the relationship of metastatic nodes to major vessels in the neck.[29] In indicated cases Colour Doppler can be used.

FNAC is helpful in the assessment of palpable node in the evaluation of a patient with an unknown primary tumour. The nature of histology may help in the search for primary tumour. In the case of a clinically palpable node in the presence of proven primary disease, FNAC may not be sufficiently reliable.

Ultrasound guided FNAC (USG-FNAC) is gaining popularity because the borderline lymph nodes cannot be reliably scored on ultrasound, Computerized tomography (CT) or Magnetic resonance imaging (MRI). USG-FNAC proved to be a quick (10-20 min) and safe (no complications) method. Although some reports of

seedling of tumour cells along the needle tract are present, this is a rare finding and has never occurred with thin aspiration needle.[26]

Aspiration can be obtained from the lymph nodes as small as 5 mm.[30] It has been shown that USG-FNAC has a very high specificity (100%) and sensitivity (73%).[31] The specificity and sensitivity of USG - FNAC is better than CT or MR imaging. The sensitivity of USG- FNAC can be enhanced by P53 mutational assays.[29] Another technique to increase the accuracy of USG- FNAC is to select the sentinel node for aspiration. The sentinel node is the first node to take up the dye. The technique involves injecting around the primary tumour site with TC-99m labelled sulphur colloid. The localization of the sentinel node is performed by planner scintigraphy and gamma probe. Dye technique is easier to perform and is also fairly effective but not as sensitive as radioisotope study.

Computerized tomography scan (CT scan) is more accurate than clinical examination in detecting metastatic lymph nodes. It is particularly important in the necks that are difficult to examine, for restaging and for inaccessible areas such as retropharyngeal space. The rapid advances in imaging technology have enhanced the ability to identify the metastatic disease in head and neck. CT and MRI have significantly improved the accuracy of detecting occult metastasis.

C.T. Scan criteria to define a node as metastatic node includes[27]:

1. Spherical lymph nodes

2. Peripheral enhancement

3. Central necrosis (Low attenuation areas)

4. Clustering of three or more lymph nodes.

5. Scattered calcification.

6. Area of Drainage.

MRI has similar accuracy rates as CT scan. MRI differentiates nodes from surrounding tissues rather more clearly than CT scan. However, limitations of CT and MRI in the assessment of small lymph node and inability to ascertain with confidence the presence or absence of metastases in any one lymph node makes CT and MRI not universally acceptable.

The metastatic nodes can be demonstrated with radio isotopes like Gallium Citrate, technetium labelled DMSA. These agents do not label normal lymph nodes. But all these investigations suffer from a low sensitivity and specificity and inability to detect nodes less than 2 cm in size by which time they are usually clinically palpable.[32]

Positron Emission Tomography (PET) will assess the metabolic activity of cervical nodes using 18 fluorodeoxyglucose (18 FDG). The role of PET is confined to the detection of the occult primary and in the assessment of residual and recurrent disease following surgery and irradiation.[32]

Single Photon Emission Computed Tomography (SPECT) gives three dimensional isotopic images and can detect tumour more than 4 mm in size. Immuno SPECT using TC-99 labelled monoclonal antibodies can detect tumour measuring 2 mm. These techniques depend on the uptake of radionuclide into tumour which is often related to high blood flow which explains overlap in the detection of

inflammatory disease. Although the expense of PET prohibits wide spread usage, these techniques will be used to detect occult recurrences, occult primaries or distant metastases.[32] PET has high incidence of false positive nodes, some of these can be eliminated by PET-CT i.e. superimposition of PET with CT scan. Ideally it has to be done after three months of surgery to reduce the false positive rate because of inflammatory changes following surgery.

THERAPEUTIC MODALITIES FOR ORAL CANCER [13, 33]

The factors that influence the choice of initial treatment are those related to the characteristics of the primary tumour (tumour factors), those related to the patients (patient's factors) and those related to the treatment delivery team (physician factors).

PHYSICIAN FACTORS: -

- Surgery
- Radiotherapy
- Chemotherapy
- Combined modality treatment
- Dental
- Rehabilitation services
- Prosthetics
- Support services

- Photodynamic therapy

- Immunotherapy

- Gene therapy

Most therapies other than surgery are not known to be effective against large tumours. Therefore, the most promising results may be obtained with therapy of nonmetastatic tumours in an adjuvant setting after surgical removal of the primary tumour.

TUMOUR FACTORS:

-Site

- Size (T stage)

- Location (anterior versus posterior)

- Proximity to bone (mandible)

- Lymph node metastasis

- Previous treatment

- Histology (type, grade, depth of invasion)

PATIENT FACTORS:

-Age

- General medical condition

- Tolerance

- Occupation

- Acceptance and compliance with regards to treatment

- Life style (smoking, drinking, tobacco chewing)

- Socio-economic consideration

- Nutrition

TREATMENT OF CERVICAL METASTASIS

The presence of cervical lymph node metastases has an adverse effect on survival. At the same time, careful and effective treatment can provide a cure in a significant number of patients with node positive neck. In the untreated neck, the patterns of spread are often predictable. Once patient has had previous radiotherapy or surgery or infection, drainage patterns are often altered. Hence, although the neck may be clinically negative (N_0) all five levels in the neck should be treated by surgery or radiotherapy. In patients with palpable neck disease (N_1, N_2, N_3), non palpable spread may be present anywhere in the neck and correct approach for such patients is to completely encompass the disease i.e. full neck dissection.[32]

The primary goal in the treatment of patients with head and neck cancer is control of the disease. However, with increasing recognition of the substantial morbidity of radical surgical treatment, more emphasis is being placed on surgical conservatism if it does not negatively impact disease control and if it offers improved post treatment function and cosmesis. The evolution of neck dissection is

representative of this trend. Radical neck dissection (RND), first described by Crile[34] in 1906, has served as the gold standard method of managing cervical metastases in patients with head and neck cancer for most of the century. RND accomplishes en bloc removal of all cervical lymphatic contents believed to be involved with or at risk for metastatic disease from head and neck malignancy and includes removal of the sternocleidomastoid muscle, internal jugular vein, submandibular gland, and spinal accessory nerve. This operation produces substantial postoperative morbidity from cosmetic and functional standpoints, with typical shoulder dysfunction seen after this surgery. With time, surgeons have challenged the necessity of such radical neck surgery and have explored the feasibility of modifications to it.

Evolution of neck dissection

A. 1906 - The en bloc cervical lymphadenectomy known as the RND was developed by Crile.

B. Blair and Brown encourage the removal of the SAN.

C. 1945 - Dargent and Papillon advocate the preservation of the SAN in clinically N_0 necks.

D. 1950 - Martin popularizes the RND explaining that "Any technique that is designed to preserve the SAN should be condemned unequivocally."

E. 1963 - Suarez indicates that based on his necropsy specimens which had Lymphatics only within the fibro fatty tissues, a complete cervical Lymphadenectomy could be accomplished while sparing the Sternocleidomastoid muscle, the IJV, and the SAN.

F. 1967 - 1980 Bocca and Pignataro popularize Suarez's version of neck dissection and coined the terms functional, conservative, and conservation neck dissection.

G. 1969 - 1981 Roy and Beahrs, Carenfelt and Eliasson proposed the Preservation of CNXI in clinically positive necks.

H. 1972 Lindberg's classic study indicates consistent patterns of Lymphatic drainage for carcinomas in various locations of the upper aero digestive tract.

I. 1990 - Shah's work confirms that of Lindberg's in a review of over 1000 neck dissection specimens.

J. 1986 - 1991 Byers, Medina, and Spiro report their results with Selective neck dissection**.**

The rationale for such modifications is based on the finding that modified radical neck dissection results in improved postoperative shoulder function and on the realization that neck recurrence is still a significant problem despite the extensiveness of radical neck dissection. Improved understanding of lymph node drainage patterns[35,36] and fascial compartments of the neck and better understanding of the indications for adjuvant postoperative radiation therapy have given further impetus to the trend away from the routine use of radical neck dissection in all patients.

CLASSIFICATION OF NECK DISSECTION

A. Comprehensive neck dissections - includes the radical neck dissection and three modifications, but always refers to a procedure in which all of groups I - V are removed.

1. Radical neck dissection

Involves the removal of all lymphatics from the inferior border of the mandible and line joining angle of the mandible to the mastoid tip, to the clavicle between the lateral border of the sternohyoid and the anterior border of the Trapezius. The deep margin of resection is the fascial carpet of the scalene muscles and the levator scapulae. The sternocleidomastoid, the internal jugular vein, and the spinal accessory nerve are removed with the specimen. Traditionally, this was the only surgical method of treating the neck but with the development of the more limited, less morbid modifications this is no longer indicated in the N_0 neck. Many surgeons no longer advocate this approach in N+ necks unless the metastatic nodes involve the muscle, vein, or nerve.

2. Modified Radical Neck Dissection

Based on the work of Suarez as well as that of Bocca and Pignataro it indicates that an en bloc removal of the cervical lymphatics can be accomplished by stripping the fascia from the Sternocleidomastoid and internal jugular vein. No lymphatic communication was ever noted between these structures and the cervical lymphatics. These studies point out that both the spinal accessory and the hypoglossal nerve do not follow the aponeurotic compartments, but rather run across them; however, their conclusion was that if the tumour did not directly involve the nerves,

they could be spared. From the above information and a desire to minimize the shoulder dysfunction associated with spinal accessory nerve sacrifice came the development of the modified radical neck dissection.

3. Type I Modified Radical Neck Dissection

Accomplishes the removal of the same regions of lymphatics as in the radical neck dissection, but the spinal accessory nerve is spared. It is used less commonly in the N_0 neck, but would be a reasonable choice with neck disease that involved the Sternocleidomastoid or jugular vein without involving the spinal accessory nerve.

4. Type II Modified Radical Neck dissection

Involves the same dissection as in the radical neck, but the spinal accessory nerve and internal jugular vein are spared. It is indicated in N+ necks with metastatic involvement of the Sternocleidomastoid, but without involvement of the nerve and vein.

5. Type III Modified Radical Neck dissection - "Functional Neck Dissection"

It is similar to the radical neck dissection with preservation of all three above mentioned non lymphatic structures. The indications for this procedure are controversial. In Europe, this operation is popular in the treatment of hypo pharyngeal and laryngeal tumors with N_0 neck. Molinari, Lingeman, and Gavilan propose this procedure for N_1 necks when the involved nodes are mobile and no greater than 2.5 to 3cm. Bocca proposes this operation for any neck that has indications for a radical neck dissection as long as the nodes are not fixed.

B. Selective Neck Dissections

This type of dissection arose from the work of Shah, Lindberg and Byers who identified the pathways of lymphatic spread in the head and neck. The regions who have high risk for metastasis are removed.

Types of selective neck dissection:

a. Supraomohyoid (anterolateral) neck dissection

Levels I, II, and III are removed sparing the Sternocleidomastoid, IJV, and CNXI. This is indicated in the treatment of oral cavity lesions.

b. Lateral neck dissection

Levels II, III, and IV are removed sparing the Sternocleidomastoid, IJV, and CNXI. This is indicated in tumours of the larynx, Oropharynx, and hypopharynx when the neck is N_0, although some advocate this approach with the N_1 neck with nodes limited to level II.

c. Posterolateral neck dissection

Levels II, III, IV, and V are removed sparing the Sternocleidomastoid, IJV, and CNXI. This is useful in the treatment of skin tumours with metastatic potential located in the posterior scalp or neck such as melanomas, squamous cell carcinomas, and Merkel cell carcinomas.

C. Extended neck dissections - describes any of the above dissections that include the removal of additional structures or other groups of lymph nodes.

Selective neck dissection (SND), which involves selective removal of nodal groups most at risk for metastasis with preservation of all non-lymphatic structures, has gradually gained acceptance in the clinically N_0 neck and has demonstrated regional control and survival rates similar to those of more extensive neck dissections.[37]

Although SND has been accepted by many as appropriate for use in the clinically node-negative neck, its use in patients with clinically obvious (palpable) metastatic disease remains extremely controversial; however, extension of the indications for its use in this setting seems logical. In the absence of factors that would alter normal lymphatic flow in the neck, such as previous neck surgery, radiotherapy, or the presence of massive obstructive adenopathy, the rationale behind the operation, which like its more radical counterpart seeks to remove the lymph nodes involved by or at risk for involvement by head and neck cancer, remains valid.

The present classification of MRND does not classify it as types 1 and 2 but only names the non-lymphatic structures spared.

Elective neck dissection: This is the neck dissection done in N_0 cases where metastasis is expected.

Elective Selective neck dissection: This is done as a staging procedure e.g.; Supraomohyoid neck dissection.

Treatment of N_0 Neck

The evaluation and treatment of N_0 neck remains controversial. The problem is whether to treat the neck electively or not. The controversy extends into when, and how, the N_0 neck should be treated.

The treatment option for N_0 neck includes:

1. Elective surgery

2. Elective radiotherapy

3. Elective neck investigation

4. Adopt a policy of wait and watch.

In patients with a greater than 20-25% chance of sub clinical neck disease, Where vigilant follow up is not possible, where clinical evaluation of the neck has proved difficult, where the neck is being entered for access for reconstruction or where imaging of the neck suggests possible nodal spread, there elective treatment with surgery or external beam radiotherapy should be considered.[32]

If the primary tumour is being treated with radiotherapy, then elective treatment to the neck should be radiotherapy. Where the primary tumour is being treated surgically, elective neck surgery can be carried out.

Elective surgery provides further information for clinical staging of lymph nodes(staging procedure) in the area are cleared to give access to vessels for reconstructive purposes, local recurrence rates may be reduced and survival enhanced.

The choice of selective neck dissection is based on site of primary tumour e.g., SOND for oral cancers.

A further option in the treatment of N_0 neck is to consider elective neck investigation. But false positive result is inevitable in the presence of inflammatory neck nodes and false negatives do occur.[23]

It is perfectly reasonable to adopt a policy of "wait and watch" in low risk necks. But in patients with high risks "wait and watch" policy will have detrimental effect.[13] This does not justify its routine use.

Treatment of N_1 Neck

In palpable neck disease all five levels may be involved and the minimum operation that should be performed is a MRND. As extra nodal spread may be uncommon in this group, conservation or FND is considered.[32]

There are proponents of a "less than five level" neck dissection for N_1 disease on the basis that in the untreated neck, the arguments for the distribution of in first echelon lymph nodes in non-palpable disease can be applied to early palpable disease. However, this sort of surgery requires considerable expertise and postoperative radiotherapy at all five levels.

The role of radiotherapy in the treatment of N_1 disease is controversial. It is less efficient than surgery for N_1 Neck and is a less preferred option unless the primary site is also being treated with radiotherapy.

RECONSTRUCTION[38]

Oro-mandibular reconstruction continues to be one of the most challenging areas of head and neck reconstruction. Reconstruction of resulting defect can be done by the following methods:

1. Split thickness skin grafts Full thickness skin grafts
2. Mucous membrane flaps
3. Tongue flaps
    a. Posteriorly based lateral tongue flap
    b. Posteriorly based bilateral tongue flap
    c. Anteriorly based ventral tongue flap
4. Masseter flap
5. Naso-labial flap
6. Medial based delto-pectoral flaps
7. Forehead flap
8. Sterno-cleidomastoid myocutaneous flap
9. Trapezius

10. Platysma myo-cutaneous flap

11. Pectoralis major myocutaneous flap

12.Latissimus myocutaneous flap

13.Costochondral grafts

14.Osteo-myocutaneous flap-fifth rib with pectoralis major myocutaneous flap -Spine of scapula with trapezius

15.Free osteo-cutaneous groin flap

16.Free osteo-cutaneous fibula flap

17.Scapular Osseo-cutaneous flap

18.Radial forearm flap (microvascular free flap)

19.Radial forearm free osteo-cutaneous flap

20.Free fibula and osseo-integrated implants

21.Anterolateral thigh free flap

Whenever possible, immediate single stage reconstruction is preferred over delayed reconstruction, when the former can be achieved with acceptable success rates and low morbidity. Immediate restoration of the mandible prevents the development of muscle contracture and restores mandibular form. Delayed reconstruction interferes with the radiotherapy and later healing.

The bone to mucosa relationship of the periosteum of the alveolar ridge and gingival mucosa is most difficult to duplicate and is necessary for wearing dentures. Preservation of chewing, provision of a base for dental appliances and preservation of a normal appearing lower third of the face are achieved by preservation of the buccal sulcus and the oral floor, which are all essential reasons for maintenance or restoration of the mandibular contour.

Tumour thickness, depth of invasion and lymph node metastasis

Cervical metastasis has a huge impact on the prognosis in patients with carcinomas of the head and neck. Lymph node metastasis reduces the survival by almost 50%, and the frequency of such spread is greater than 20% for most squamous cell carcinomas . The presence of cervical lymph-node metastasis is considered as a strong determinant of survival in patients with squamous cell carcinoma of the oral cavity (OSCC). The incidence of occult lymph-node metastasis in early-stage tumors (primary site T-categorization T1 or T2) has been reported to be between 27% and 40%.[39]

It is described that 49% occult metastasis in cervical lymph nodes in patients presenting with squamous cell carcinoma of buccal mucosa.[40] Level I was the most common site for nodal metastases (100%), followed by level II (32%), level III (16%), and level IV (8%).[41] Though there are multimodal treatment options, the prognosis is usually poor The presence of occult lymph node metastasis of buccal carcinoma following oral tongue , is observed more often than in any other cancer of the oral cavity.[42] Literature shows an overall 5-year survival rate of 65% ,even though the tumour stage distribution remained same compared to the preceding 10-year period.[43] Survival was better related to a more aggressive treatment of the neck even in early tumor stages and to adjuvant radiotherapy in advanced tumor stages. Only a few investigations have been done into the metastasis of squamous cell carcinoma of the buccal mucosa. But it is of interest to note that the incidence of cervical lymph node metastasis from cancer of the buccal mucosa is significant.

The presence of extra capsular spread reduces the chances of cure by 50%. As mentioned earlier the site, size, differentiation of tumor, perineural invasion, perivascular invasion, inflammatory response, and DNA content predicts cervical lymph node metastasis.[43,44]

Elective neck dissection is both diagnostic as well as therapeutic and is usually advised when the risk of cervical lymph-node involvement is greater than 15%-20%.[45] It provides pathological information on the status of neck nodes, and helps if adjuvant therapies are needed. Many number of patients with early stage OSCC undergo END and later are found to have no evidence of cervical lymph node metastasis, while they have risk of potential morbidity of a neck dissection. Efforts to identify the factors

that help in predicting the risk of cervical lymph-node metastais should provide better improvement in elective neck management.[45-47]

Breslow established a strong link between tumor thickness (TT) and both tumor-free survival and metastasis in patients with cutaneous melanoma.[48,49] Mohit-Tabatabai and his team and Spiro and his team according to Breslow's hypothesis regarded the relationship between lymph-node involvement and tumour thickness to oral cavity malignancy.[50,51] Since then, many studies have been carried out to test this relationship. These studies have shown that tumour thickness is an important predictor for lymph-node involvement in OSCC. Studies have revealed that the most influential parameter in the prognosis of a patient with cancer of the tongue is the tumour thickness. Many authors have found that the thickness of the tumour correlates better with survival and involvement of the lymph nodes than does its superficial diameter.[52-54] Tumour thickness measurement has not been uniform. Many studies used an optical micrometer to measure the thickness did not specify how the data were obtained.[51-56] In literature different measurements are identified, some measured the distance from the deepest point of tumour invasion to the most protruding part of the tumour (tip of the papilla) in exophytic lesions and to the ulcer base in ulcerated lesions, and some measured from the deepest point of the tumour to an imaginary line that reconstructed the healthy mucosa. And some did not consider the keratin layer and inflammatory infiltrate.[56,57] The most aggressive tumours are those with the greatest capacity to grow downwards vertically. Literature shows that the tumour mass which has the capacity of vertical growth and its aggressiveness is that which can be observed below an imaginary line reconstructing the healthy oral mucosa, because below this line the tumour must destroy healthy tissue in order to invade. The exophytic growth of the tumour should not be considered, because it does not

represent the overcoming of tissue resistance, whereas the space left by the ulcerated tumour should be included, because it represents tissue destroyed by the downwards growth of the tumour.[58]

The Martinez-Gimeno Scoring System was designed to evaluate the risk of neck metastasis in squamous cell carcinoma of oral cavity. The parameters included tumour thickness, grades of differentiation, inflammatory infiltration, vascular embolus, perineural spread, inflammatory infiltration.[2] This predicts metastasis better than scan and palpation. **Tumour thickness is defined as the vertical extent in a perpendicular fashion. Tumour depth is taken as the infiltrative portion of the tumour which extend below the surface of mucosa.**

Primary tumour thickness and depth of invasion has also been used as a predictor in lymph node metastasis in oral tongue cancer. Studies have indicated that the thickness of primary tumour has a strong predictive value for lymph node metastasis. In some studies the thickness of more than 5mm was statistically correlated with lymph node metastasis.[4,52,59] In other studies the optimal cut off point was found to be 4mm. For tumours thicker than this prophylactic neck management is recommended.[60,61] . In another study, the risk of metastasis in the neck with tumour thickness of 6 mm or less was 11%, whereas when tumour thickness was 7 mm or more this risk was 44%.[62]

Similar study was done to correlate the tumour thickness in floor of the mouth and cervical lymph node metastasis. Different studies showed different cut off points. 1.5 mm, 5mm and 7.5 mm cut off points were established .[50, 63-65]

Depth of tumour invasion is considered as an independent predictor tor cervical lymph node metastasis. Infiltration depth was defined as the maximum depth of

tumour infiltration (millimetres) below the mucosal surface. In case of ulcerated or exophytic tumours, the reconstructed mucosal surface was used.[66]

In literature, definitions of depth of invasion are different. In a review paper where the study was one depth of invasion and tumour thickness in oral cancer, around fifty studies were included.[67]Depth of invasion is known to be a better predictor for nodal status, because it compensates for exophytic growth or tissue destruction by the tumour.[58, 68, 69] Few more studies on infiltration depth were published.[70, 71] One study found a significant cut-off at 2.2 mm.[72] The other studies found a significant cut-off in the range 5 mm.

The use of depth of invasion in predicting lymph node metastasis in oral cancer are many. It is easy, quick and cheap to perform. Depth of invasion is already a standard item in the histopathology report according to the Royal College of Pathologists (UK) and the Dutch Working Group Head– Neck Tumours, amongst others.[73, 74] So by studying the depth of invasion in buccal mucosa squamous cell carcinoma to predict lymph node metastasis can be readily implemented in clinical practice.

MATERIALS AND METHODS:

Source of data:

This prospective cohort study was conducted from November 2012 to 0ctober 2014 at R. L. Jalappa Hospital and Research Centre, Tamaka, which is serving a rural population with 40% incidence of oral cavity malignancies, among all cancer patients attending ENT outpatient department (unpublished data).

Fifty three patients with buccal mucosa cancer with T2 and T3 lesions were selected for the study material.

The following data were obtained for each patient:

a. History
b. Addiction habits
c. Clinical examination
d. Biopsy report
e. Surgery details
f. Histological evaluation
g. Follow up to evaluate oncological outcome

METHOD OF COLLECTION OF DATA:

INCLUSION CRITERIA

T2 or T3 squamous cell carcinoma of buccal mucosa.

EXCLUSION CRITERIA

1. Prior chemotherapy.
2. Prior radiotherapy.
3. Prior surgery for malignancy in the head and neck region
4. Positive margins on histopathological examination of resected primary tumour.
5. T1 and T4 squamous cell carcinoma of the buccal mucosa.

The staging was performed on the basis of TNM staging. All the patients were treated with wide excision of primary tumour and simultaneous neck dissection as primary treatment. The excised specimen was evaluated for tumour thickness (taken as the vertical extent of the tumour from its surface to its deepest extent in perpendicular fashion) and tumour depth (taken as the infiltrative portion of the tumour which extends below the surface of the mucosa).

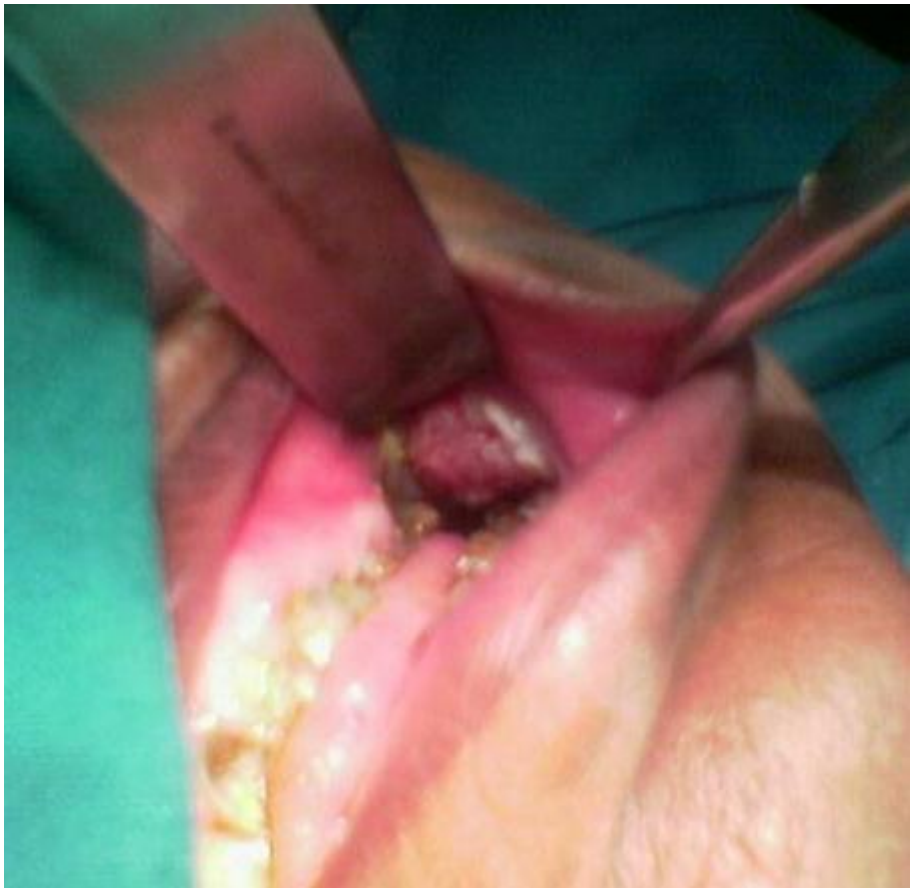
The resected neck dissection specimen was histologically examined to look for metastasis. The results were documented. An attempt was made to correlate thickness of primary tumour and depth of invasion of the primary tumour with cervical lymph node metastasis .

Each patient was assessed as follows:

PREOPERATIVE:

- Clinical examination
- Addiction habits
- Associated premalignant condition
- Biopsy

Photo 2 : Squamous cell carcinoma of buccal mucosa



OPERATIVE: The patients underwent wide excision of the tumour and either supromohyoid neck dissection or modified radical neck dissection based on their clinical nodal status. Patients with N0, N1 underwent supraomohyoid neck dissection and patients with N2a, N2b underwent modified radical neck dissection. The surgical defect was reconstructed by either forehead flap reconstruction, pectoralis major myocutaneous flap reconstruction, anterolateral thigh flap reconstruction, radial forearm free flap reconstruction and supraclavicular flap reconstruction.

Photo 3: Intraoperative photo-draping of the patient

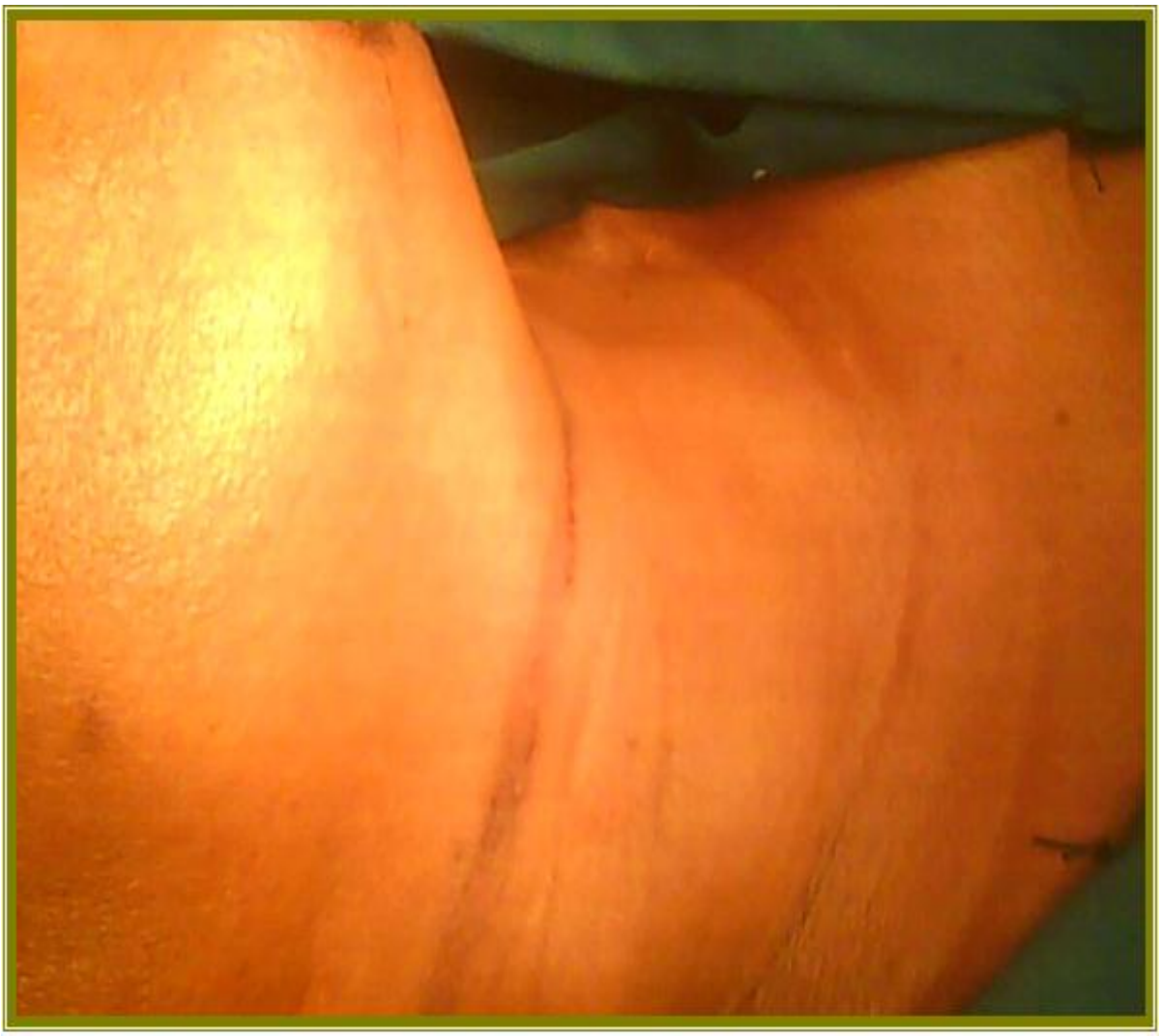


Photo 4 : Marking of incision for neck dissection

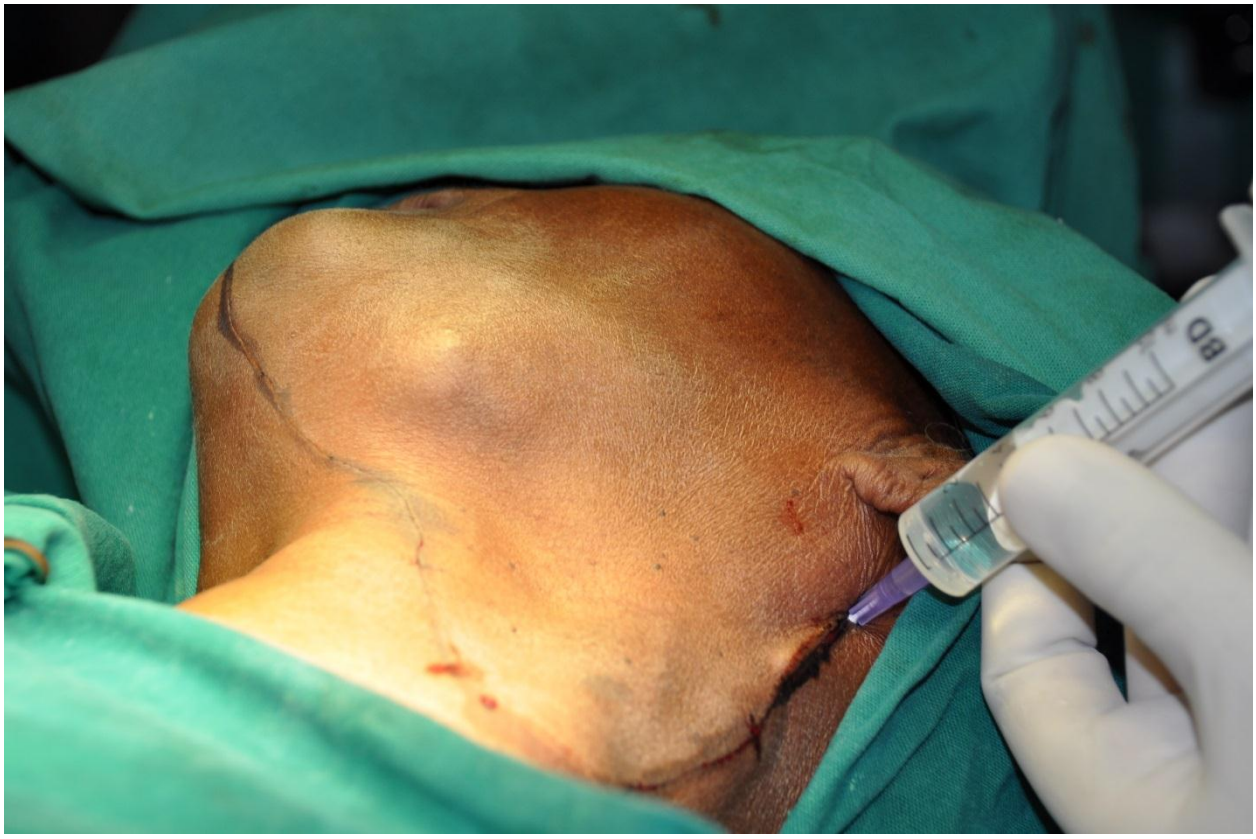


Photo 5 : Neck dissection

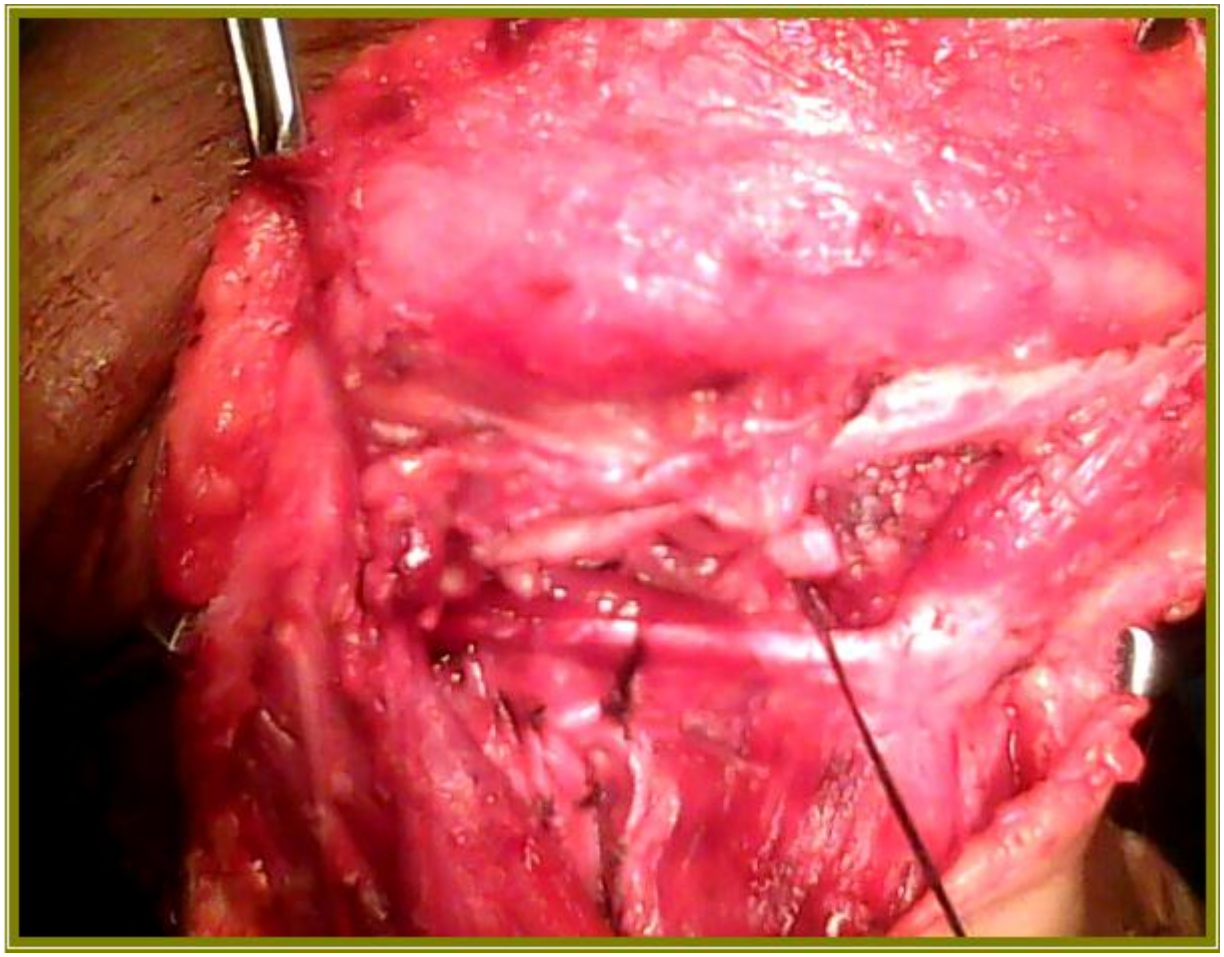


Photo 6 : Neck dissection specimen

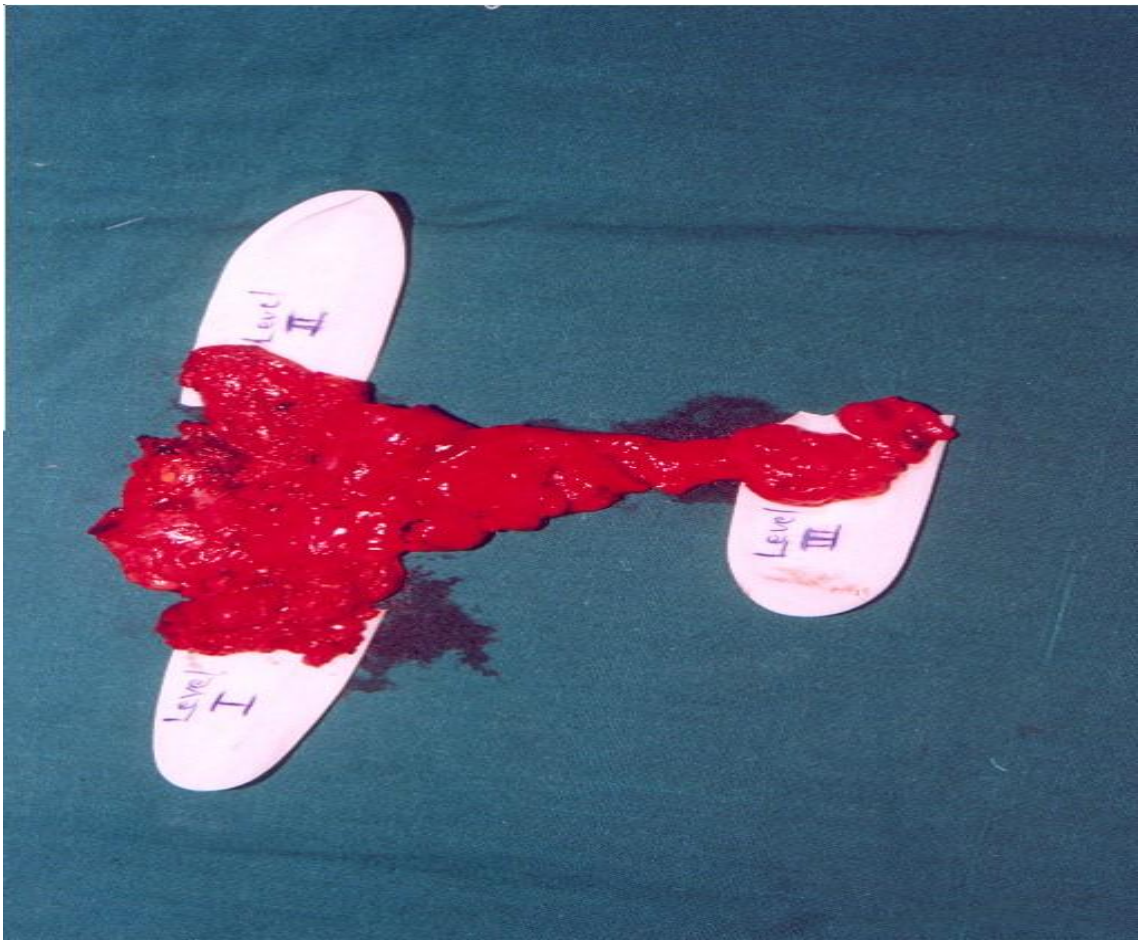


Photo 7 : Composite resection of T_3 tumour

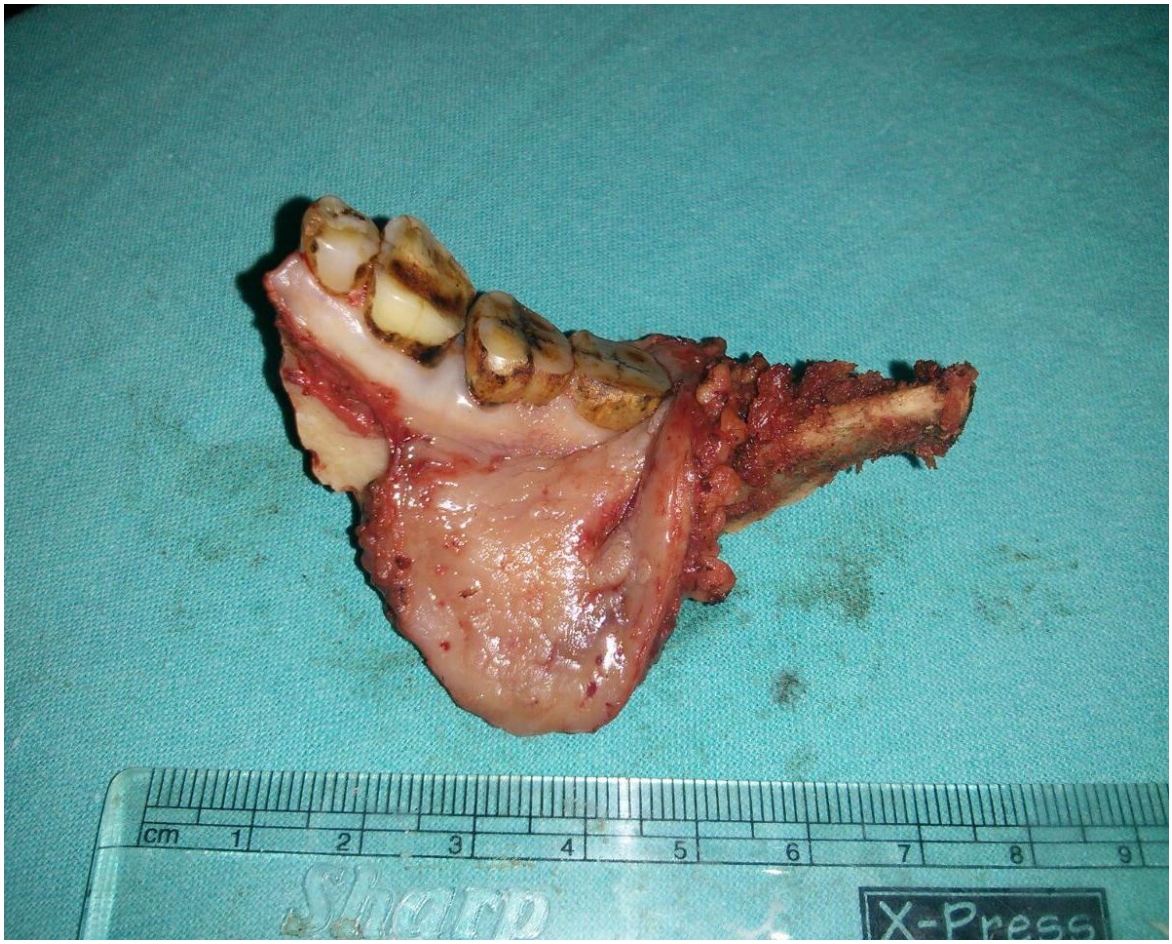


Photo 8 : Skin closure

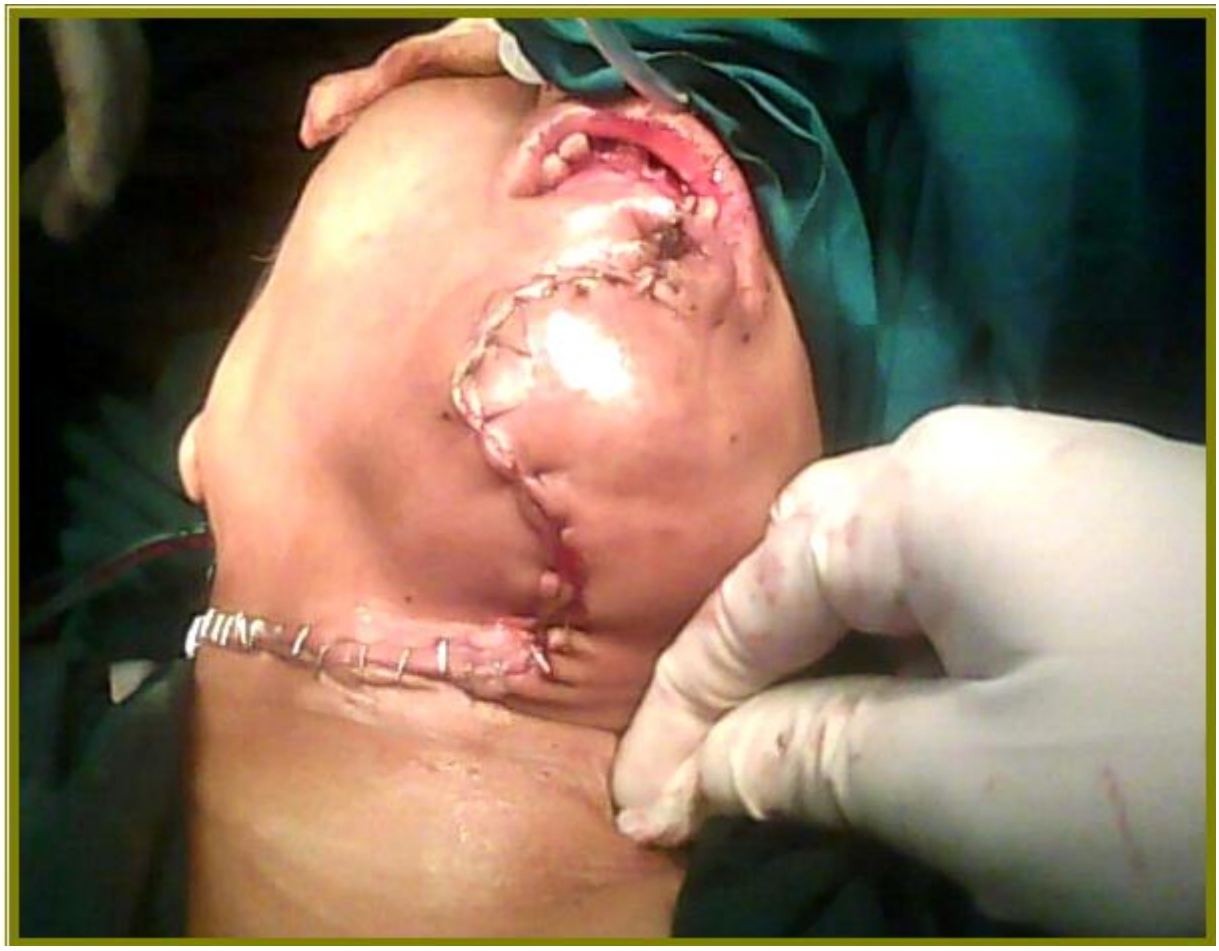
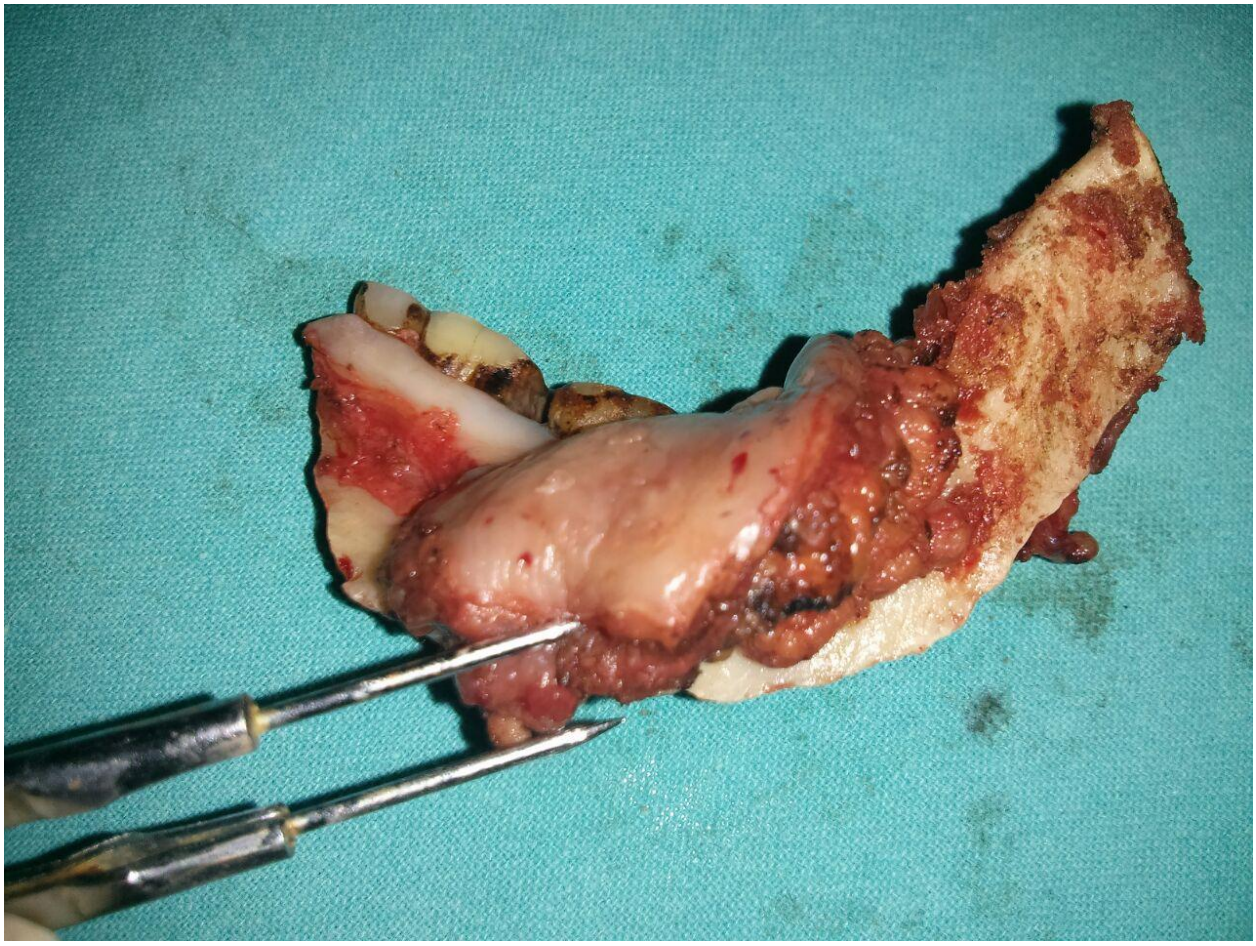


Photo 9 : Lymph node specimen for HPE

Photo 10 : Measuring the TT before immersing in formalin



POST OPERATIVE: - Histopathological examination of each specimen was done for:

TUMOUR SIZE :

HISTOLOGICAL TYPE :

DIFFERENTIATION :

Tumour thickness

Tumour depth

VASCULAR INVASION :

NERVE INVASION :

BONE / CARTILAGE INVASION :

SALIVARY GLAND INVASION :

LYMPH NODE STATUS

TOTAL NUMBER OF LYMPH NODES :

NO OF POSITIVE NODES :

LEVEL OF POSITIVE NODE :

MICROMETASTASIS (<2mm in diameter) :

EXTRA CAPSULAR SPREAD :

Photo 11 : HPE showing well differentiated squamous cell carcinoma

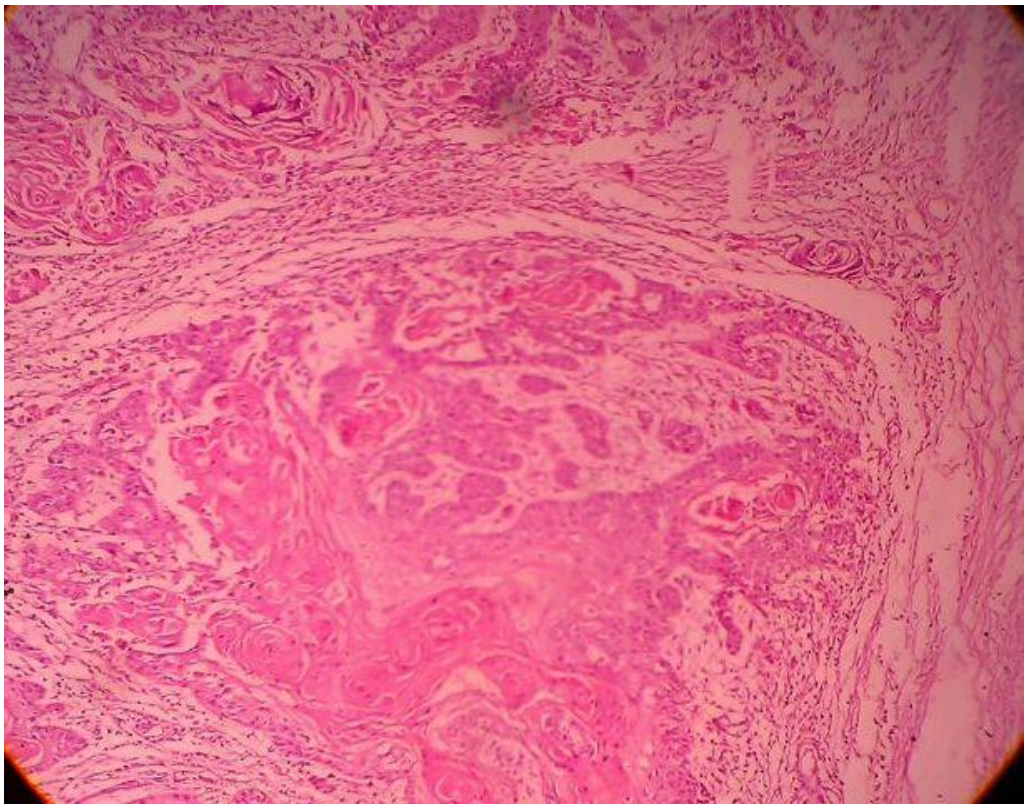
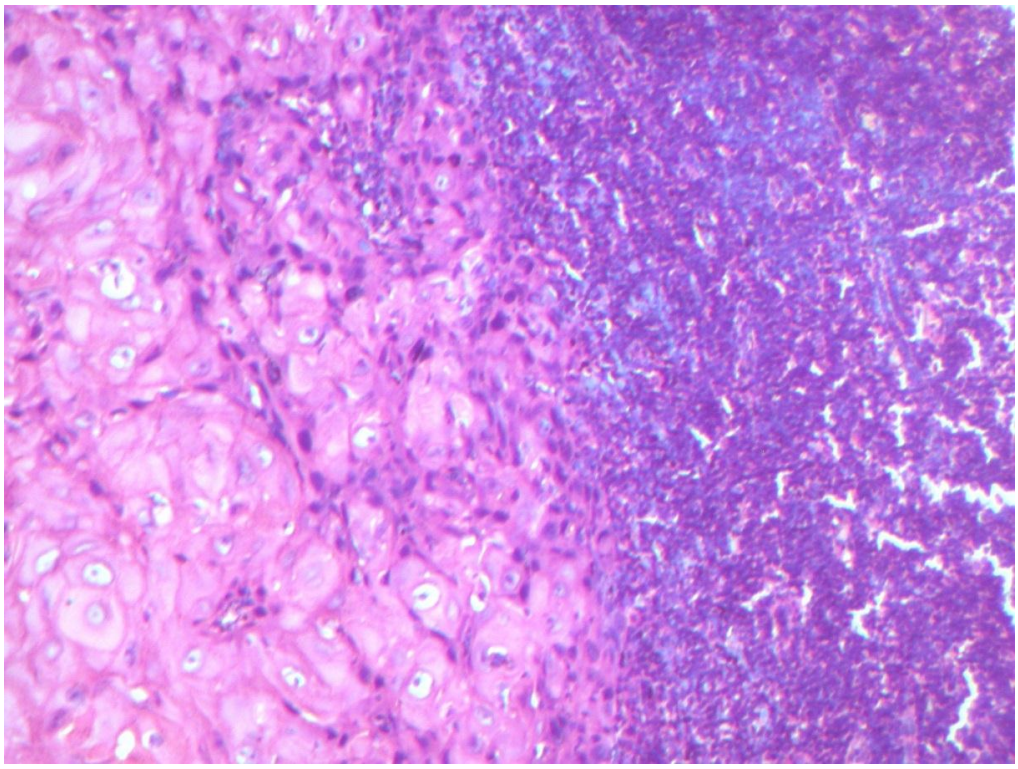


Photo 12: HPE showing tumour metastasis in lymph node



FOLLOW UP: All operated patients were followed up for 3, 6 and 9 months.

Clinically for: - Local recurrence --- Ulceration, growth

- Regional recurrence--- Lymphadenopathy

- Distant metastasis

And for :

- lost to follow up

- Died due to the disease

- Died due to other cause.

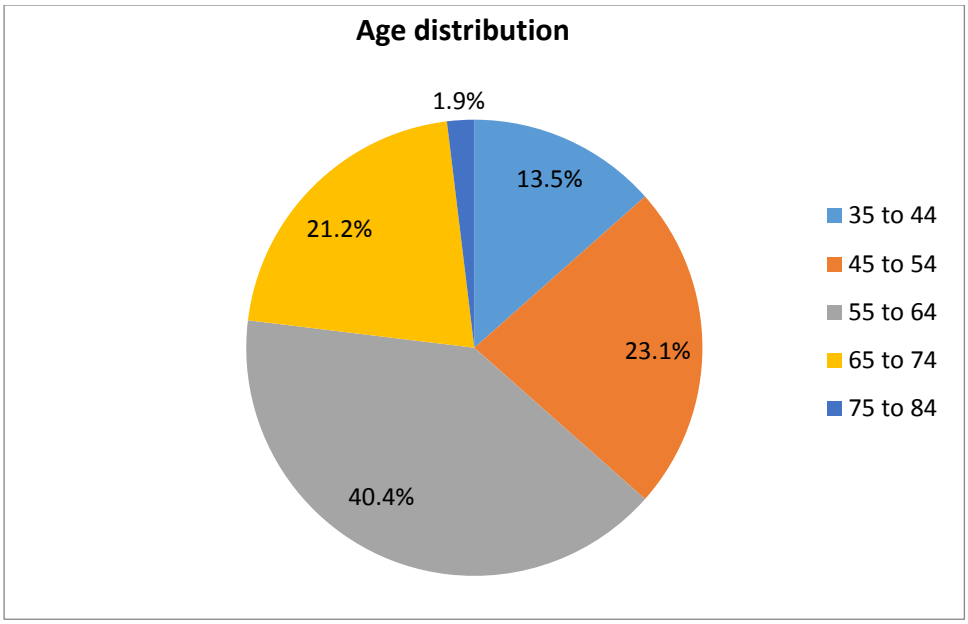
RESULTS:

In our study, we have analysed different parameters.

Table 2 – Showing age distribution in study groups:

Age group	Number of patients	% of patients
35 to 44	7	13.5%
45 to 54	12	23.1%
55 to 64	21	40.4%
65 to 74	11	21.2%
75 to 84	1	1.9%

Figure 5: Showing age distribution in study groups:

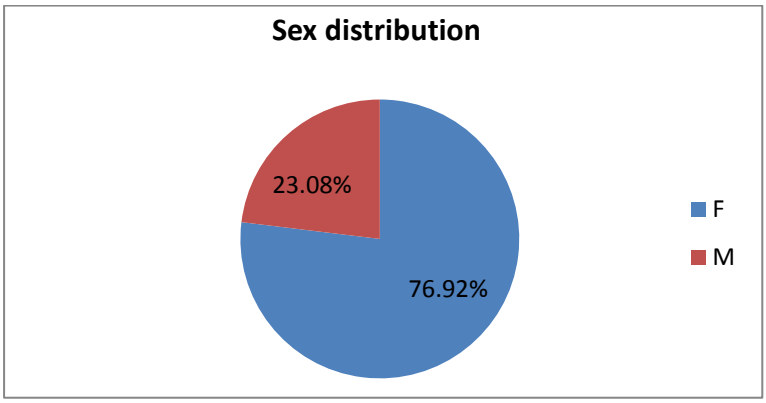


40.4% of the patients are between the age group 55 to 64 years. About 76.9% of patients are between 35 to 64 years age group.

Table 3: Sex distribution

Sex	Number of patients	% of patients
F	40	76.92%
M	12	23.08%

Figure 6: Sex distribution

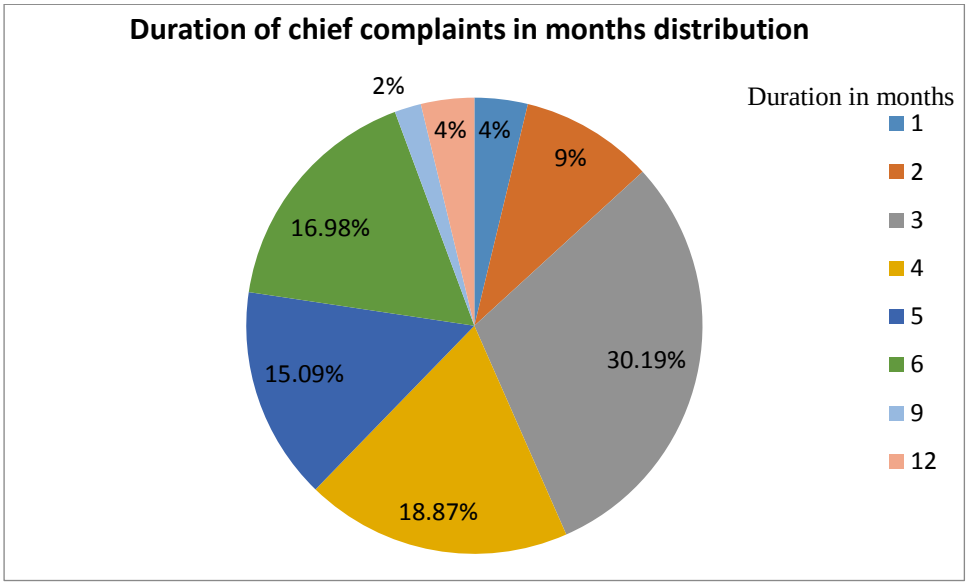


In our study 76.92% of the patients were females and 23.08% were males.

Table 4: Duration of chief complaints

Duration of chief complaints		
Duration in months	Number of patients	% of patients
1	2	4%
2	5	9%
3	16	30%
4	10	19%
5	8	15%
6	9	17%
9	1	2%
12	2	4%

Figure 7 : Duration of chief complaints

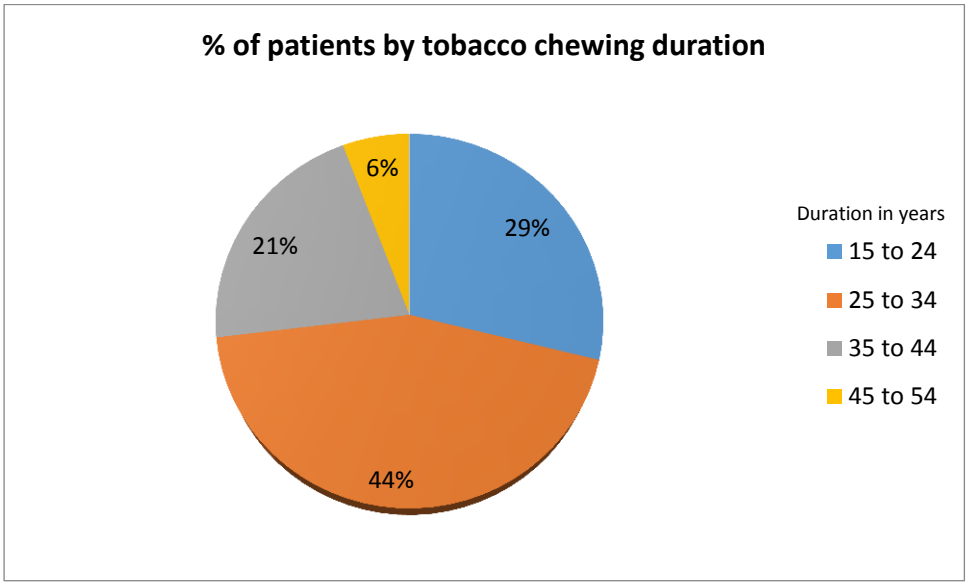


Weighted mean duration of chief complaints is 4.28 months. Almost 81.1% of patients had duration of chief complaints ranging from 3 to 6 months.

Table 5: Tobacco chewing duration

Tobacco chewing Duration in years	Number of patients	% of patients
15 to 24	15	29%
25 to 34	23	44%
35 to 44	11	21%
45 to 54	3	6%

Figure 8: Tobacco chewing duration



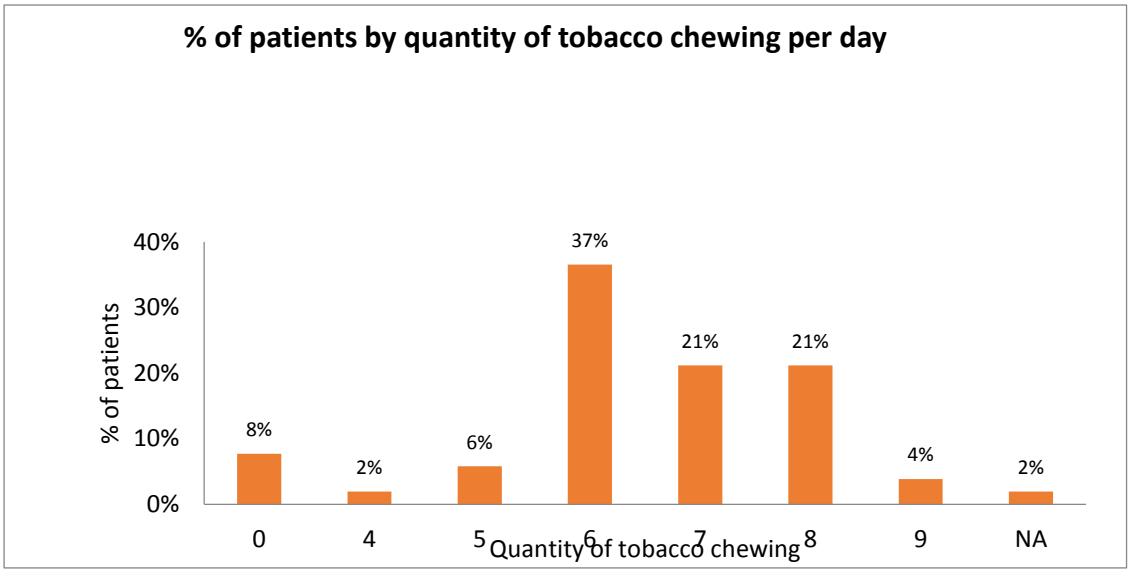
Weighted mean duration	28.154 years

Weighted mean duration of tobacco chewing is 28.154 years. Almost 71% of the patients are chewing tobacco 25 to 54 years.

Table 6: Quantity of tobacco chewing per day:

Quantity of tobacco chewing per day		
Quantity of tobacco chewing(number of times/day)	Number of patients	% of patients
0	4	8%
4	1	2%
5	3	6%
6	19	37%
7	11	21%
8	11	21%
9	2	4%
NA	1	2%

Figure 9: Quantity of tobacco chewing per day

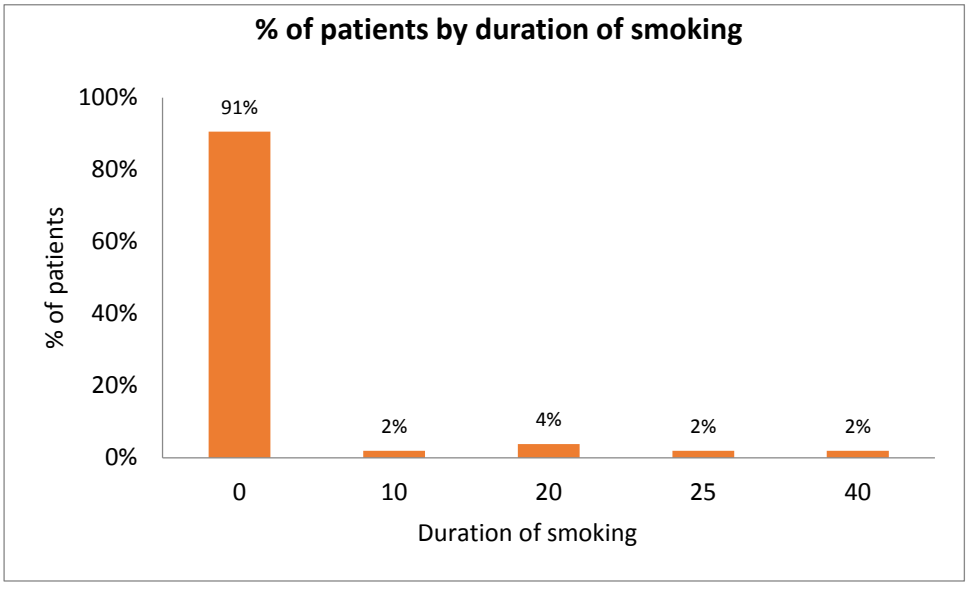


Almost 79% of the patients chew 6 to 8 times of tobacco per day. Average quantity of tobacco chewing per day among all patients is 5.57.

Table 7: Duration of smoking (years)

Duration of smoking		
Duration in years	Number of patients	% of patients
0	48	91%
10	1	2%
20	2	4%
25	1	2%
40	1	2%

Figure 10: Duration of smoking (years)

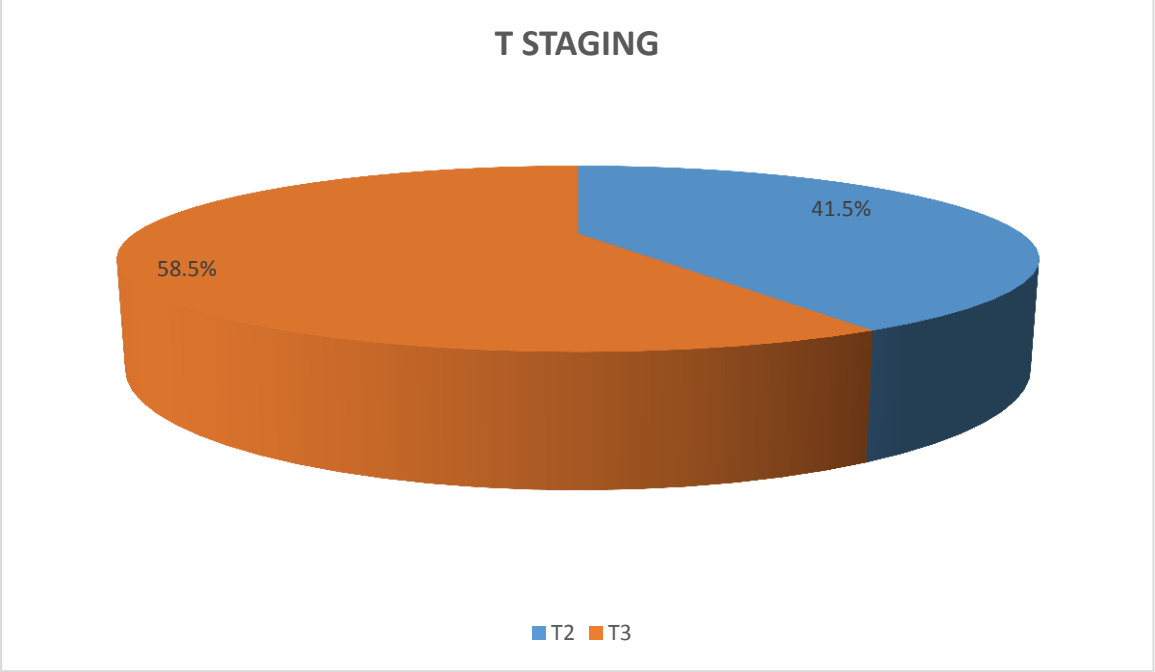


91% of patients do not smoke Beedi or Cigarette.

TABLE 8: T STAGING

T STAGING	NO OF PATIENTS	% of patients
T2	22	41.5%
T3	31	58.5%

Figure 11 : T STAGING

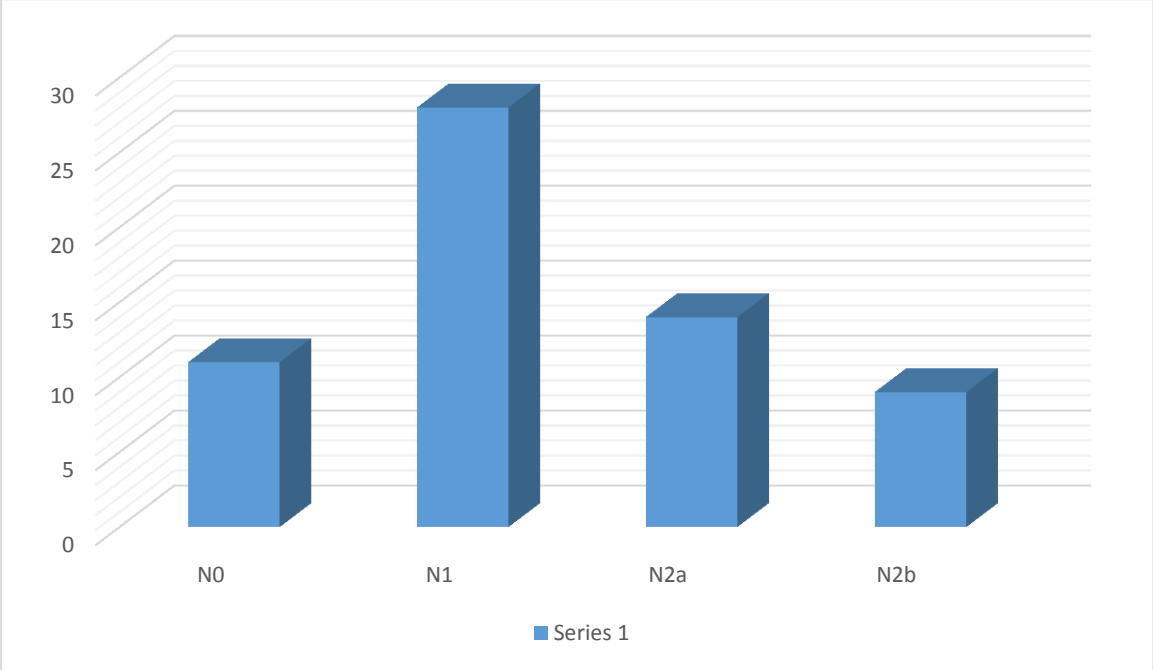


41.5 % of the patients were T2 and 58.5% were T3 .

TABLE 9 :Clinical nodal status of the patients

CLINICAL NODAL STATUS	NO OF PATIENTS
N0	11
N1	28
N2a	5
N2b	9

Figure 12: Clinical nodal status of patients



In our study 11 (20.75%) patients have N0 status, 28 (52.83%) patients have N1 status and 14(26.41%) patients have N2 status.

Table 10: Patients with cervical lymph node metastasis on HPE

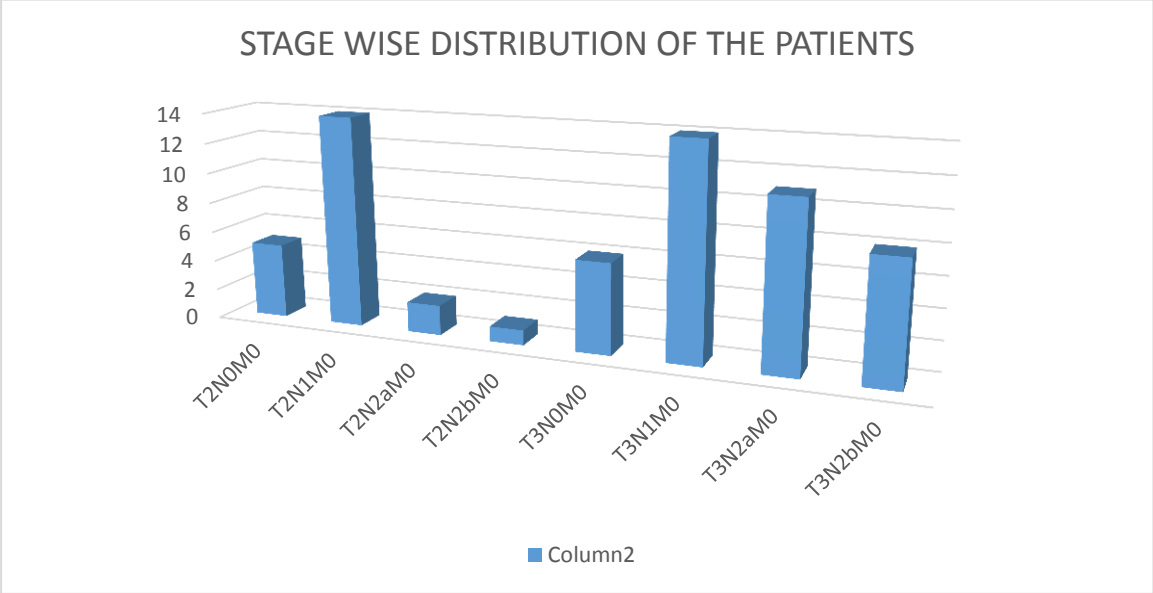
Total number of patients	Patients with cervical lymph node metastasis	% of patients with cervical lymph node metastasis
53	21	39.6%

39.6% of the patients had cervical lymph node metastasis on histopathological examination

TABLE 11 : CLINICAL STAGING OF THE PATIENTS

CLINICAL DIAGNOSIS	No OF PATIENTS
T2N0M0	5
T2N1M0	14
T2N2aM0	2
T2N2bM0	1
T3N0M0	6
T3N1M0	14
T3N2aM0	3
T3N2bM0	8

Figure 13: CLINICAL STAGING OF PATIENTS

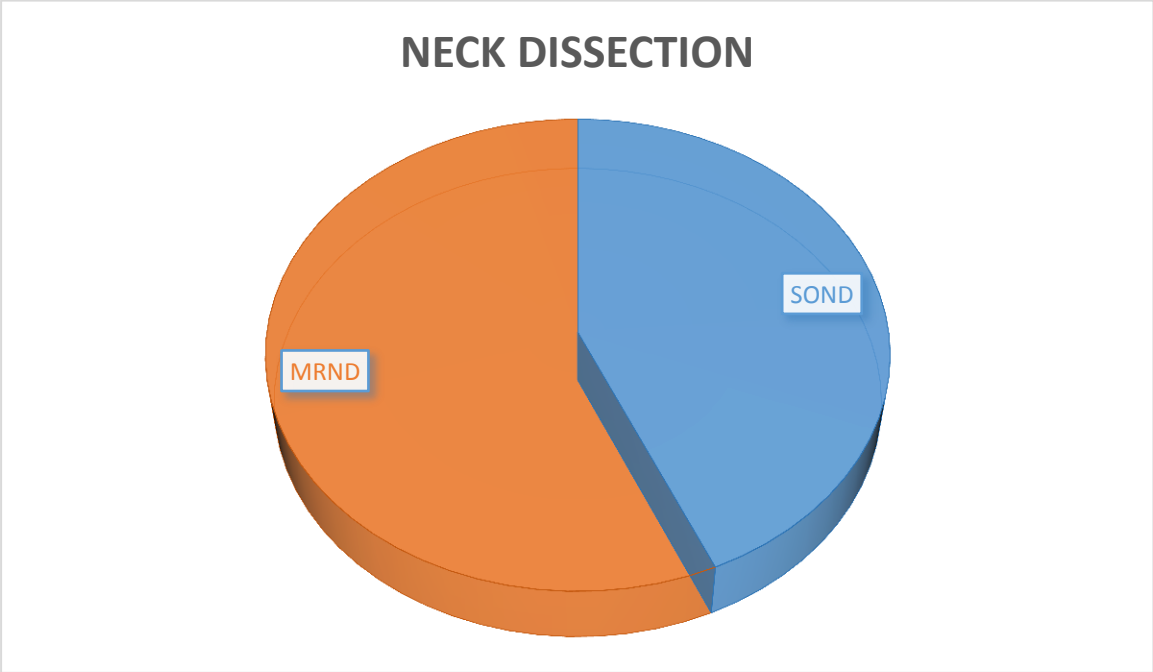


There were 5 patients with T2N0M0 staging, 14 patients with T2N1M0 staging, 2 patients with T2N2aM0 staging, 1 patient with T2N2bM0, 6 patients with T3N0M0 staging, 14 patients with T3N1M0 staging, 3 patients with T3N2aMx0staging and 8 patients had T3N2bM0 staging.

Table 12 : Surgical procedure – Neck dissection

Neck dissection	SOND	MRND
No of patients	23	30

Figure 14 : Surgical procedure – Neck dissection

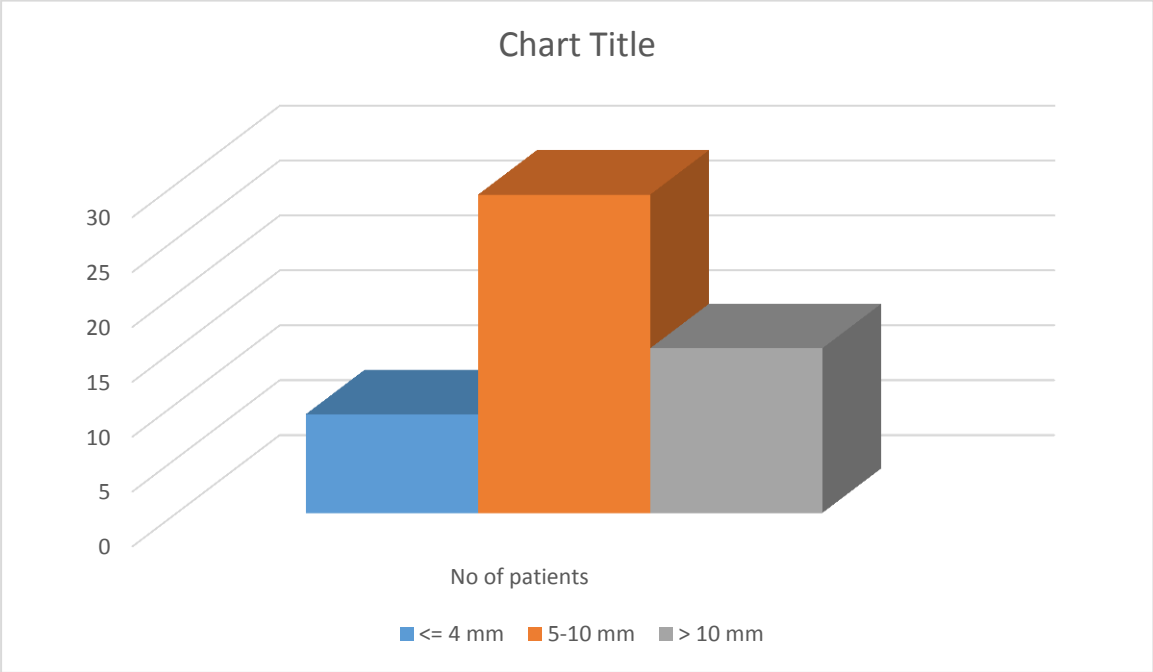


23 patients underwent SOND and 30 patients underwent MRND.

Table 13 : Distribution of patients in tumour thickness group

Tumour thickness group	<=4mm	5-10 mm	>10 mm
No of patients	9	29	15

Figure 15 : Distribution of patients in tumour thickness groups

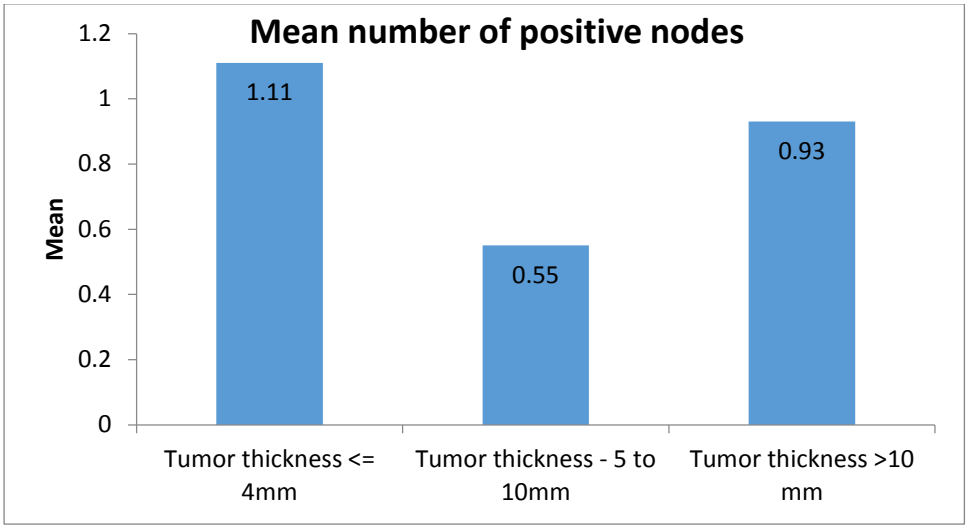


9 (16.98 %) patients were included in <=4 mm tumour thickness group, 29 (54.71%) patients in 5-10 mm group and 15 (28.3%) patients in >10 mm group.

Table 14: Metastasis distribution in Tumour thickness groups:

Metastasis	Tumour thickness <= 4mm		Tumour thickness – 5 to 10mm		Tumour thickness >10 mm		P-value between groups with Tumour thickness <=4mm and 5mm to 10mm	P-value between groups with Tumour thickness <=4mm and >10mm	P-value between groups with Tumour thickness 5mm to 10mm and >10mm
	No of patients	% of patients	No of patients	% of patients	No of patients	% of patients			
Absent	5	55.56%	19	65.52%	8	53.33%	0.5884	0.9155	0.4312
Present	4	44.44%	10	34.48%	7	46.67%			

Figure 16: Metastasis distribution in Tumour thickness groups



Percentage of Metastasis present in the group tumour thickness <=4mm is 44.44%.Percentage of metastasis present in the group tumour thickness 5 to 10m is 34.48%. Percentage of metastasis present in the group tumour thickness >10mm is 46.67%.

The p-value between the percentage of metastasis present in the groups tumour thickness <=4mm and tumour thickness 5 to 10mm is 0.5884. The p-value is greater than 0.05. Hence the p-value is statistically insignificant. It indicates that the percentage of metastasis present in both the groups is same.

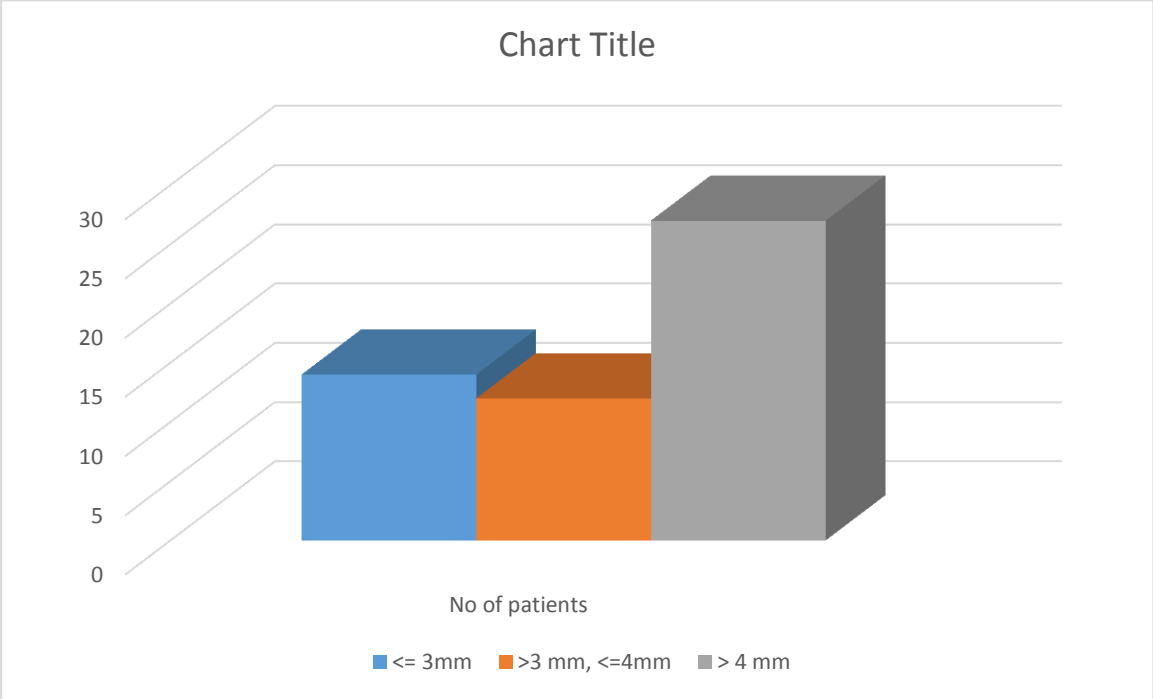
The p-value between the percentage of metastasis present in the groups tumour thickness <=4mm and tumour thickness >10mm is 0.9155. The p-value is greater than 0.05. Hence the p-value is statistically insignificant. It indicates that the percentage of metastasis present in both the groups is same.

The p-value between the percentage of metastasis present in the groups tumour thickness 5mm to 10mm and tumour thickness >10mm is 0.4312. The p-value is greater than 0.05. Hence the p-value is statistically insignificant. It indicates that the percentage of metastasis present in both the groups is same.

Table 15: Distribution of patients in tumour depth group

Tumour depth	<=3 mm	>3 mm - <=4 mm	> 4 mm
No of patients	14	12	27

Figure 17: Distribution of patients in tumour depth group

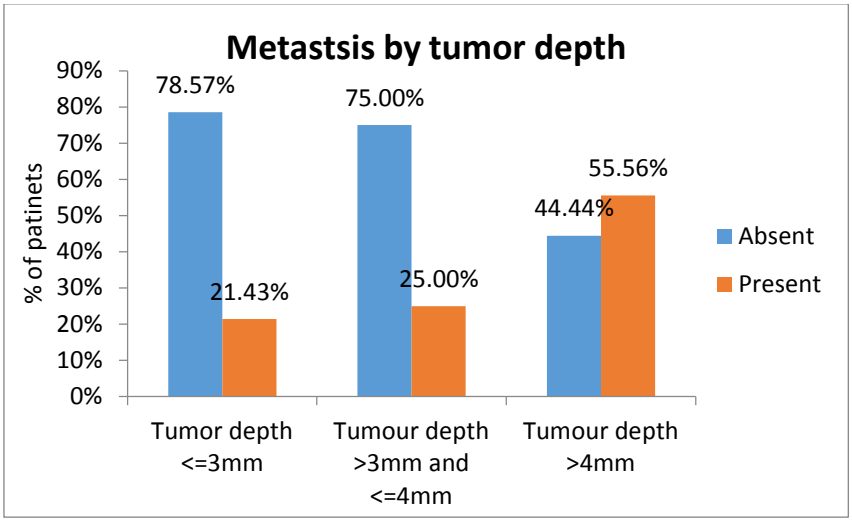


14 (26.4%) patients were in <=3 mm tumour depth group, 12 (22.65%) patients were in >3 mm , <= 4mm group and 27 (50.94%) patients in > 4 mm group.

TABLE 16: Metastasis distribution in Tumour depth groups

Metastasis	Tumor depth <=3mm		Tumour depth >3mm and <=4mm		Tumour depth >4mm		P-value between groups with Tumour depth <=3mm and >3mm & <4mm	P-value between groups with Tumour depth <=3mm and >5mm	P-value between groups with Tumour depth >3mm & <4mm and >5mm
	No of patients	% of patients	No of patients	% of patients	No of patients	% of patients			
Absent	11	78.57%	9	75.00%	12	44.44%			
Present	3	21.43%	3	25.00%	15	55.56%	0.8295	0.0368	0.0772

Figure 18: Metastasis distribution in Tumour depth groups



Percentage of Metastasis present in the group tumour depth <=3mm is 21.43%.Percentage of metastasis present in the group tumour depth >3mm and <=4mm is 25.00%. Percentage of metastasis present in the group tumour depth >4mm is 55.56%.

The p-value between the percentage of metastasis present in the groups tumour depth <=3mm and tumour depth >3 to <=4mm is 0.8295. The p-value is greater than 0.05. Hence the p-value is statistically insignificant. It indicates that the percentage of metastasis present in both the groups is same.

The p-value between the percentage of metastasis present in the groups tumour depth <=3mm and tumour depth >4mm is 0.0368. The p-value is less than 0.05. Hence the p-value is statistically significant. It indicates that the percentage of metastasis present in both the groups is different.

The p-value between the percentage of metastasis present in the groups tumour depth >3mm to <=4mm and tumour thickness >4mm is 0.072. The p-value is greater than 0.05. Hence the p-value is statistically insignificant. It indicates that the percentage of metastasis present in both the groups is same.

Table 16: Distribution among the cases of last follow up

Status of last follow up	Number of patients
Local recurrence	**2**
Regional recurrence	**0**
Distant metastasis	**1**
Lost to follow up	**3**
Died of disease	**0**
Died due to other cause	**1**

3 of our patients were lost to follow up.

2 of our patients had local recurrences after follow up of 9 months. They were clinically diagnosed to have T3N2bMx, one of them had tumour thickness of 10mm and depth of invasion of 5 mm . The other patient had tumour thickness of 21 mm and depth of invasion of 10 mm. Both the patients had received radiation.

1 patient had liver metastasis who was clinically diagnosed to have T2N1Mx. The patient had tumour thickness of 10mm and tumour depth of 5 mm. This patient had refused postoperative radiotherapy.

DISCUSSION

Initially, squamous cell carcinoma of the head and neck spreads locally and then it metastasizes to the lymph nodes of the neck. Surgical treatment of these tumours include local resection and neck dissection.

Lymph node metastasis has been considered as one of the most significant prognostic factors in oral cancer, hence it is important to note its occurrence.

This study was conducted at R.L.Jalappa Hospital, Kolar. A total number of 53 patients were included in our study. Increased incidence was seen in the 4^{th}-6^{th} decade of life. In the Bangalore registry for oral cancer, majority of patients included were in the seventh or eighth decade.[75] There is a progressive rise in the incidence of oral cancer with age. But, we had come across early age distribution mainly because of tobacco chewing habits of patients in this region.

In our study, majority (76.92%) of the patients were females. Such high incidence among women is mainly related with the differences in practices of chewing a betel quid, consisting of betel leaf, areca palm nut, slaked lime and catechu, along with other additives and flavourings. A study by Nandkumar A has reported similar major difference in rates between males and females.[75]

In our study, 60% of patients presented with left sided oral cancer, which does not have any clinical importance. But the side involved by cancer mainly corresponded with the habit of placing the quid at that particular site causing repeated contact of carcinogens.

In our study 71% of the patients were chewing tobacco from 25 to 54 years. The mean duration of tobacco chewing is 28.154 years. This is similar to the other

study by Gosselin BJ and his team,which showed 90% of tobacco chewers with oral cavity cancer.[75]

41.5 % patients in our study were of T2 status and 58.5% patients were of T3 status. There is definite late presentation of disease due to lack of awareness in rural patient population and low socio-economic conditions of the patients.

20.75 % of patients had clinically N0 status, 52.83% patients had N1 status and 26.41 %patients had N2 status on presentation.

In our study, there was an equal distribution of the patients having T2N1M0 (26%) and T3N1M0 (26%) staging.

All of our patients underwent wide excision of the tumour and neck dissection and subsequent reconstruction.

11 of our patients had clinically N0 neck, all of them underwent SOND. However none of them had any occult metastasis. Occult metastasis is defined as metastasis in lymph nodes on final HPE in the absence of clinically detectable enlarged lymph nodes. In a study by Narendra H it was 24%. This was due to the inclusion of T4 lesions in their study.[76]

After the excision of the tumour and neck dissection, histopathological examination was done to look for cervical lymph node metastasis of whom 26 (39.6%) patients had cervical lymph node metastasis.

The number of patients whose excised tumour specimen was measured for tumour thickness were divided into 3 groups of <=4 mm, 5-10 mm and > 10 mm.

9 (16.98 %) patients were included in <=4 mm tumour thickness group, 29 (54.71%) patients in 5-10 mm group and 15 (28.3%) patients in >10 mm group.

The metastasis in the lymph nodes in the tumour thickness group < 4 mm was observed to be 44.44%, in the group 5-10 mm was 34.48% and in the group > 10 mm was 46.67%.

The p-value between the percentage of metastasis present in the groups tumour thickness <=4mm and tumour thickness 5 -10mm is 0.5884. The p-value is greater than 0.05. Hence the p-value is statistically insignificant. The p-value between the percentage of metastasis present in the groups tumour thickness <=4mm and tumour thickness >10mm is 0.9155. The p-value is greater than 0.05. Hence the p-value is statistically insignificant. The p-value between the percentage of metastasis present in the groups tumour thickness 5mm to 10mm and tumour thickness >10mm is 0.4312. The p-value is greater than 0.05. Hence the p-value is statistically insignificant.

Tumour thickness is an important factor to predict lymph node metastasis in malignancies of tongue, floor of the mouth[56], lower lip, soft palate and oral cavity.[77,78]

In a similar study by Loddar and his team on oral cavity cancer have shown that risk of metastasis in the neck with tumour thickness of 6 mm or less was 12%, whereas tumour thickness in the group > 7 mm this risk was 57%.[62] Ragson and his team have recorded that the percentage of metastasis in lesions less than 5 mm thickness was significantly lower compared with those lesions with a thickness more than 5 mm.[79]

In a large clinical review by Pentenero, tumour thickness was shown to be an important parameter for predicting nodal metastasis and for survival. They showed that in literature the cut-off thickness predicting neck metastasis and survival varied from 1.5mm to 10 mm.[67]

A meta-analysis by Huang showed an association between tumour thickness and cervical lymph node involvement and they stated that the optimal cut-off point for tumour thickness is 4 mm.[3]

Various literature involving study of oral tongue cancer have shown that the tumour thickness exceeding 5 mm was statistically significant when correlated with metastasis.[52,59,68]

Many studies involved lip cancer and the tumour thickness of 3mm, 4mm and 6 mm were significant in correlating with metastasis.[80,81]

In literature tumour thickness has known to have its effect on the survival of patients. Brown and his team have described the cut-off point as being 3 mm, whereas Spiro and his team have shown that patients showed a significantly lower survival rate above a tumour thickness of 2 mm.[51,56] Moore in his study has differentiated five groups of patients according to their tumour thickness and found that the survival reduced significantly with increasing tumour thickness.[82] Urist and his team performed a survival analysis and concluded that a thickness of 6 mm was the cut-off point to divide patients with tumours of the oral mucosa according to their survival.[83]

The number of patients whose excised tumour specimen was measured for tumour depth were divided into 3 groups of <=3 mm, >3mm, <=4mm and > 4mm.

Percentage of Metastasis present in the group tumour depth <=3mm is 21.43%.Percentage of metastasis present in the group tumour depth >3mm and <=4mm is 25.00%. Percentage of metastasis present in the group tumour depth >4mm is 55.56%.

The p-value between the percentage of metastasis present in the groups tumour depth <=3mm and tumour depth >3 to <=4mm is 0.8295. The p-value is greater than 0.05.

Hence the p-value is statistically insignificant. *The p-value between the percentage of metastasis present in the groups tumour depth <=3mm and tumour depth >4mm is 0.0368. The p-value is less than 0.05. Hence the p-value is statistically significant.* The p-value between the percentage of metastasis present in the groups tumour depth >3mm to <=4mm and tumour thickness >4mm is 0.072. The p-value is greater than 0.05. Hence the p-value is statistically insignificant.

Tumour depth > 4 mm showed statistically significant correlation with lymph node metastasis.

A study by Melchers and his team showed that tumour depth is an independent predictor for nodal status in pathological T1–2 stage of oral cavity cancer. They recommend depth of invasion of 4 mm as an indication to perform a neck dissection in N_0 oral cavity cancer.[66]

Spiro and his team retrospectively analysed 92 patients treated with surgery for tongue and floor of the mouth cancers. They concluded that for clinically N_0 cancer, elective neck dissection was indicated in patients with depth of invasion of more than 2 mm because in these tumours risk of metastasis reached 40%.[51]

3 of our patients were lost to follow up.

2 of our patients had local recurrences after follow up of 9 months. They were clinically diagnosed to have T3N2bMx, one of them had tumour thickness of 10mm and depth of invasion of 5 mm. The other patient had tumour thickness of 21 mm and depth of invasion of 10 mm. Both the patients had received radiation.

1 patient had liver metastasis who was clinically diagnosed to have T2N1Mx. The patient had tumour thickness of 10mm and tumour depth of 5 mm. this patient had refused postoperative radiotherapy.

However in our study tumour thickness was not found to be statistically correlating in predicting cervical lymph node metastasis whereas tumour depth of 5 mm and more showed statistical correlation in predicting lymph node metastasis.

Tumour thickness of more than 10 mm showed a prediction for aggressive lymph node metastasis though not statistically.

CONCLUSION

1. There is a high incidence of buccal mucosa cancers among lower socioeconomic group, especially females, in Kolar region.
2. Majority of our patients had T3 lesions. There is definite late presentation of disease due to lack of awareness in rural patient population and low socio-economic conditions of the patients.
3. All the oral cancers in our series which had thrown metastases were to submandibular and upper deep cervical nodes.
4. Though the tumour thickness was not affecting the lymph node metastasis in this study, few studies have shown positive correlation between these two entities. More number of multi institutional studies with a larger sample size is required to evaluate this aspect.
5. However, tumour thickness of more than 10mm predicted aggressive lymph node metastasis, though not observed to be statistically significant.
6. There is a statistically significant correlation between tumour depth of more than 4mm and cervical lymph node metastasis.
7. Other studies have shown similar cut off point of 4mm of tumour depth to be correlated with aggressive lymph node metastasis.
8. Tumour thickness and depth of invasion may turn out to be reliable criteria to predict lymph node metastasis in buccal mucosa cancer during surgery and as prognostic markers.
9. Based on this we conclude that it is preferable to do an elective neck dissection even for N_0 neck, if tumour depth is more than 4 mm

SUMMARY

This study was conducted at R.L.Jalappa Hospital, Kolar. A total number of 53 patients were included in our study. Increased incidence was seen in the 4^{th}-6^{th} decade of life. In our study, majority (76.92%) of the patients were females.

In our study 71% of the patients were chewing tobacco from 25 to 54 years. The mean duration of tobacco chewing is 28.154 years.

41.5 % patients in our study were of T2 status and 58.5% patients were of T3 status. 20.75 % of patients had clinically N0 status, 52.83% patients had N1 status and 26.41 %patients had N2 status on presentation.

In our study, there was an equal distribution of the patients having T2N1M0 (26%) and T3N1M0 (26%) staging.

After the excision of the tumour and neck dissection, histopathological examination was done to look for cervical lymph node metastasis of whom 26 (39.6%) patients had cervical lymph node metastasis.

The number of patients whose excised tumour specimen was measured for tumour thickness were divided into 3 groups of <=4 mm, 5-10 mm and > 10 mm. 9 (16.98 %) patients were included in <=4 mm tumour thickness group, 29 (54.71%) patients in 5-10 mm group and 15 (28.3%) patients in >10 mm group.

The metastasis in the lymph nodes in the tumour thickness group was not statistically significant

The number of patients whose excised tumour specimen was measured for tumour depth were divided into 3 groups of <=3 mm, >3mm, <=4mm and > 4mm.

Percentage of Metastasis present in the group tumour depth <=3mm is 21.43%.Percentage of metastasis present in the group tumour depth >3mm and <=4mm is 25.00%. Percentage of metastasis present in the group tumour depth >4mm is 55.56%.

Tumour depth > 4 mm showed statistically significant correlation with lymph node metastasis.

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ANNEXURES

PROFORMA

IMPACT OF PRIMARY TUMOUR THICKNESS AND DEPTH OF INVASION ON CERVICAL LYMPH NODE METASTASIS IN SQUAMOUS CELL CARCINOMA OF BUCCAL MUCOSA

Name of the patient: **Age:** **Sex:**

Occupation: **Hospital no:** **Phone:**

Address:

COMPLAINTS OF	YES/NO	SINCE
Ulcer/mass in oral cavity		
Mass/swelling in neck		
Restricted mouth opening		
Excessive salivation		
Difficulty in swallowing		
Voice change		
Loss of appetite		
Weight loss		
Generalized weakness		

COMORBIDITIES	YES/NO	SINCE
Hypertension		
Diabetes Mellitus		
Pulmonary Tuberculosis		
Acid Peptic Disease		

Family History:

CONTRIBUTORY :
NOT CONTRIBUTORY :

PERSONAL HISTORY	
Sleep, bowel, bladder habits	
Appetite	

HABITS	YES/NO	QUANTITY/DAY	SINCE
Tobacco chewing			
Bidi			
Cigarette			
Alcohol			

GENERAL PHYSICAL EXAMINATION

BUILT: NOURISHMENT:
PALLOR: ICTERUS:
PULSE: BLOOD PRESSURE:
WEIGHT:

Local examination:

Oral cavity:
Orodental hygiene:
Lips:
Mouth opening: Trismus : +/-

Lesion	Site	Greatest Antero Posterior diameter in cms	Greatest Transverse diameter in cms	Type of growth

NECK NODES:

NUMBER:
LEVEL OF NODE:
SIZE:
CONSISTENCY:
TENDERNESS:
SKIN OVER THE NODE:

CLINICAL DIAGNOSIS:

Investigations:

Hb: **TC:** **DC:** **Plt Count:**
BT: **CT:** **HIV:** **HbsAg:**
RBS :

Biopsy:

Treatment:

OPERATION DONE:

WIDE EXCISION
SOND MRND
HEMIMANIBULECTOMY : +/-
MARGINAL MANDIBULECTOMY : +/-

DATE OF SURGERY:

EXCISED SPECIMEN: SITE:
RIGHT LEFT MIDLINE
TUMOUR SIZE:

cms AWAY FROM SUPERIOR MARGIN
cms AWAY FROM INFRIOR MARGIN
cms AWAY FROM ANTERIOR MARGIN
cms AWAY FROM POSTERIOR MARGIN

HISTOPATHOLOGICAL REPORT:
Of the primary tumour:

DIFFERENTIATION: WELL
MODERATELY
POOR

Tumour thickness
Tumour depth

RESECTED MARGIN OF TUMOUR:

	ANTERIOR	POSTERIOR	SUPERIOR	INFERIOR
FREE FROM TUMOUR				
INVOLVED BY THE TUMOUR				

VASCULAR INVASION: +/ -
NERVE INVASION: +/-
BONE / CARTILAGE INVASION: +/-
SALIVARY GLAND INVASION: +/-

LYMPH NODE STATUS

TOTAL NUMBER OF LYMPH NODES:
NO OF POSITIVE NODES:
LEVEL OF POSITIVE NODE:
MICROMETASTASIS (<2mm in diameter): PRESENT NOT IDENTIFIED
EXTRA CAPSULAR SPREAD: PRESENT NOT IDENTIFIED

SUMMARY
TUMOUR SITE:
TUMOUR TYPE:
pTNM stage p T p N p M

FOLLOW UP

	3 MONTHS	6 MONTHS	9 MONTHS
DISEASE FREE			
LOCAL RECURRENCE			
REGIONAL RECURRENCE			
DISTANT METASTASIS			
LOST TO FOLLOW UP			
DIED OF DISEASE			
DIED DUE TO OTHER CAUSE			

KEY TO MASTERCHART

F	⇨	Female
M	⇨	Male
BM	⇨	Buccal Mucosa
WE	⇨	Wide excision
T	⇨	Tumour size and extent
N	⇨	Regional nodal metastasis – clinically
M	⇨	Distant metastasis
SCC	⇨	Squamous Cell Carcinoma
SOND	⇨	Supra omohyoid neck dissection
MRND	⇨	Modified radical neck dissection
N_0	⇨	Number