Identification of socio-demographic and behavioral risk factors of oral cancer in rural and urban areas of Bangladesh

This Thesis Paper Submitted in Partial Fulfillment of the Requirement for the Degree of Master of Pharmacy, East West University

Submitted by

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EAST WEST UNIVERSITY

Dedicated

To

My Loving Parents

DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation, entitled "**Identification of socio-demographic and behavioral risk factors for oral cancer in rural and urban areas of Bangladesh**" is an authentic and genuine research work carried out by me under the guidance of Dr. Shamsun Nahar Khan, Associate Professor, Department of Pharmacy, East West University, Dhaka.

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ENDORSEMENT BY HEAD OF THE DEPARTMENT

This is to certify that the dissertation entitled "**Identification of socio-demographic and behavioral risk factors for oral cancer in rural and urban areas of Bangladesh**" is a genuine research work carried out by Tanjina Hossain, under the supervision of Shamsun Nahar Khan (Ph. D, Postdoc, Harvard University, Associate Professor, Department of Pharmacy, East West University, Dhaka). I further certify that no part of the thesis has been submitted for any other degree and all the resources of the information in thus connection are duly acknowledged.

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Prof. Dr. Chowdhury Faiz Hossain

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CERTIFICATE

This is to certify that, the thesis on "**Identification of socio-demographic and behavioral risk factors for oral cancer in rural and urban areas of Bangladesh**" submitted to Department of Pharmacy, East West University, Aftabnagar, Dhaka, in partial fulfillment of the requirements for the degree of Masters of Pharmacy (M. Pharm), was carried out by Tanjina Hossain (ID # 2014-1-79-026) under our guidance and supervision and that no part of the thesis has been submitted for any other degree. We further certify that all the sources of information of in this connection are duly acknowledged.

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Abstract

Abstract: This study was conducted as a cross sectional survey in the National Institute of Cancer Research and Hospital, Dhaka Bangladesh. A questionnaire was designed and comprised of relevant questions to determine socio-demographic information, awareness and knowledge of oral cancer and risk factors and questions on participant's exposure to risk factors were also included.

Method: Subjects above the age of 30 years (n=114) were randomly selected during the period from 1 June 2016 to October 2017. The questionnaire was distributed to complete while they were waiting for their treatment at the National Institute of Cancer Research and Hospital (NICRH). Data was analyzed using Microsoft Excel 2010 and statistical package

Result: The study revealed that, female adult was more susceptible to oral cancer than male. The mean age of the participants was 48.7 ± 10.8 years ranging from 30 to 85. Among the 114 patients, 85% came from rural areas and 69% of those population found illiterate. From the study we found that, tobacco smoking, smokeless tobacco (betel leaf, betel nut, quid chewing, jorda, gull) and alcohol was the major risk factors of oral cancer. Also, sun or radiation exposure and fungal infection was identified as a risk factors of oral cancer. In this study, we also found that local factor such as faulty teeth, sharp teeth, loose teethe and denture are important factor for oral cancer. As a sign and symptom, non-healing mouth ulcer and Lump in neck could be major signs of oral cancer. Among these all cancer patients, 38.6% were affected in buccal mucosa, 25.44% were affected in alveolar region and few of them are in lip (14.04%). The study shows that TNM stage of most patients were $T_2N_1M_x$, $T_2N_3M_x$ that means tumor size 2 to 6 cm and cancer cell present in lymph node and metastasis information could not be assessed. Our study about chemotherapeutic treatment indicate that 5-flurouracil, Paclitaxel, Cisplatin and Carboplatin are most commonly use in Oral Cancer.

Conclusion: At current circumstance, all through the world and our nation, number of oral cancer patient increased day by day. Respondents were found having a low level of knowledge scores on the risk factor, sign and symptoms, diagnosis and treatment of oral cancer. The present investigation primarily gives a thought that there might be some connection between oral cancer and different risk factors.

Key Words: Oral Cancer, tobacco, risk factor, teeth, tumor, treatment, knowledge etc.

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Introduction

Chapter One: Introduction

Oral cancer affects around 14.1 million people, making it a well-known of the most common cancers in the world. Developing countries, specifically those from the South Asian region relish Bangladesh, have a higher function of oral cancer compared to extended countries. (Khan, Muller, Ahmed et all, 2015)

Head and neck cancer (HNC) is one of the most common type of cancer worldwide, and has a poor survival rate and been found not changed for years. A high prevalence of Head and neck cancer has been reported in the southwestern region of Saudi Arabia, as compared to other areas of the country (Alhazzari and Alghamdi et all, 2016). In recent review in İstanbul, Turkey on Among 170 participant dentists, largest number of oral cancer patients identified tobacco (98.8%) and alcohol usage (91.2%), prior oral cancer lesions (95.3%), viral infections (90.0%), UV exposure (86.5%), and betel quid chewing (80.6%), and lower numbers reported older age (56.5%) and low consumption of fruit and vegetables (52.4%). (Kebabcıoğlu & Pekiner et all, 2017)

In Sudan, clinic based cross-sectional study, expressed females and those living in urban locale scores higher than their partner in information of risk factor of oral cancer. (Babiker, Osman, Mohamed, and Almahdi et all, 2017)

A similar observation was made by Amel S Eltayeb, Asim Satti, Ahmed M Sulieman geographic in areas of the Sudan, there were 1,370 participants, 634(46.3%) were males and 736(53.7%) were females. (Eltayeb and Satti et all, 2017)

Comparative overview on Australian populace, the most well-known risk factors thought to be related with oral cancer were smoking (87.5%), poor oral hygiene (67.9%) and family history (61.1%). Just 50.2% of respondents knew about alcohol drinking as a risk factor. (Dost and Farah et all, 2016)

A survey was conducted on oral most cancers inserted dental patients in Saudi. This research discovered that only 62.4 % were conscious of oral cancer. Some 68.2 and 56.5 %, respectively. More than two thirds of patients had low level of knowledge about any signs of oral cancer.

Respondent with lower than university education was expressively less attentive, and had much less knowledge of the signs and risk factors of oral cancer. (Al-Mawer & Al-Soneidar et all, 2017)

In Similar survey it was found that Only 45.6% of the subjects had heard about oral cancer. Some 66.9% and 33.8% respectively, were able to appropriately identify tobacco and alcohol as risk factors. Some 24.1% had no knowledge about any signs of oral cancer. Male subjects, smokers, alcohol drinkers, older participants (>40 years), and participants with less than a university education were significantly less aware, and had much less knowledge, of the signs and risk factors of oral cancer. (Hassona, Abu Ghosh and Sawair et all, 2015)

It was also found in North Queensland, Australia52.3% of the respondents were aware of the existence of OPC but only 19.0% were aware of PMODs. Of those who were aware of oral cancer, 92% agreed or strongly agreed that smoking is a strong risk factor for OPC. Similarly, a relatively high proportion of the respondents agreed or strongly agreed that tobacco chewing (84%), tobacco chewing with areca nut (68%), chewing areca nut alone (51%) and exposure to actinic radiation (71%) as risk factors. However, the results for alcohol intake, age, and HPV infection were found to be relatively poor with proportions 33%, 34%, and 23% respectively. (Formosa and Ariyawardana et all, 2015)

Tobacco was identified as a risk factor by 54.8% of individuals and this knowledge was associated with their education level, dentist visits, and tobacco consumption. Fewer subjects (24.6%) referred to alcohol as a risk factor, and this knowledge was associated with their education level and dentist visits. [10] (Silva Monteiro and Warnakulasuriya et all, 2015)

The goal of this paper is to provide an impression, including a quantitative analysis Socio-Demographic and Behavioral risk factors in rural and urban areas in field of oral cancer. The specific objectives are: *i*) to analyze the growth pattern of oral cancer in Bangladesh, *ii*) to analyzed risk factor of oral cancer *iii*) understanding the treatment pattern of oral cancer in Bangladesh

Description of the Oral cancer

Chapter Two: Description of the Oral cancer

2.1 Cell

Our body is made up of millions of tiny cells and different parts of the body such as organs, bones, muscles, skin and blood are made up of from different specialized cells. Nucleus is the Centre of most of cells which contains thousands of genes made up from a chemical called DNA. These genes control the functions of the cell. From time to time most types of cell divide and multiply in the body. Old cells are replaced by new cells as old cells become damaged. A normal cell may become abnormal when one or more gene in the cell becomes damaged or altered. Then from the original cells lots of abnormal cells develop to form a group of abnormal cells leading to the formation of tumor. Sometimes tumor may lead to the formation of cancer.

2.2 Cancer

The word cancer is derived from the Latin word for crab because cancers are often very irregularly shaped, and because, like a crab, they ‘’grab on and don’t let go’’. Cancer is a term used for diseases in which abnormal cells divide without control and are able to invade other tissues. Cancer cells can spread to other parts of the body through the blood and lymph systems. The process of cancer spreading is called ‘metastasis’. Growth of cancer cell is different from normal cells. Cancer cells continue to grow and from new abnormal cells instead of dying. Due to the damage of DNA normal cells become cancer cells. DNA is present in every cell and conducts their functions. Normally when DNA is damaged in normal cells they rapidly repair the damage or die but in cancer cells the damage DNA is not repaired or dies. It produces new cells containing the damage which is not necessary for the body. The cancer develops inside the body.

2.3 Definition of Oral/Pharyngeal Cancer

Oral cancer, also known as mouth cancer, is a type of head and neck cancer and is any cancerous tissue growth located in the oral cavity. It may arise as a primary lesion originating in any of the tissues in the mouth, by metastasis from a distant site of origin, or by extension from a neighboring anatomic structure, such as the nasal cavity. Alternatively, the oral cancers may originate in any of the tissues of the mouth.

2.4 Types of oral cancer

2.4.1 Squamous cell carcinoma: More than 90% of cancers that occur in the oral cavity and oropharynx are squamous cell carcinoma. Normally, the throat and mouth are lined with so-called squamous cells, which are flat and arranged in a scale-like way. Squamous cell carcinoma means that some squamous cells are abnormal.

2.4.2 Verrucous carcinoma: About 5% of all oral cavity tumors are verrucous carcinoma, which is a type of very slow-growing cancer made up of squamous cells. This type of oral cancer rarely spreads to other parts of the body but can invade the tissue surrounding the site of origin.

2.4.3 Minor salivary gland carcinomas: This category includes several kinds of oral cancer that can develop on the minor salivary glands, which are found throughout the lining of the mouth and throat. These types include adenoid cystic carcinoma, mucoepidermoid carcinoma, and polymorphous low-grade adenocarcinoma.

2.4.4 Lymphomas: Oral cancers that develop in lymph tissue, which is part of the immune system, are known as lymphomas. The tonsils and base of the tongue both contain lymphoid tissue. See our pages on Hodgkin lymphoma and non-Hodgkin lymphoma for cancer information related to lymphomas in the oral cavity.

2.4.5 Benign oral cavity and oropharyngeal tumors: Several types of non-cancerous tumors and tumor-like conditions can arise in the oral cavity and oropharynx. Sometimes, these conditions may develop into cancer. For this reason, benign tumors, which usually don't recur, are often surgically removed. The types of benign lesions include:

- Eosinophilic granuloma
- Fibroma
- Granular cell tumor
- Karatoacanthoma
- Leiomyoma
- Osteochondroma
- Lipoma
- Schwannoma
- Neurofibroma

- Papilloma
- Condyloma acuminatum
- Verruciform xanthoma
- Pyogenic granuloma
- Rhabdomyoma
- Odontogenic tumors (lesions that begin in tooth-forming tissues)

2.4.6 Leukoplakia and erythroplakia:

These non-cancerous conditions mean that there are certain types of abnormal cells in the mouth or throat. With leukoplakia, a white area can be seen, and with erythroplakia, there is a red area, flat or slightly raised, that often bleeds when scraped. Both conditions may be precancerous; that is, they can develop into different types of cancer. When these conditions occur, a biopsy or other test is done to determine whether the cells are cancerous.

2.5 Pathophysiology

Carcinogenesis and the Hallmarks of Cancer

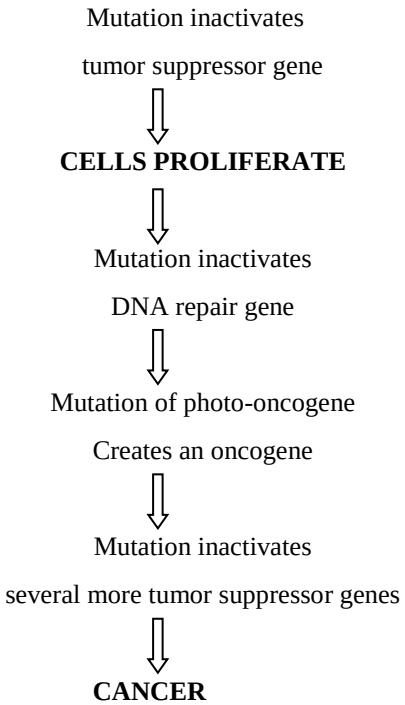


Figure: 1: -Carcinogenesis and the Hallmarks of Cancer

Oral carcinogenesis like any other cancer is a progressive disease and normal epithelium passes through stages starting from dysplasia to finally transforming into invasive phenotypes. Although all types of carcinomas are seen in oral cavity, the most common form of is squamous cell carcinoma. Use of genetic and proteomic approach in recent years have revealed the molecular pathological picture of. There is active search to identify genetic alterations in oncogenes or tumour suppressor genes, role of genomic instability and epigenetic modifications and to generate a gene expression profile in oral oncogenesis (Khandekar, Bagdey and Tiwari et all, 2006). Understanding these genetic changes and gene expression patterns are keys to the understanding of molecular pathogenesis of. Though, there are some significant leads achieved, the complete understanding of molecular pathology of and its association with causative agent will require another decade of intensive research. We have discussed some of the important updates in this area of active research.

2.5.1 Genetic Susceptibility

It is now established that up to 10% of all cancers have a strong hereditary component. Role of genetic component in the development of is being suggested by several studies showing familial clustering (Boring and Clin et all, 1992). A clustering of has been seen in certain ethnic groups, like Askenazi group in Israel; with incidence being double as compared to other Jewish population in that country. However, the basis of this genetic susceptibility is not well understood, as yet.

Evaluation of specific genetic polymorphism in key genes involved in oral carcinogenesis has been the major area of study. Glutathione S-transferase M1 (GSTM1) null genotype appears to be the most consistent polymorphic susceptibility marker for head and neck cancer including. Meta-analyses by Tripathy and Roy showed that the GSTM1 null genotype conferred a 20–50% significantly increased HNSCC risk. (Boring and Clin et all, 1992)

The variant val allele of the CYP1A1 (Cytochrome P450, family 1, member A1) polymorphism is another fairly consistent susceptibility marker with a 35% increased risk in a meta- analysis of 12 studies (Rockville et all, 1982). The studies on many other gene polymorphisms have been inconclusive. (Wynder and Bross et all, 1957) found that ALDH1B and ALDH2 (Aldehyde dehydrogenase 2) genes were associated with HNSCC and showed significant correlation with alcohol consumption.

2.5.2 Proto-oncogenes, Oncogenes and Genetic Alterations:

Genetic alterations define molecular basis of carcinogenesis which includes point mutations, amplifications, rearrangements, and deletions. Several oncogenes have also been implicated in oral carcinogenesis (McCoy et all, 1978). Aberrant expression of epidermal growth factor receptor (EGFR), K-ras, c-myc, int-2, Parathyroid adenomatosis 1 (PRAD-1) and B-cell lymphoma (bcl) like oncogenes have been reported in development (US Department of Health and Human Services). Over expression and amplification of cellular oncogene EGFR have been reported in a 7,12-Dimethylbenz(a)anthracene (DMBA) induced hamster cheek pouch malignant model (Wynder and Bross et all, 1957). Transforming growth factor-alpha (TGF-α) is known to promote neovascularization and mitogenesis. It has been shown to be aberrantly expressed in human and in hamster oral tumor (PK and Califano et all, 2004).

2.5.3 Tumor Suppressor Genes

More than 50% of all primary HNSCC harbour p53 mutation (Kreimer and Clifford et all, 2005). Inactivation of p53 represents the most common genetic change in all human cancers (Schildt and Eriksson et all, 1998). The most commonly deleted region in HNC is located at chromosome 9p21–22 (Shillitoe and Greenspan et all, 1982D). Loss of chromosome 9p21 occurs in the majority of invasive tumors in head and neck cancer (Boring and Clin et all, 1992). Homozygous deletions in this region are frequent and represent one of the most common genetic changes identified. p16 (CDKN2) present in this deleted region, is a potent inhibitor of cyclin D1 (Kassim and Daley et all, 1988). Loss of p16 protein has been observed in most advanced pre-malignant lesions also (US Department of Health and Human Services, 1986) have identified an alternative RNA transcript for p16 termed as Alternative Rating Frame (ARF; or p16β). Introduction of p16 or p16ARF into HNC cell lines result in potent growth suppression (Starr and Daling et all, 2001).

Loss of chromosome 17p is also frequent in most human cancer including. It is seen in approximately 60% of invasive lesions. Although p53 inactivation correlates closely with loss of 17p in invasive lesions, p53 mutations are quite rare in early lesions that contain 17p loss. Loss of chromosome arm 10 and 13q are also noted in primary tumors (*GBD 2013 Mortality Causes of Death Collaborators 2015).*

Many other regions of chromosomal loss have been seen in Oral Cancer. Further, fine mapping of these critical genes within these areas may provide important information in the understanding of genomic instability leading to the development of this neoplasm.

2.5.4 Genomic Instability

Genomic instability such as loss of hetrozygosity (LOH) and microsatellite instability (MSI) are frequently observed in cancer and such instability has been investigated and several reports are available in OC. Chromosome 9p21 containing p16 tumor suppressor gene is frequently lost in HNSCC and oral preneoplastic lesions (Wynder and Bross et all, 1957) (PK and Califano et all, 2004).Chromosome 3p14 contains the tumor suppressor gene fragile histidine triad (FHIT) as well as a common fragile site, FRA3B which is also found to be frequently deleted in early tumorigenesis (PK and Califano et all, 2004) and its deletion is assiated with exposure to cigarette smoke (US Department of Health, Education, and Welfare, 1979). Loss of chromosome 17p13 harboring p53 tumour suppressor gene is also common in multistep head and neck tumorigenesis (Schildt and Eriksson et all, 1998). Loss of function of the tumour suppressor p53 can result in uncontrolled cell division and progressive genomic instability (Boring and Clin et all, 1992). The increased frequency of LOH in invasive tumours at the 9p21 locus is also reported and may suggest that the region, probably the p16 gene is important in early malignant progression. Several studies have demonstrated these by using microsatellite markers. Alterations in certain regions of chromosomes 3p, 9p, 17p and 18q are associated with the development of HNSCC (Squier, Cox and Hall et all, 1986). (Kremer and Lesch et all, 1991) performed a microsatellite analysis of cells sampled from the oral cavity of oral and oro-pharyngeal cancer patients and observed LOH in 84% of samples. In another study, (Spafford ,Social inequalities in oral health et al, 2015) identified genomic alterations in all of the malignant lesions of the oral cavity included in their sample.

2.5.5 Epigenetic Alterations

The major epigenetic modification in tumours is methylation. Changes in the methylation patterns can play an important role in tumorigenesis. Epigenetic modifications are frequently connected with the loss of genetic expression and important for the multiple indispensable genetic events

during carcinogenesis. Malignant progression takes place because these alterations can inactivate DNA repairing genes.

Methylation patterns of p16, methylguanine-DNA methyltransferase (MGMT) and Death-associated protein kinase (DAP-K) genes in smears of patients suffering from head and neck cancer showed abnormal hypermethylation patterns by a methylation specific polymerase chain reaction (PCR). (Social inequalities in oral health et al, 2015)

2.5.6 Molecular Progression Model

(Califano *GBD 2013 Mortality Causes of Death Collaborators* et al, *(2015)* tested ten most common allelic events in a large number of primary pre-invasive lesions and invasive HNSCC to develop a molecular progression model. It involves inactivation of many putative suppressor gene loci. Chromosomes 9p and 3p appear to be lost early, closely followed by loss of 17p. Mutations in p53 gene are seen in the progression of pre-invasive to invasive lesions. Many other genetic events occur later during progression. Other genetic events, such as amplification of cyclin D1 and inactivation of p16 have been tested predominantly in invasive lesions, but their precise order in the model was not determined (McCoy et all, 1978).

2.5.7 Molecular Epidemiology

The pattern of specific gene mutation in patient may give a clue to the aetiology of that particular tumor (Schildt and Eriksson et all, 1998) analyzed the pattern of p53 mutation in HNSCC. They found that the incidence of p53 mutation was much higher in patients who were exposed to both tobacco and alcohol versus non-users.

It has been suggested that alcohol appears to augment the effect of smoking due to an increase in the absorbance of carcinogens contained within the cigarette smoke. Several epidemiologic evidences suggest that abstinence from cigarette smoking may decrease the overall incidence of HNSCC (Kassim and Daley et all, 1988).

HPV positive oral and oro-pharyngeal cancer comprise a distinct clinico-pathological entity. They are less likely to occur among heavy smokers and drinkers, have lesser likelihood of p53 mutation and have better cancer-specific survival. It has been suggested that HPV positive tumours may have better prognosis by inactivating retinoblastoma (Rb) (Starr and Daling et all, 2001).

2.6 Epidemiology

In 2013 oral cancer resulted in 135,000 deaths up from 84,000 deaths in 1990. Oral cancer occurs more often in people from the lower end of the socioeconomic scale (*Cancer Research UK. Retrieved 28 October 2014).*

> In 2011, close to 37,000 Americans are projected to be diagnosed with oral or pharyngeal cancer. 66% of the time these will be found as late stage three and four diseases. It will cause over 8,000 deaths. Of those 37,000 newly diagnosed individuals, only slightly more than half will be alive in 5 years. Similar survival estimates are reported from other countries. For example, five-year relative survival for oral cavity cancer patients in Germany is about 55% (The Oral Cancer Foundation). Survival rates of patients diagnosed with oral cancer have not significantly improved in decades. The death rate for oral cancer is higher than cervical cancer, Hodgkin's lymphoma, laryngeal cancer, cancer of the testes, and endocrine system cancers such as thyroid, or skin cancer (malignant melanoma). If the definition of oral cancer is expanded to include cancer of the larynx, for which the risk factors are the same, the numbers of diagnosed cases grow to approximately 50,000 individuals, and 13,500 deaths per year in the U.S. Worldwide, the problem is much greater, with over 640,000 new cases being found each year (Werning, John W et al, 2007).Low public awareness of the disease is a significant factor, but these cancers could be found at early highly survivable stages through a simple, painless, five-minute examination by a trained medical or dental professional.

Oral cancer is the sixteenth most common cancer in the UK (around 6,800 people were diagnosed with oral cancer in the UK in 2011), and it is the nineteenth most common cause of cancer death (31 around 2,100 people died from the disease in 2012).

Oral cancer is the most common form of cancer in India. 130,000 people succumb to oral cancer in India annually. The reason for this high prevalence of oral cancer in India is primarily tobacco consumed in the form of gutka, quid, snuff or misri. In the North-East India, the use of areca nut is also a risk factor for oral cancer.

2.7 Oral cancer symptoms

The earliest signs of oral cavity and oropharyngeal cancer may be mistaken for other problems, such as a toothache or cold. If symptoms persist for several days or weeks, it is important to see your doctor so that, if oral cancer is present, it can be diagnosed as soon as possible. Many of these symptoms can be due to other, less serious problems or other cancers.

2.7.1 Oral cancer symptoms

Some of the most common oral cancer symptoms and signs include:

- **Persistent mouth sore:** A sore in the mouth that does not heal is the most common symptom of oral cancer
- **Pain:** Persistent mouth pain is another common oral cancer sign
- A lump or thickening in the cheek
- A white or red patch on the gums, tongue, tonsil, or lining of the mouth
- A sore throat or feeling that something is caught in the throat that does not go away
- Difficulty swallowing or chewing
- Difficulty moving the jaw or tongue
- Numbness of the tongue or elsewhere in the mouth
- Jaw swelling that makes dentures hurt or fit poorly
- Loosening of the teeth
- Pain in the teeth or jaw
- Voice changes
- A lump in the neck
- Weight loss
- Persistent bad breath

If any of these oral cancer symptoms or signs are present for days or weeks, your doctor may recommend tests to check for oral cancer. As with any cancer, having your cancer diagnosed as soon as possible will help ensure that any treatment is as effective as possible.

Table 1: Frequent Signs and Symptoms of Oral Cancer

Early	Late
Persistent red and/or white patch	Indurated area
Progressive swelling or enlargement	Paresthesia, dysesthesia of the tongue or lips
Sudden tooth mobility without apparent cause	Airway obstruction
Unusual oral bleeding or epistaxis Prolonged hoarseness	Chronic earache (chronic serous otitis media)/otalgia
Nonhealing ulcer	Trismus Dysphagia
Unusual surface changes	Cervical lymphadenopathy Persistent pain or referred pain Altered vision

2.8 Oral cancer stages

Making an educated treatment decision begins with the stage, or progression, of the disease. The stage of oral cancer is one of the most important factors in evaluating treatment options. Our cancer doctors use a variety of diagnostic tests to evaluate oral cancer and develop an individualized treatment plan. If you have been recently diagnosed, we will review your pathology to confirm you have received the correct diagnosis and staging information, and develop a personalized treatment plan. If you have a recurrence, we will perform comprehensive testing and identify a treatment approach that is suited to your needs.

2.8.1 TNM system for oral cancer (Rockville et al, 1982)

We stage oral cancer using The American Joint Committee on Cancer's (AJCC) TNM system, a commonly accepted method based on three key components:

Tumor (T) describes the size of the original tumor.

Node (N) indicates whether the cancer is present in the lymph nodes.

Metastasis (M) refers to whether cancer has spread to other parts of the body.

A number (0-4) or the letter X is assigned to each factor. A higher number indicates increasing severity. For instance, a T1 score indicates a smaller tumor than a T2 score. The letter X means the information could not be assessed.

Once the T, N, and M scores have been assigned, an overall stage is assigned.

T Categories for Oral Cavity and Oropharyngeal Cancers. These measurements refer to the primary oral cancer tumor.

- TX: primary tumor cannot be assessed; information not known.
- TO: no evidence of primary tumor Tis: carcinoma in situ. This means that the disease is still localized, or contained within the top layers of cells lining the oral cavity and oropharynx. Cancer cells have not invaded the deeper layers of oral or oropharyngeal tissue.
- T1: tumor is 2 cm across or smaller.

- T2: tumor is larger than 2 cm across, but smaller than 4 cm.
- T3: tumor is larger than 4 cm across.
- T4 is divided into two subgroups:
- T4a: the tumor is growing into nearby structures. At this stage, the oral cancer is called a moderately advanced local disease. The areas to which cells have spread vary according to the type of oral cancer:
  - For oral cavity cancers: the tumor is growing into nearby structures such as the bones of the jaw or face, deep muscle of the tongue, skin of the face, or maxillary sinus.
  - For lip cancers: the tumor is growing into nearby bone, the inferior alveolar nerve (the nerve to the jawbone), the floor of the mouth, or the skin of the chin or nose.
  - For oropharyngeal cancers: the tumor is growing into the larynx (voice box), the tongue muscle, or bones such as the hard palate or jaw.
- T4b: the tumor has grown through nearby structures and into deeper areas or tissues. At this stage, the cancer is called very advanced local disease, and may include any of the following conditions:
  - The tumor is growing into other bones, such as the pterygoid plates (in the skull) and/or the skull base. This type of spreading can occur with any oropharyngeal or oral cancer.
  - The tumor surrounds the internal carotid artery. This type of spreading can occur with any oropharyngeal or oral cancer.
  - For lip and oral cavity cancers: the tumor is growing into an area called the masticator space
  - For oropharyngeal cancers: the tumor is growing into a muscle called the lateral pterygoid muscle, which is used for chewing.
  - For oropharyngeal cancers: the tumor is growing into the nasopharynx (the area of the throat that is behind the nose).

N Categories for Oral Cavity and Oropharyngeal Cancers

- NX: nearby lymph nodes cannot be assessed; information not known.
- N0: the oral cancer has not spread to any nearby lymph nodes.
- N1: the cancer has spread to one lymph node on the same side of the head or neck as the primary tumor. This lymph node is smaller than 3 cm across.

- N2 is divided into three subgroups:
- N2a: the oral cancer has spread to one lymph node on the same side as the primary tumor, and the lymph node measures 3–6 cm across.
- N2b: the cancer has spread to 2 or more lymph nodes on the same side as the primary tumor. No lymph nodes are larger than 6 cm across.
- N2c: the oral cancer has spread to one or more lymph nodes on both sides of the neck or on the side opposite the primary tumor. No lymph nodes are larger than 6 cm across.
- N3: the cancer has spread to a lymph node that measures more than 6 cm across.

M Categories for Oral Cavity and Oropharyngeal Cancers

- M0: no distant spread.
- M1: the oral cancer has spread to distant sites outside the head and neck region (for example, the lungs, liver or bones).

2.9 Etiology and Major risk Factors

Numerous risk factors or possible causative agents for OC have been described. Chemical factors like tobacco and alcohol, biological factors like human papillomavirus (HPV), syphilis, oro-dental factors, dietary deficiencies, chronic candidiasis and viruses have been shown to be significantly associated with Oral cancer.

2.9.1 Lifestyle

2.9.1.1 Cigarettes

Reports by the U.S. Public Health Service have clearly established a direct causal relationship between cigarette smoking and cancer of the oral cavity.A number of major prospective cohort (US Department of Health and Human Services) (PK and Califano et al, 2004) (US Department of Health and Human Services,Public Health Service, 1982) mortality studies have been critical in both elucidating the causal nature of the association and estimating the magnitude of the disease burden. Two such studies, Cancer Prevention Study (CPS) I and II, sponsored by the American Cancer Society (ACS), are the largest epidemiological studies ever undertaken, each following

more than 1 million men and women. Evidence from these and 5 other epidemiological studies has provided key documentation of the association between cigarette smoking and oral cancer.

The mortality risk for oral cancer in cigarette smokers is substantially greater than that observed among lifelong "never smokers." Although estimates vary, most studies have reported mortality 4, 5 ratios for smokers versus never smokers of about 5-6:1, with several reporting ratios in excess of 10:1. Furthermore, the risk for death from oral cancer is consumption related; the more cigarettes consumed daily and the more years one has smoked, the greater the risk (US Department of Health and Human Services, Public Health Service, 1986) (Squier and Cox et al, 1986). In CPS II, which followed over 1.2 million individuals for 6 years beginning in 1982, male cigarette smokers had a relative risk for oral cancer 27.7 times greater than that of a male never smoker; the rates among women who smoked were nearly 6 times greater. Estimates of the percentage of oral5 cancers attributable to cigarette smoking have been quite consistent, generally ranging from 75% to 90%(Shopland and Eyre et al, 1991) (Centers for Disease Control and Prevention, 1990) (Doll and Peto et al, 1994) than for those who continued to smoke. These studies have found that Cigars and Pipes Although cigarette smoking is the form of tobacco use most often linked with increased incidence of oral cancer, regular use of pipes or cigars also increases the risk of disease. Both prospective (US Department of Health, Education, and Welfare, Public Health Service, 1973) and retrospective studies have consistently documented that pipe and cigar smokers experience mort alit y rates for oral cancer either similar or higher than those risks observed among cigarette smokers.

2.9.1.2 Smokeless Tobacco (Snuff and Chewing Tobacco)

Only recently has the scientific and public health community turned its attention to the possible health implications of smokeless tobacco use. In 1981, Winn and colleagues published a seminal (US Department of Health and Human Services, Public Health Service, National Cancer Institute, 1992) (Winn and Blot et al, 1981) study involving 255 women living in rural North Carolina; they found a fourfold increased risk of oral cancer among nonsmokers who dipped snuff. This association could not be explained by smoking or alcohol consumption, dentures, poor dentition, diet, or use of mouthwash. For long- term users there was a 50-fold increased risk for cancer of the gum and buccal mucosa. Even women who had used smokeless tobacco less than 25 years had a 14-fold greater risk for these cancers.

2.9.1.3 Alcohol

Most patients with oropharyngeal cancer drink alcohol. One study found rates as high as 94% in men and 82% in women.1 However, one problem with identifying alcohol as an independent risk factor for oral cancer is that heavy drinkers are usually heavy users of tobacco products. Another problem is that consumption of alcohol and a poor diet might affect the risk for oral cancer. Furthermore, assessment of alcohol intake is inherently imprecise because of a bias toward underreporting and the often-episodic nature of usage. Thus, it is hard for a patient to estimate "average" use. All three forms of alcohol (beer, hard liquor, and wine) have been associated with oral cancer, although hard liquor and beer have a higher associated risk. Studies (Brunneman and Scott et al, 1982) (Mashberg and Garfinkel et al, 1981) (SKC, Kabat and Wynder) (Cristallini and

Padalino Et al, 1989) that have found alcohol use to be a factor for oral carcinogenesis have usually concluded that the level of consumption was important; one study found elevated risk only if 56 or more glasses of wine per week were consumed. 34 Another study showed a significant increase only if the average *daily* consumption of alcohol exceeded 120 grams. That evidence is contradictory about the role of alcohol in oral cancer may relate to the difficulty in measuring intake or to alcohol's effect on other variables (or both), but it is reasonable to assume that any form of alcohol taken in excess may promote oral cancer.

2.9.1.4 Cigarettes and Alcohol

A combination of "heavy" smoking and "heavy" drinking results in odds ratios (ORs) for oral cancer of up to 38 for men and 100 for women.1 (An *odds ratio* is a measure of association that quantifies the relationship between an exposure and health outcome.) An OR of 38 in men indicates a multiplicative effect because the OR for "heavy" smoking alone among men is 5.8; for "heavy" drinking alone it is 7.4. Another study of smoking and drinking showed these factors to have a greater than additive but less than multiplicative effect. In this study, the risk of oral cancer attributed to smoking (76%) was higher than the risk attributed to alcohol consumption (55%).35 Similarly, Brunneman et al. found the oral cancer risk attributable to tobacco to be higher (72%) than for alcohol (23%).29 It is apparent that, used in combination, alcohol and tobacco exert a synergistic effect that substantially increases the risk for oral cancer. Blot et al. estimated that tobacco smoking and alcohol drinking combine to account for approximately three-fourths of all oral and pharyngeal cancers in the United States.1 Research on pigs has shown that applying 5% or 15% ethanol enhances the permeability of tobacco carcinogens in porcine mucosa, especially in the floor of the mouth. (Squier, Cox and Hall et al, 1986) (Kremer and Lesch et al, 1991).

2.9.2 General

2.9.2.1 Diet

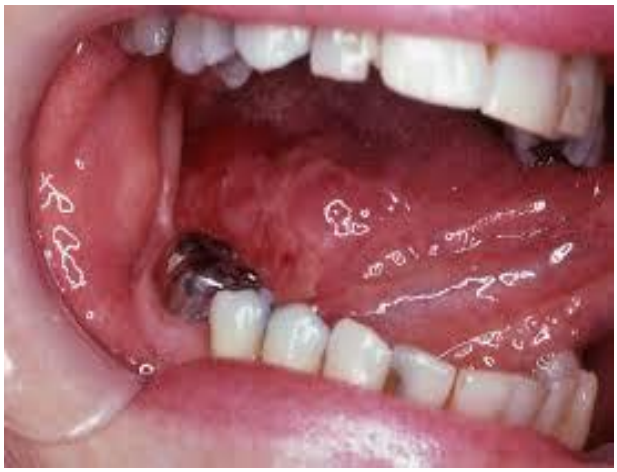
Although dietary factors have been identified as having a possible association with oral cancer, accumulated scientific evidence that use of tobacco and alcohol increases oral cancer risk far outweighs any evidence linking a deficient diet to increased risk.

2.9.2.2 Actinic Radiation

Sunlight, through actinic radiation, helps to produce cancer along the vermilion border of the lip.Because these “sunlight” induced cancers are much more common in fair-skinned individuals exposed to the outdoor life than in individuals with darker pigmentation, it appears that darker pigment protects against actinic radiation damage. The wavelengths of the light thought to be responsible for the actinic damage are in the 2900-3200 ' range.

2.9.2.3 Dental Factors

There is little evidence to suggest that poor oral hygiene, improperly fitting dental prostheses, defective dental restorations, or misaligned or sharp teeth promotes oral cancer. Gorsky and Silverman63 evaluated 400 patients with oral cancer to determine whether dentures were a risk factor and found no correlation between the wearing of dentures and the patient’s cancer.



2.9.2.4 Gender:

Oral cancer and orpharyngeal cancer are twice as common in men as in women. This difference may be related to the use of alcohol and tobacco, a major oral cancer risk factor that is seen more commonly in men than women. According to the American Cancer Society, the gender difference is decreasing among oral cancer patients as more women are using tobacco and drinking.

2.9.2. 5 Age: The average age at diagnosis for oral cancer is 62, and two-thirds of individuals with this disease are over age 55.

2.9.2.6 Genetics:

- Genetic syndromes: Some inherited genetic mutations, which cause different syndromes in the body, carry a high risk of oral and oropharyngeal cancer. These include:
- Fanconi anemia: This blood condition is caused by inherited abnormalities in several genes. Problems can begin at an early age and often lead to leukemia or aplastic anemia. The risk of oral cancer among people with Fanconi anemia is up to 500 times higher than among the general population.
- Dyskeratosis congenita: This genetically linked syndrome can also cause aplastic anemia, and carries a very high risk of mouth and throat cancer occurring at an early age.

2.9.2.7 OTHER

- **Immune system suppression**: Taking drugs that suppress the immune system, such as those used to prevent rejection of a transplant organ or to treat certain immune diseases, may increase the risk of oral cancer.

- **Lichen planus:**

People with a severe case of this illness, which usually causes an itchy rash but sometimes appears as white lines or spots in the mouth and throat, may have a higher risk of oral cancer. Lichen planus usually affects middle-aged people.

- **Graft-versus-host disease (GVHD):**

This condition can occur after a stem-cell transplant, in which bone marrow is replaced following cancer occurrence or treatment. The new stem cells may have an immune response against the patient's own cells, and tissues in the body may be destroyed as a result. GVHD increases the likelihood of oral cancer, which can develop as soon as 2 years later.

- **Viruses and Their Interactions with Oncogenes:**

Alterations of cellular oncogenes, which lead to altered expression of their products, have been implicated in human cancers. 64 Cellular oncogenes, also known as proto-oncogenes, acquire their

transforming properties or become activated by gene amplification, point mutations, and gene rearrangements. Oncogenes can encode growth factors and growth factor receptors, act on internal signaling molecules, and regulate DNA transcription factors. (Somers and Glickman et al, 1992) (Scully et al, 1993) (Greer and Douglas et al, 1990). Other genes encode proteins that inhibit the cell cycle or promote programmed cell death (apoptosis). Tumor suppressor genes may become inactivated or mutated with consequential loss of control over cell division (SKC, Kabat and Wynder). Theretinoblast and p53 gene products are examples.Chemical Factors Consideration of risk factors should recognize that many molecular events governing control of cell cycles are influenced by viruses. Those most commonly implicated in oral cancer transformation have been the human papillomavirus (HPV), herpes group viruses, and the adenoviruses. (Greer and Shroyer et al, 1992) (Kabat and Wynder et al, 1989) (Park and Byung et al, 1992) (Johnson Et al, 1991). Of these, HPV and herpes have been the most thoroughly studied and are now considered to be the most likely "synergistic viruses" involved in human oral cancer. The herpes viruses most often linked to oral cancer are the Epstein-Barr virus (EBV) and cytomegalovirus (CMV); both EBV DNA and CMV DNA have been demonstrated in oral carcinomas (Park and Byung et al,1992). The hamster cheek pouch model has been used to evaluate the role of herpes simplex virus (HSV) (Johnson Et al, 1991) and reports indicate that HSV can act synergistically with chemical carcinogens to initiate oncogenic transformation in this animal model (Johnson Et al, 1991) (Odukoya and Shklar et al, 1984). However, there is still debate as to whether the presence of HSV in such tissues shows a cause-and effect association between virus and cancer. More than 100 different HPV types have been isolated from benign and malignant neoplasms. HPV antigens and gene products have been detected in biopsies of oral cancer and precancer; HPV has also been identified in nodal metastases from oral, head, and neck cancers. The genotypes most often found in oral carcinoma are HPV 16 and 18, but HPV can also be found in normal oral mucosa. Whether or not HPV plays an active role in the initiation of oral malignancy, whether it is simply a passenger virus, and whether the virus acts in synergy with exogenous agents such as tobacco or alcohol to promote neoplasia are all questions that still await answers. Some viruses, particularly HPV and herpes, interact with oncogenes and tumor suppressors. Recent evidence suggests that the HPV 16/E5 gene can induce malignant transformation in epithelial cells, possibly acting by enhancing growth-factor-mediated intercellular signal transduction (Vambutas and Lorenzo et al, 1993). The E6 and E7 HPV 16 and 18 gene products act as oncoproteins by interacting with host cell p53

poptotic protein, promoting its elimination (Woods and Shillitoe et al, 1994) (Gimenez and Slaga et al, 1993). Loss of p53, in turn, removes inhibition of cell-cycling influences. Still, there are substantial gaps in our knowledge about how oncogenes, tumor suppressorgenes, and viruses promote oral cancer.

2.9.3 Unproven risk factor:

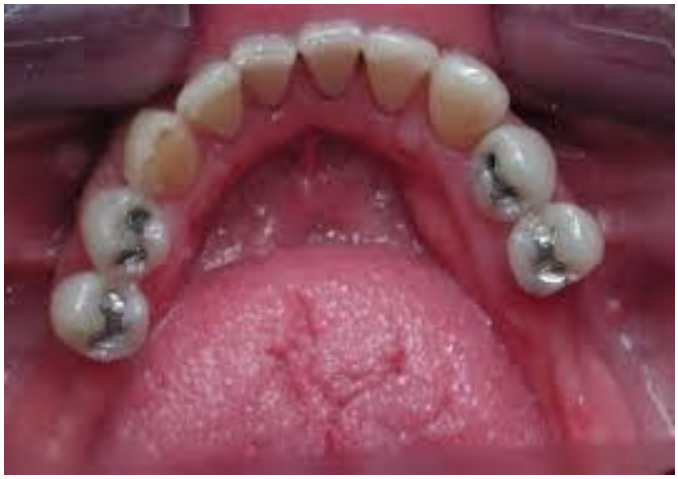
Recent years, concern has been raised about some products heightening the risk of oral cancer. These concerns are controversial and have not yet been proven in scientific studies. The products some believe to increase cancer risk factors include:

2.9.3.1 Mouthwash:

Some studies have shown a link between mouthwash that is high in alcohol content and the risk of oral and oropharyngeal cancer. However, other research has raised doubts about this concern. The frequent use of mouthwash by people who smoke and drink—two confirmed risk factors for oral cancer—makes it difficult to establish a clear link between mouthwash and oral cancer.

2.9.3.2 Irritation from dentures:

Poorly fitting dentures that cause long-term irritation of the mouth lining have also been a point of concern regarding oral cancer risk. This link has not been confirmed in several studies. However, loose dentures may trap substances that are known to cause oral cancer, such as alcohol and tobacco. Individuals who wear dentures should be sure to have their fit checked by a dentist regularly, remove them at night, and clean and rinse them thoroughly each day.



2.10 Diagnostic

2.10.1 Medical history and physical exam:

As a first step, doctor will probably ask you questions about symptoms, possible risk factors, and any other medical conditions may have. doctor will examine to look for possible signs of an oral or oropharyngeal cancer (or pre-cancer). These could be bumps or other abnormal areas on your head, face or neck, or problems with the nerves of the face and mouth. The doctor will look at the entire inside of your mouth,and might feel around in it with a gloved finger. He or she may also use other tests to look for abnormal areas in the mouth or throat, or to get a better sense of what an abnormal area might be. If there is a reason to think might have cancer, your doctor will refer you to a doctor who specializes in these cancers, such as an oral and maxillofacial surgeon or a head and neck surgeon (also known as an ear, nose, and throat [ENT] doctor or an otolaryngologist). This specialist will probably do other exams and tests.

2.10.2 Complete head and neck exam:

The specialist will pay special attention to the head and neck area, being sure to look and feel for any abnormal areas. This exam will include the lymph nodes of the neck, which will be felt carefully for any signs of cancer. Because the oropharynx is deep inside the neck and some parts are not easily seen, the doctor may use mirrors or special fiber-optic scopes to examine these areas while you are in the doctor's office. Indirect pharyngoscopy and laryngoscopy: For this exam, the doctor uses small mirrors placed at the back of your mouth to look at the throat, base of the tongue, and part of the larynx (voice box).

2.10.3 Direct (flexible) pharyngoscopy and laryngoscopy:

For this exam, the doctor inserts a flexible fiber-optic scope (called an *endoscope*) through the mouth or nose to look at some areas that can't easily be seen with mirrors, such as the region behind the nose (nasopharynx) and the larynx, or to see certain areas clearer.Both types of exams can be done in the doctor's office. For either type of exam, the doctor may spray the back of your throat with numbing medicine first to help make the exam easier.

2.10.4 Panendoscopy:

During a panendoscopy, the doctor uses different types of endoscopes passed down the mouth or nose to perform laryngoscopy, esophagoscopy, and (at times) bronchoscopy. This lets the doctor thoroughly examine the oral cavity, oropharynx, larynx (voice box), esophagus (tube leading to the stomach), and the trachea (windpipe) and bronchi (breathing passageways in the lungs).

This exam is usually done in an operating room while you are under general anesthesia (asleep). The doctor uses a laryngoscope to look for tumors in the throat and larynx. Other parts of the mouth, nose, and throat are examined as well. If a tumor is found that is large or seems likely to spread, the doctor may also need to use an esophagoscope to look into the esophagus or a bronchoscope to look into the trachea and bronchi.

Your doctor will look at these areas through the scopes to find any tumors, see how large they are, and see how far they may have spread to surrounding areas. A small piece of tissue from any tumors or other abnormal areas may be removed (biopsied) to be looked at under a microscope to see if they contain cancer. Biopsies can be done with special instruments operated through the scopes.

2.10.5 Biopsy:

In a biopsy, the doctor removes a sample of tissue to be looked at under a microscope. The actual diagnosis of oral and oropharyngeal cancers can only be made by a biopsy. A sample of tissue or cells is always needed to confirm that cancer is really present before treatment is started. Several types of biopsies may be used, depending on each case.

2.10.6 Exfoliative cytology:

In this technique, the doctor scrapes a suspicious area and smears the collected tissue onto a glass slide. The sample is then stained with a dye so the cells can be seen under the microscope. If any of the cells look abnormal, the area can then be biopsied.

The advantage of this technique is that it is easy, and even only slightly abnormal-looking areas can be examined. This can make for an earlier diagnosis and a greater chance of cure if there is

cancer. But this method does not detect all cancers. Sometimes it's not possible to tell the difference between cancerous cells and abnormal but non-cancerous cells (dysplasia) with this approach, so a biopsy would still be needed.

2.10.7 Incisional biopsy

For this type of biopsy, the doctor cuts a small piece of tissue from an area that looks abnormal. This is the most common type of biopsy to sample areas in the mouth or throat.

The biopsy can be done either in the doctor's office or in the operating room, depending on where the tumor is and how easy it is to get a good tissue sample. If it can be done in the doctor's office, the area around the tumor will be numbed before the biopsy is taken. If the tumor is deep inside the mouth or throat, the biopsy might be done in the operating room with the patient under general anesthesia (in a deep sleep). The surgeon uses special instruments through an endoscope to remove small tissue samples.

2.10.8 Fine needle aspiration (FNA) biopsy:

For this test, the doctor uses a very thin, hollow needle attached to a syringe to draw (aspirate) some cells from a tumor or lump. These cells are then looked at under a microscope to see if cancer is present.

FNA biopsy is not used to sample abnormal areas in the mouth or throat, but is sometimes used when a patient has a neck mass that can be felt or seen on a CT scan. FNA can be helpful in several different situations, such as:

- Finding the cause of a new neck mass:
- An FNA biopsy is sometimes used as the first test for someone with a newly found neck lump.
- The FNA may show that the neck mass is a benign (non-cancerous) lymph node that has grown in reaction to a nearby infection, such as a sinus or tooth infection. In this case, treatment of the infection is all that is needed. Or the FNA may find a benign, fluid-filled cyst that can be cured by surgery. But even when the FNA results are benign, if the patient has symptoms suggesting cancer, more tests (such as pharyngoscopy and panendoscopy) are needed.

If the FNA finds cancer, the doctor looking at the sample can usually tell what type of cancer it is. If the cells look like a squamous cell cancer, more exams will be done to search for the source of the cancer in the mouth and throat. If the FNA shows a different type of cancer, such as lymphoma or a cancer that has spread to a lymph node in the neck from another organ (like the thyroid, stomach, or lungs) more tests will be done to find it, and specific treatment for that type of cancer will be given.

2.10.9 Lab tests of biopsy samples:

All biopsy samples are sent to a lab to be viewed under a microscope by a pathologist, a doctor who is specially trained to diagnose cancer with lab tests. The doctor can usually tell cancer cells from normal cells, as well as what type of cancer it is, by the way the cells look. In some cases, the doctor may need to coat the cells with special stains to help tell what type of cancer it is.

2.10.10 HPV testing:

For cancers of the throat, doctors often have the biopsy samples tested to see if HPV infection is present. This information can help the doctor predict the probable course of the cancer, as people whose cancers are linked to HPV tend to do better than those whose cancers are not.

This testing is not routinely used to guide treatment at this time, but in the future, it might help doctors decide which patients might be able to get less aggressive treatment.

2.10.11 Imaging tests:

Imaging tests use x-rays, magnetic fields, or radioactive substances to create pictures of the inside of your body. Imaging tests are not used to diagnose oral cavity or oropharyngeal cancers, but they may be done for a number of reasons both before and after a cancer diagnosis, including:

- To help look for a tumor if one is suspected
- To learn how far cancer may have spread
- To help determine if treatment has been effective
- To look for possible signs of cancer recurrence after treatment

2.10.12 Chest x-ray:

An x-ray of your chest may be done to see if the cancer has spread to your lungs. Unless your cancer is far advanced, it is not likely that it will have spread. This x-ray is most often done in an outpatient setting. If the results are not normal, your doctor may order a computed tomography (CT) scan or other test to look at your lungs in more detail.

2.10.13 Computed tomography (CT):

The computed tomography (CT) scan uses x-rays to produce detailed, cross-sectional images of your body. Instead of taking one picture, like a standard x-ray, a CT scanner takes many pictures as it rotates around you. A computer then combines these pictures into an image of a slice of your body. Unlike a regular x-ray, a CT scan creates detailed images of the soft tissues and organs in the body.

This test can help your doctor determine the size and location of a tumor, if it is growing into nearby tissues, and if it has spread to lymph nodes in the neck. The test also may be done to look for spread of cancer to the lungs.

A CT scanner has been described as a large donut, with a narrow table that slides in and out of the middle opening. You will need to lie still on the table while the scan is being done. CT scans take longer than regular x-rays, and you might feel a bit confined by the ring while the pictures are being taken.

For some scans, you might be asked to drink a contrast solution. This helps better outline the digestive tract so that tumors can be seen more clearly and certain areas are not mistaken for tumors. After the first set of pictures is taken you might also receive an intravenous (IV) injection of a contrast dye. This can also help tumors be seen more clearly. A second set of pictures is then taken.

The injection may cause some flushing (a feeling of warmth, especially in the face). Some people are allergic and get hives, or rarely, have more serious reactions like trouble breathing or low blood pressure. Be sure to tell the doctor if you have any allergies or have ever had a reaction to any contrast material used for x-rays.

2.10.14 Magnetic resonance imaging (MRI)

MRI scans use radio waves and strong magnets instead of x-rays. The energy from the radio waves is absorbed by the body and then released in a specific pattern formed by the type of body tissue and by certain diseases. A computer translates the pattern into detailed images of parts of the body. As with a CT scan, a contrast material might be injected, but this is a different substance than what is used for CT (so being allergic to one, doesn't mean you are allergic to the other.

Because it provides a very detailed picture, an MRI scan may be done to look for spread of the cancer in the neck. These scans can also be very useful in looking at other areas of the body as well, especially the brain and spinal cord.

MRI scans are a little more uncomfortable than CT scans. First, they take longer — often up to an hour. During the scan, you need to lie still inside a narrow tube, which is confining and can upset people who have claustrophobia (fear of enclosed spaces). Special, more open MRI machines can sometimes help with this if needed, although the images may not be as sharp in some cases. The machine also makes clicking and buzzing noises that disturb some people. Some places provide earplugs to block this noise out.

2.10.15 Positron emission tomography (PET):

For a PET scan, a form of radioactive sugar (fluorodeoxyglucose or FDG) is injected into the blood. The amount of radioactivity used is very low and it will pass out of the body over the next day or so. Because cancer cells use glucose at a higher rate than normal cells, they will absorb more of the radioactive sugar, and the radioactivity will to concentrate in the cancer. After about an hour, you will be moved onto a table in the PET scanner. You lie on the table for about 30 minutes while a special camera creates a picture of areas of radioactivity in the body. The picture is not finely detailed like a CT or MRI scan, but it provides helpful information about your whole body.

A PET scan may be used to look for possible areas of cancer spread, especially if there is a good chance that the cancer is more advanced. This test also can be used to help tell if a suspicious area seen on another imaging test is cancer or not.

A PET scan is often combined with a CT scan using a machine that can perform both scans at the same time (PET/CT scan). This lets the doctor compare areas of higher radioactivity on the PET with the more detailed appearance of that area on the CT.

2.10.16 Barium swallow

A barium swallow can be used to examine the lining of the upper part of the digestive system, especially the esophagus (the tube connecting the throat to the stomach). In this test, you drink a chalky liquid called *barium* to coat the walls of your throat and esophagus. A series of x-rays of the throat and esophagus is taken as you swallow, which the barium outlines clearly.

Because patients with oral and oropharyngeal cancers are at risk for cancer of the esophagus, your doctor may order this test to check for this cancer. It is also useful to see if the cancer is causing problems with normal swallowing.

For more information on imaging tests, see our document Imaging (Radiology) Tests.

2.11 Oral cancer treatment

If one is diagnosed with oral cancer, your doctor will discuss the best options to treat it. This depends on several factors, including the type and stage of the cancer and your general health.

Your treatment for oral cancer will be customized to your particular needs. One or more of the following therapies may be recommended to treat the cancer or help relieve symptoms.

2.11.1 Surgery:

Surgery is the most frequent treatment for oral cancer. The type of surgery depends on the type and stage of the tumor. Surgical techniques to treat oral cancer and deal with the side effects of treatment include:

- Removal of the tumor or a larger area to remove the tumor and surrounding healthy tissue
- Removal of part or all of the jaw
- Maxillectomy (removal of bone in the roof of the mouth)
- Removal of lymph nodes and other tissue in the neck
- Plastic surgery, including skin grafts, tissue flaps or dental implants to restore tissues removed from the mouth or neck
- Tracheotomy, or placing a hole in the windpipe, to assist in breathing for patients with large tumors or after surgical removal of the tumor
- Dental surgery to remove teeth or assist with reconstruction

2.11.2 Radiation Therapy:

In cancer of the mouth, Radiation Therapy may be used alone to treat small or early-stage tumors. More often, radiation therapy is used after surgery, either alone or with chemotherapy for more advanced tumors. The method of radiation treatment used depends on the type and stage of cancer.

External-beam radiation therapy is the most frequently used method to deliver radiation therapy to the mouth. Intensity-modulated radiotherapy (IMRT) and proton therapy are aimed at treating the tumor while minimizing damage to surrounding normal tissue.

Internal radiation or brachytherapy delivers radiation with tiny seeds, needles or tubes that are implanted into the tumor. It is used sometimes for treating small tumors or with surgery in advanced tumors.

2.11.3 Proton Therapy:

The Proton Therapy means this cutting-edge therapy is backed by all the expertise and compassionate care for which MD Anderson is famous.

Proton Therapy delivers high radiation doses directly into the tumor, sparing nearby healthy tissue and vital organs. For many patients, this results in a higher chance for successful treatment with less impact on the body.

2.11.4 Chemotherapy:

Chemotherapy may be used to shrink the cancer before surgery or radiation, or it may be combined with radiation to increase the effectiveness of both treatments. It also may be used to shrink tumors that cannot be surgically removed.

2.11.5 Tumor Growth Factor Inhibitors:

Tumor growth factors are hormone-like substances that occur naturally in the body and cause cell growth. An epidermal growth factor (EGF) receptor on the surface of some oral cancer cells can bind to certain substances that stimulate tumor growth. New drugs are being tested that target EGF receptors and may stop cancer cells from growing.

2.11.6 After Treatment: Reconstruction and Rehabilitation:

Oral cancer and its treatment often cause difficulty in speaking, swallowing and breathing. We work with you, defining your needs and making sure you receive the care you need. This may include speech, occupational and physical therapies and other methods.

After treatment, some patients with oral cancer need plastic or reconstructive surgery to help restore their appearance or regain the ability to speak or swallow. MD Anderson'splastic and reconstructive surgeons are among the most skilled and experienced in the world.

Sometimes the surgeon can perform reconstructive surgery at the same time as your cancer surgery; in other cases, it is best to wait. Your doctor will recommend the method that is best for you. If reconstructive surgery isn't possible, you may be fitted for a dental prosthesis or implant. A therapist will show you how to use the device. Sometimes, grafts of skin, muscle or bone, which are moved from another part of body to the mouth, are used.

2.11.7 Treatment options for oral cavity and oropharyngeal cancer by stage:

The type of treatment your doctor will recommend depends on the tumor site and how far the cancer has spread. This section lists the options usually considered for each stage of oral cavity or oropharyngeal cancer. These are general comments about treatment,because the approach to each site may be different. Your doctor may have reasons for suggesting a treatment option not mentioned here.

- **Stage 0 (carcinoma in situ)**

Although cancer in this stage has not become invasive (started to grow into deeper layers of tissue), it can do so if not treated. The usual treatment is to remove the top layers of tissue along with a small margin of normal tissue. This is known as *surgical stripping* or *thin resection*. Close follow-up to see if any cancer has come back (recurrence) is important. Carcinoma in situ that keeps coming back after resection may require radiation therapy.

Nearly all patients at this stage survive a long time without the need for more intensive treatment. But it is important to note that continuing to smoke increases the risk that a new cancer will develop.

- **Stages I and II**

Most patients with stage I or II oral cavity and oropharyngeal cancer can be successfully treated with either surgery or radiation therapy. Chemotherapy (chemo) may be given with radiation, especially to treat any cancer left after surgery. Both surgery and radiation work well in treating these cancers. The choice of treatment is influenced by the expected side effects, including how the treatment might affect your appearance and ability to speak and swallow.

Lip: Small cancers are often removed with surgery, with Mohs surgery as an option. Radiation alone may also be used as the first treatment. Surgery may be needed later if radiation doesn't completely get rid of the tumor.

Large or deep cancers often require surgery. If needed, special reconstructive surgery can help correct the defect in the lip.

If the tumor is thick, this increases the risk that the cancer may have spread to lymph nodes in the neck, so the surgeon may remove them (lymph node dissection) to be checked for cancer spread.

Oral cavity: For cancers of the floor of the mouth, front of the tongue, inside of the cheek, gums, and hard palate, surgery is the main treatment. Lymph nodes in the neck may be removed (lymph node dissection) to check for cancer spread. If the cancer does not appear to have been completely removed by surgery or if has a high risk of coming back based on how the cancer cells look under the microscope, radiation (often combined with chemo) may be added.

Radiation can be used instead of surgery as the main treatment in some patients. This is most often used in patients who can't have surgery because of medical problems.

Oropharynx: For cancers of the back of the tongue, soft palate, and tonsils, the main treatment is radiation therapy aimed at the cancer and the lymph nodes in the neck. Surgery can be used as the main treatment (instead of radiation) in some cases. This would mean removing lymph nodes in the neck as well (lymph node dissection). If any cancer remains after surgery, radiation (often with chemo) is often used.

- **Stages III and IVA**

Oral cavity cancers (cancers of floor of the mouth, front of the tongue, inside of the cheek, gums, and hard palate): Stages III and IVA include larger cancers, those that have grown into nearby tissues, and those that have spread to nearby lymph nodes in the neck. These cancers are often treated with a combination of surgery and radiation. Surgery is often done first and includes removal of neck lymph nodes (lymph node dissection).

Oropharyngeal cancers (cancers of the back of the tongue, soft palate, and tonsils): Stages III and IVA include larger cancers, those that have grown into nearby tissues, and those that have spread to nearby lymph nodes in the neck. These cancers are often treated with a combination of radiation and chemo (chemoradiation), although radiation and cetuximab may be used in some cases. The effect of combining radiation with both chemo and cetuximab is also being studied. Any cancer that remains after chemoradiation is removed with surgery. If the cancer has spread to neck lymph nodes, they may also need to be removed (a lymph node dissection) after chemoradiation is done.

Another option is to treat first with surgery to remove the cancer and neck lymph nodes. This is often followed by radiation or chemoradiation to lower the chance of the cancer coming back.

The choice of treatment is influenced by where the cancer is, how much it has spread, the expected side effects, and the patient's current health status.

Some doctors give chemo as the first treatment, followed by chemoradiation (chemo and radiation given together), and then surgery if needed. Not all doctors agree with this approach, though.

- **Stage IVB**

Cancers that have already spread to other parts of the body are usually treated with chemo, cetuximab, or both. Other treatments such as radiation may also be used to help relieve symptoms from the cancer or to help prevent problems from occurring.

Clinical trials are looking at different ways of combining radiation and chemo with or without cetuximab or other new agents to improve survival and quality of life, and reduce the need for radical or deforming resection of advanced oral cavity and oropharyngeal cancers.

Recurrent oral cavity or oropharyngeal cancer

When cancer come backs after treatment, it is called recurrent cancer. Recurrence can be local (in or near the same place it started), regional (in nearby lymph nodes), or distant (spread to bone or organs such as the lungs). Treatment options for recurrent cancers depend on the location and size of the cancer, what treatments have already been used, and on the person's general health.

If the cancer comes back in the same area and radiation therapy was used as the first treatment, surgery is often the next treatment, if the cancer can be removed completely and the patient is healthy enough for surgery. Usually, external beam radiation therapy cannot be repeated in the same site except in selected cases. However, brachytherapy can often be used to control the cancer if it has come back in the place it started. If surgery was used first, more surgery, radiation therapy, chemo, cetuximab, or a combination of these may be considered.

If the cancer comes back in the lymph nodes in the neck, these are often removed with surgery (lymph node dissection). This may be followed by radiation.

If the cancer comes back in a distant area, chemo (and/or cetuximab) is the preferred form of treatment. This may shrink or slow the growth of some cancers for a while and help relieve symptoms, but these cancers are very difficult to cure.

If chemo is no longer working, a newer option might be treatment with the immunotherapy drug pembrolizumab. This drug can help the body's own immune system attack the cancer.

If further treatment is recommended, it's important to talk to your doctor so that you understand what the goal of treatment is — whether it is to try to cure the cancer or to keep it under control for as long as possible and relieve symptoms. This can help you weigh the pros and cons of each treatment. Because these cancers are hard to treat, clinical trials of newer treatments may be a good option for some people.

Material and method

Chapter Three: Material and method

A retrospective study was conducted with ambulatory and inpatients at the National Institute of Cancer Research and Hospital (NICRH), those are the renowned cancer hospital in Dhaka. In this, information was collected from 114 patients. The questionnaire and the study procedures were approved by the institutional review board and its ethical committee. A pilot study was conducted which not only helped to discern the sample size but also allowed assessment of the validity, reliability and acceptability of the questionnaire. The questionnaire comprised 45 closed-ended questions that assessed the subjects' awareness of oral cancer, knowledge of signs/symptoms, risk factors and treatment for oral cancer. Socio-demographic information such as age, sex, occupation, address, educational level, risk factor and treatment pattern was also recorded.

Disease diagnosed, and drugs prescribed to each patient were studied. Problems were faced while the survey works were (1). The treatment and follow of up sheet of the hospitals were no properly maintained. (2) In many cases women patients are not co-operative to provide information. Data were analyzed using the Statistical Package using Microsoft Excel 2010 for windows. In this survey Selection of Disease and A literature review of earlier studies regarding risk factors, signs and symptoms, and risk perceptions was used to identify items for this survey was taken 1 month, Selection and Collection information from questionnaire to patient's and Prescriptions was taken 6 Months. Review and Analysis data was taken 4 Months.

Research Protocol with Time Line

Chapter Four: Research Protocol with Time Line

- Selection of Disease and Literature Review: 1 Month
- Selection, Collection and Identification of the Prescriptions: 3 Months
- Prescription Review and Analysis: 2 Months
- Prepare and Print the Research Paper: 1 Months

Literature review

Chapter Five: Literature review

Rao, S. V. K., Mejia, G., Roberts-Thomson, K., & Logan, R reported the prevalence of oral cancers (OC) is high in Asian countries, especially in South and Southeast Asia. Asian distinct cultural practices such as betel-quid chewing, and varying patterns of tobacco and alcohol use are important risk factors that predispose to cancer of the oral cavity. The aim of this review is to provide an update on epidemiology of OC between 2000 and 2012. he tongue is the leading site among oral cancers in India. The next most common sites in Asian countries include the buccal mucosa and gingiva. The 5 year survival rate has been low for OC, despite improvements in diagnosis and treatment. Tobacco chewing, smoking and alcohol are the main reasons for the increasing incidence rates (Rao and S. V. K. et al, 2013). Radoi, L., Paget-Bailly, S., Cyr, D., Papadopoulos, A., Guida, F., Schmaus, A., & Luce, D. reported that, the role of tobacco smoking and alcohol drinking in the incidence of oral cavity cancer by subsite in France, a high-incidence area. We analysed detailed data on lifelong tobacco smoking and alcohol drinking from 772 oral cavity cancer cases and 3555 controls included in a population-based case-control study, the ICARE study. Tobacco smoking increased the risk of oral cavity cancer even for the smaller quantities and durations, whereas alcohol drinking increased this risk only in heavy drinkers who were also ever smokers. Population-attributable risks for oral cavity cancer were 78.6% for tobacco smoking, 7.3% for alcohol drinking and 80.7% for tobacco and/or alcohol consumption (Radoï and Paget-Bailly et al, 2013). Sankaranarayanan, R.reported, the disease ranks number one among all cancers in male patients and number three among cancers in female patients. Causal association between oral cancer and the chewing of betel quids containing tobacco leaves or stem and other tobacco habits has been extensively studied. Sex ratio reveals a 2:1 preponderance of male patients. Only 10% to 15% of cases present in localized stages. The poor survival revealed by existing studies is mainly due to the overwhelming proportion of advanced cases (Sankaranarayanan et al, 1990)). Rahman, M., Sakamoto, J., & Fukui, T. reported,that, the cumulative cases and controls were 4778 and 6271, respectively, based on 10 case-control studies conducted in India. Among the cases, 49.1% were bidi smokers and 7.7% cigarette smokers, while they were 19.9% and 10.3%, respectively, among controls. Pooled odds ratio (OR) of bidi smoking for oral cancer was 3.3 [95% confidence interval (CI), 3.0-3.6] and 2.6 (95% CI 1.8-3.8), respectively, based on fixed- and random-effects model. Cigarette smoking, on the other hand, did

not show any significant association. PAR% of bidi smoking for oral cancer ranged from 4.7% to 51.6% on individual study basis, while they were 31.4% and 24.1%, respectively, based on OR derived from fixed- and random-effects models. PAR% was 5.8% and 8.7% based on single study estimate from Pakistan and Sri Lanka, respectively (Rahman and Sakamoto et al, 2005). Petti, S. reported about Worldwide, 25% of oral cancers are attributable to tobacco usage (smoking and/or chewing), 7-19% to alcohol drinking, 10-15% to micronutrient deficiency, more than 50% to betel quid chewing in areas of high chewing prevalence. Carcinogenicity is dose-dependent and magnified by multiple exposures. Conversely, low and single exposures do not significantly increase oral cancer risk (Petti, S. et al, 2009)). Merchant, A., Husain, S. S., Hosain, M., Fikree, reported,approximately 68% of the cases were men, 49 years old on average, the youngest being 22 years old and the eldest 80. People with oral submucous fibrosis were 19.1 times more likely to develop oral cancer than those without it, after adjusting for other risk factors. People using paan without tobacco were 9.9 times, those using paan with tobacco 8.4 times, more likely to develop oral cancer as compared with non-users, after adjustment for other covariates. This study identifies an independent effect of paan without tobacco in the causation of oral cancer. Its findings may be of significance in South Asian communities where paan is used, and among health-care providers who treat persons from South Asia (Merchant and Husain et al, 2000). Johnson, N. reported ,tobacco use, heavy alcohol consumption, and poor diet together explain over 90 percent of cases of head and neck cancer. All forms of tobacco represent risk factors for oral cancer, but on present evidence, snuff habits as they exist in Scandinavia and probably in the United States carry lower risks of serious health hazards, including oral cancer. Alcohol synergizes with tobacco as a risk factor for all upper aerodigestive tract SCC: this is super-multiplicative for the mouth, additive for the larynx, and between additive and multiplicative for the esophagus. The increase in oral cancer in the Western world has been related to rising alcohol use (Johnson, N. et al, 2001). Johnson, N. also repoted,Poor oral health often factors of oral cancer. Oral cancer is very dreadful disease that affects many people each year all over the world and it is eleventh most dominate cancer in the world. Oral cancer is also reported in Bangladesh and more than 7000 people are diagnosed each year and 6.6 % people are died. This paper shows the total oral cancer picture in Bangladesh based on different literatures and cancer registry from the web and also different risk factors that associated with this disease (Rahman and Sakamoto et al, 2005).

Results and Discussion

Chapter Six: Results and Discussion

A total 114 patients were interviewed according to the questionnaire and filled up accordingly, these questionnaires were utilized for the study (response rate-95 %), the rest of the questionnaires were either not returned or submitted without implication. Among the finished questionnaires were collected from 11 in Patients and 103 from out Patients. The socio-demographic facts of the investigation population are shown in Table 1. The illustration included 54 (47.37 %) male and 60 (52.63%) female patients. The mean age of the patients was 48.7 ± 10.8 years going from 30 to 85 years. A large portion of the participants were found illiterate (60.53%). Only 6.4% and 1.6% of the population received education at the SSC or equivalent and HSC or equivalent level.

12.28 % of the total patients (n=114) were reported with family history of oral cancer or other than oral cancer. 85.96% patients were found habitant of rural areas where not sufficient cancer treatment facilities were available. Only 5.26% and 8.77% patients were from urban and sub-urban areas respectively. 72% of the patients were belong to a poor income group and 28% population were coming from a lower income group.

Table-2: Sociodemographic appearances of the study sample (N = 114)

Variable	Frequency	Percentage (%)
Gender		
Male	54	47.37
Female	60	52.63
Age		
≤40 years	95	83.33
>40 years	19	16.63
Education		
Illiterate	69	60.53
SSC or equivalent	43	6.14
HSC or equivalent	2	1.76
Family History		
Yes	14	12.28
No	100	87.72
Residence		
Rural	98	85.96
Sub-Urban	10	8.77
Urban	6	5.26
Economic Status		
Poor	82	72
Lower middle class	32	28

Tobacco:

Smoking includes use of cigarettes, bidi, and hookah. Though cigarette smoking is seen in all Asian countries, bidi smoking is common in Bangladesh which is an important risk factor for oral cancer in Bangladesh.

Bidi smokers are 4 times at risk of developing oral cancer compared to non-smokers

The risk of oral cancer increases with the

- **amount** of tobacco used and the
- **duration** of the habit.

Out of the total 114 patients 44% and 56% patients were informed to be smokers and non-smoker respectively.

Table-3: frequency and percentage of tobacco (smoking) users

Patient type	frequency	Percentage (%)
Smoker	50	44
Non-Smoker	64	56
Total Patients	**114**	100

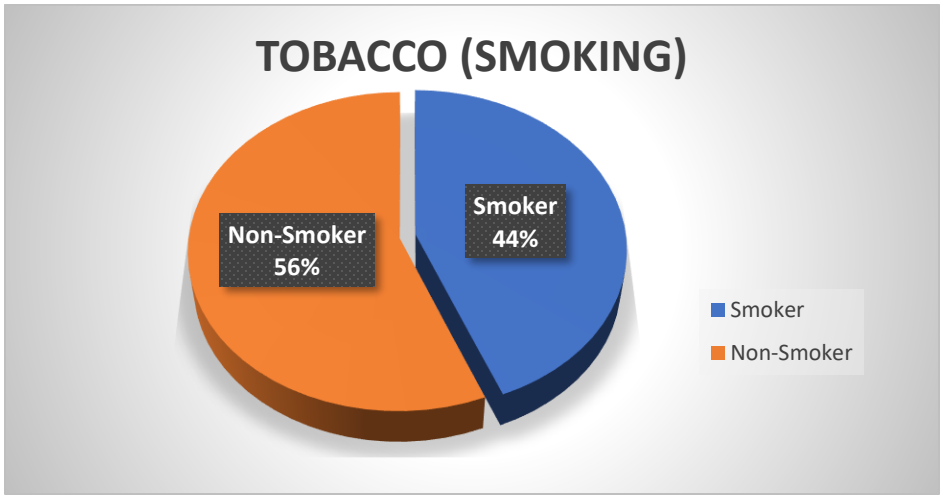


Fig 2: percentage of tobacco (smoking) users for oral cancer risk factors

Smokeless tobacco:

Smokeless tobacco (8-10 times a day) are exposed to the same nicotine as 30-40 cigarettes a day.Strong social culture peoples encourage to the combination of betel nut and tobacco. The habit

is more common in women than in men. In our study we found that Zarda and Betel Quid chewing is a major carcinogenic dominant factor in Bangladesh. Betel quid consists of betel nut, betel leaf and zarda

In this study we have found 1 single case where only betel nut was taken by the patients. A 2.63 % patient were found only taking betel leaf.

In Bangladesh a high number of populations (37.72%) were found taking betel nut with betel leaf and tobacco leaf (zarda) together. Only 28% of the patients used to take betel nut and betel leaf together. According to this result, we found that patients of this two groups has TNM stage were $T_2N_1M_x$, $T_2N_3M_x$ that means tumor size 2-4 to 4-6 cm and cancer cell present in lymph node. Only 11.40% were found taking betel leaf, betel nut in combination with zarda and gull.

Table-4: **frequency and percentage of tobacco (smokeless) users**

Factors	Percentage	Frequency	Status	stage
betel leaf	2.63	3	2cm-3 cm	$T_2N_1M_x$
betel nut	0.88	1	2cm-3 cm	$T_2N_1M_x$
gull	0.88	1	2cm-4 cm	$T_2N_1M_x$
betel leaf and betel nut	14.02	16	2cm-3cm 4cm-6 cm	$T_2N_1M_x$ $T_3N_2M_x$
betel leaf with quid chewing	0.88	1	3cm x 2.3cm	$T_2N_1M_x$
zarda with betel nut	0.88	1	2cm x 2.5 cm	$T_2N_1M_x$
Quid chewing with betel nut	0.88	1	2cm x 2.5 cm	$T_2N_1M_x$
Factors	Percentage	Frequency	Status	stage
betel leaf, betel nut combination with				
zarda	37.72	43	2cm-3 cm 4cm-6 cm	$T_2N_1M_x$ $T_3N_2M_x$
quid chewing	3.51	4	2cm-4 cm	$T_2N_1M_x$
gull	3.51	4	2cm-4 cm	$T_2N_1M_x$
zarda and gull	11.40	13	2cm-3 cm	$T_2N_1M_x$
quid chewing and zarda	6.14	7	2cm-4.5 cm	$T_3N_2M_x$
quid chewing and gull	1.75	2	1.8cm-2.5cm	$T_2N_1M_x$
quid chewing zarda and gull	5.26	6	2cm-3cm	$T_2N_1M_x$

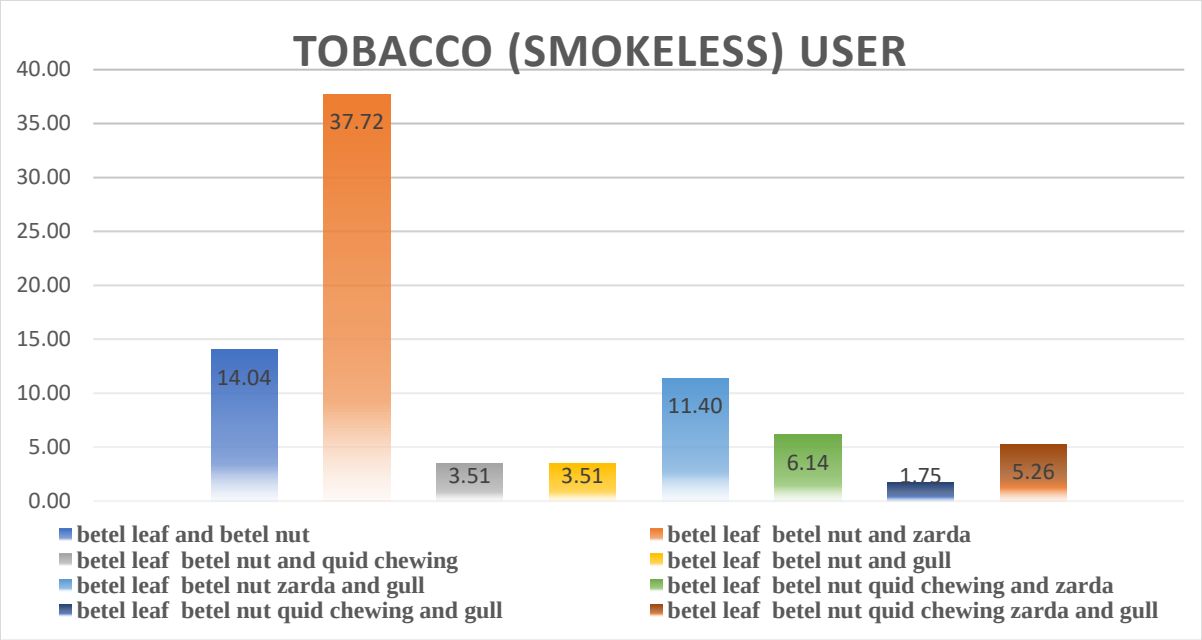


Fig. 3 Percentage of smokeless tobacco user for oral cancer risk factors

Drinking alcohol is an important risk factor for oral cancer in Bangladesh. A combination of both alcohol and tobacco provides the greatest risk of oral cancer.

In bangladesh on Among 114 participants, a lower number of oral cancer patients were reported to alcohol usage (3%) whereas alcohol is one of the major risk factor of oral cancer in worldwide.

Table-5: frequency and percentage of alcohol users:

Alcohol user	Percentage (%)	frequency
yes	2.63	3
no	97.37	111

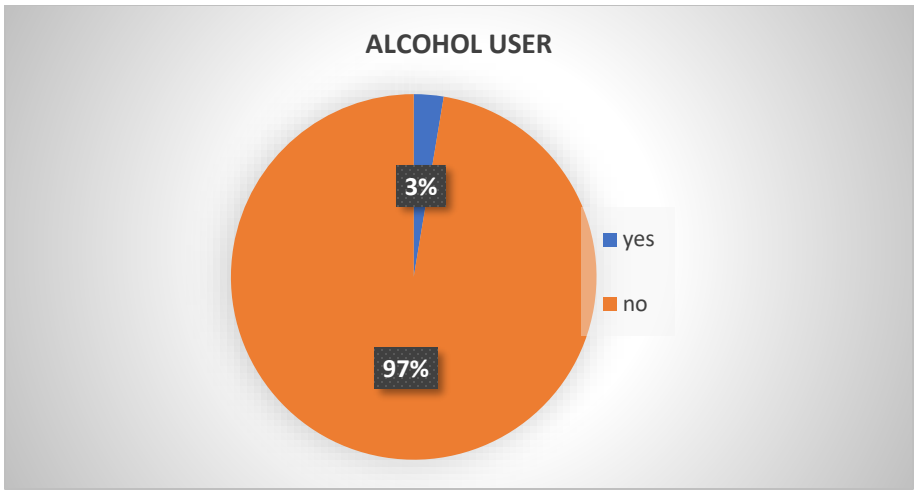


Fig 4 Percentage of alcohol user for oral cancer risk factors

In this study, Among the total patients we found that faulty teeth were 72.81%, 64.04% patients were loose teeth, 40.35% were denture and 48% were sharp teeth.
So, it shows that faulty teeth, loose teethe and denture are significant risk factors for oral cancer. It has been proposed that long-term disturbance of the coating of the mouth caused by in effectively fitting dentures which is a risk factor for oral cancer.

Table-6: frequency and percentage of dental factor for oral cancer

Factors	frequency	percentage
Sharp teeth	34	29.82
Faulty teeth	83	72.80
Denture	46	40.35
Loose teeth	73	64.03

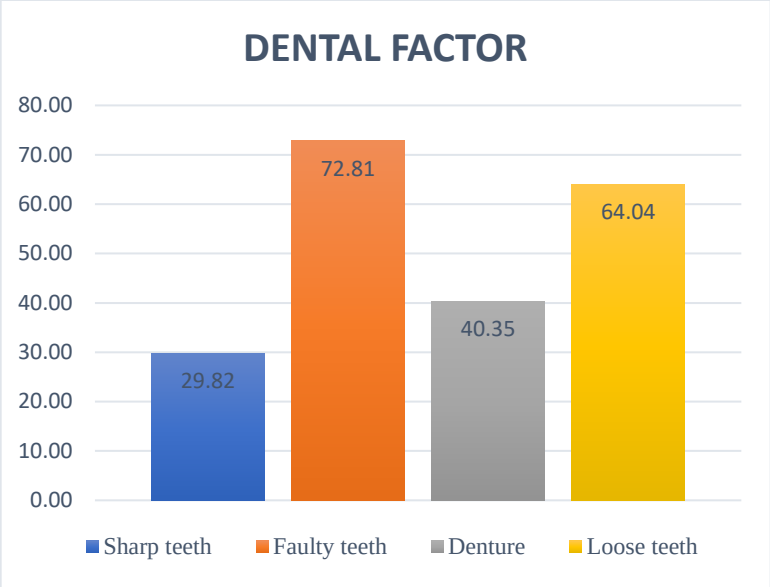


Fig. 5 Percentage of dental factor for Oral Cancer of correct responses

Figure 5 shows the relationship between risk factor and local factor. In this relationship we found that betel leaf taking responses having sharp teeth (26.32%), faulty teeth (62.28%), denture (35.96%) and loose teeth (57.89%).

In betel nut chewing patients also found having sharp teeth (26.32%), faulty teeth (61.4%), denture (35.09%) and loose teeth (56.14%).

Tobacco Leaf / Jorda taking person having sharp teeth (15.79%), faulty teeth (45.61%)%), denture (26.32%) and loose teeth (43.86%). These three relationships are most abundant from total.

Table-7: Percentage of Relationship between risk factor and dental factor for oral cancer

Factors	Sharp teeth	Faulty teeth	Denture	Loose teeth
Betel Leaf	26.32	62.28	35.96	57.89
Betel Nut Chewing	26.32	61.40	35.09	56.14
Tobacco Leaf / zarda	15.79	45.61	26.32	43.86
Quid Chewing	7.89	16.67	5.26	15.79
Gull	8.77	20.18	7.02	17.54
Alcohol	0.88	1.75	0.88	1.75

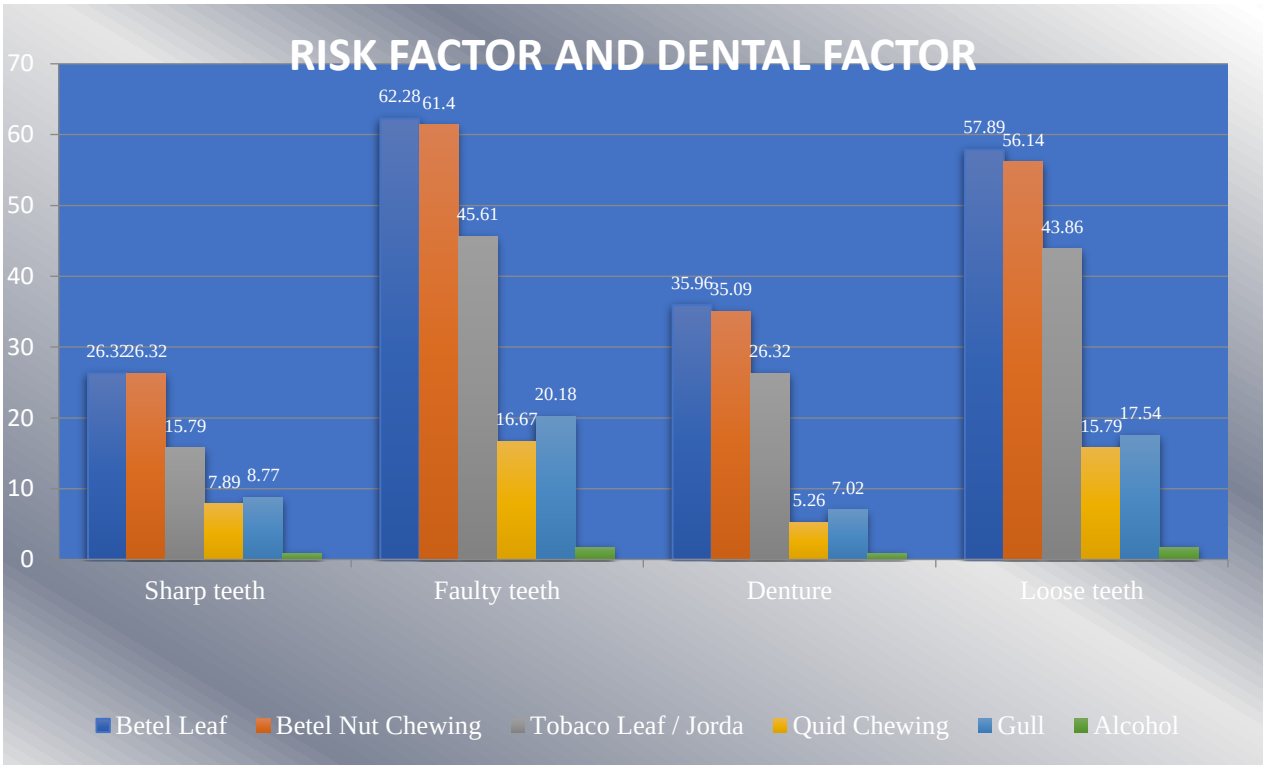


Fig. 6 Relationship between risk factor and dental factor

In bangladesh, the most recognized risk factor thought to be related with oral cancer were sun exposure (38.60 %). Also, fungal contamination (14.91%), chemical exposure (28.07%) and older age (18.42%) was incorrectly identified as a risk factors of the individuals.

Table-8: **frequency and percentage of other factors**

Other factors	Percentage (%)	Frequency
Fungal Infection	14.91	17
Sun exposure	38.60	44
Chemical Exposure	28.07	32
Old Age	18.42	21

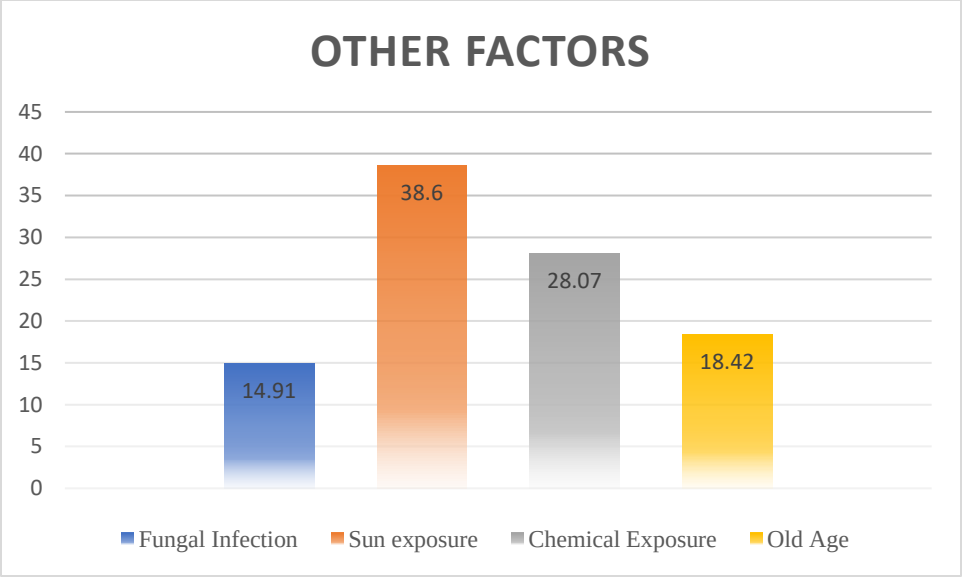


Fig. 7 Percentage of other factors for Oral Cancer of correct responses

This study revealed that 63.16% patients has non-healing mouth ulcer as an early indication of oral cancer. Only 68.42% of the patients have red and white lesions and 53.51% of the patients have lump in the neck which could be major signs of oral cancer. Most of the patients faced serious pain (difficulty with shallowing 37.72%) and dramatic weight loss (14.04%). Another major sign of oral cancer are loose teeth (45.61%), numbness in mouth (13.16%) and only 7% of the patients faced bleeding from mouth.

Table-9: frequency and percentage of sign and symptom for oral cancer

Sign and Symptom	Percentage (%)	Frequency
Non- healing mouth ulcer and bleeding ulcer	70.18	80
Pain or difficulty with Swallowing	37.72	43
Loose teeth	45.61	52
Dramatic weight loss	14.04	16
Lower Lip, face, neck or chin numbness	13.16	15
White, Red and White or Red patches in mouth or lips	68.42	78
Lump in neck	53.51	61

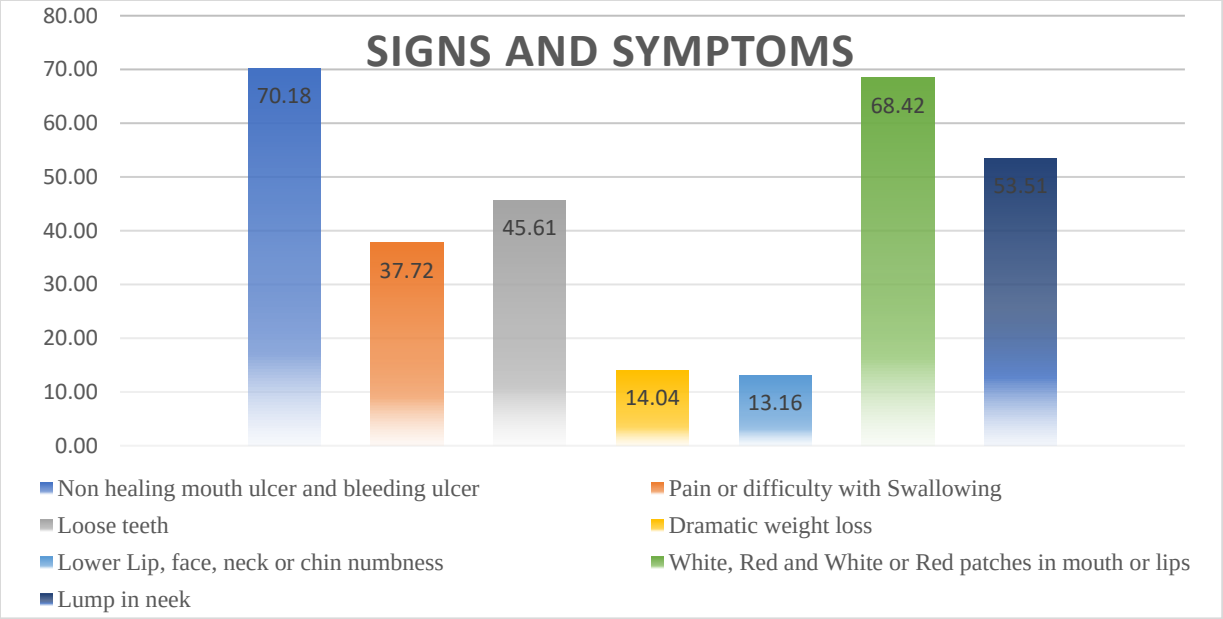


Fig. 8 Percentage of correct responses for oral cancer signs and symptoms

Oral cancer may occur on any part of the oral mucosa, but there are geographical variations in the sites particularly at risk which partly reflect different etiological factors.

In Bangladesh the buccal mucosa (39.5%), alveolar mucosa (25.4%), lip (14.0%), retromolar trigon (4.4%), tongue (2.6%) and floor of the mouth (1.8%) is the most frequent site we found in this study. Other sites are palate (2.6%), face (0.9%), maxilla (5.3%), mandible (3.5%). And this can be described to the widespread chewing of betel quid or pan and to smoking habits.

Table-10: frequency and percentage of primary site for oral cancer

site	Percentage (%)	frequency
Buccal Mucosa	39.5	45
Alveolar Region	25.4	29
Lip	14.0	16
floor of mouth	1.8	2
Face	0.9	1
Mandible	3.5	4
maxilla	5.3	6
Palate	2.6	3
Tongue	2.6	3
Retromolar trigon	4.4	5

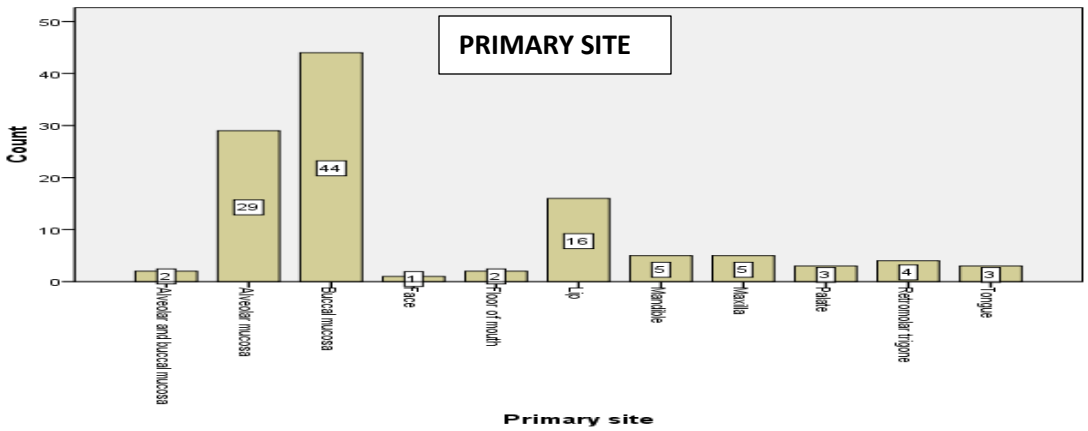


Fig. 9 Percentage of primary site for Oral Cancer of correct responses

This below Fig 9 shows the relationship between risk factor and primary site of oral cancer. Major primary site of Betel Leaf taking responses are Buccal Mucosa (37.72%) and Alveolar Region (23.68%). In case of Betel Nut Chewing responses also Buccal Mucosa (35.09%) and Alveolar Region (23.68%) are major primary site. These two relationships are most abundant from total.

Table-11: Percentage of Relationship between risk factor and Primary site of Oral Cancer

Factors	Buccal Mucosa	Alveolar Region	Lip	floor of mouth	Face	Mandible	maxilla	Palate	Tongue	Retromolar trigon	Total
Betel Leaf	37.72	23.68	10.53	0.88	0.88	2.63	4.39	2.63	1.75	3.51	88.60
Betel Nut Chewing	35.09	23.68	11.40	0.88	0.00	2.63	5.26	2.63	1.75	4.39	87.72
Tobacco Leaf / Zarda	24.56	20.18	7.02	0.00	0.88	1.75	2.63	1.75	1.75	3.51	64.04
Quid Chewing	9.65	7.89	0.88	0.00	0.88	0.00	0.00	0.00	0.00	0.00	19.30
Gull	10.53	7.02	4.39	0.00	0.88	0.00	0.88	0.88	0.00	0.00	24.56
Alcohol	0.88	0.00	0.88	0.00	0.00	1.75	0.00	0.00	0.88	0.00	4.39

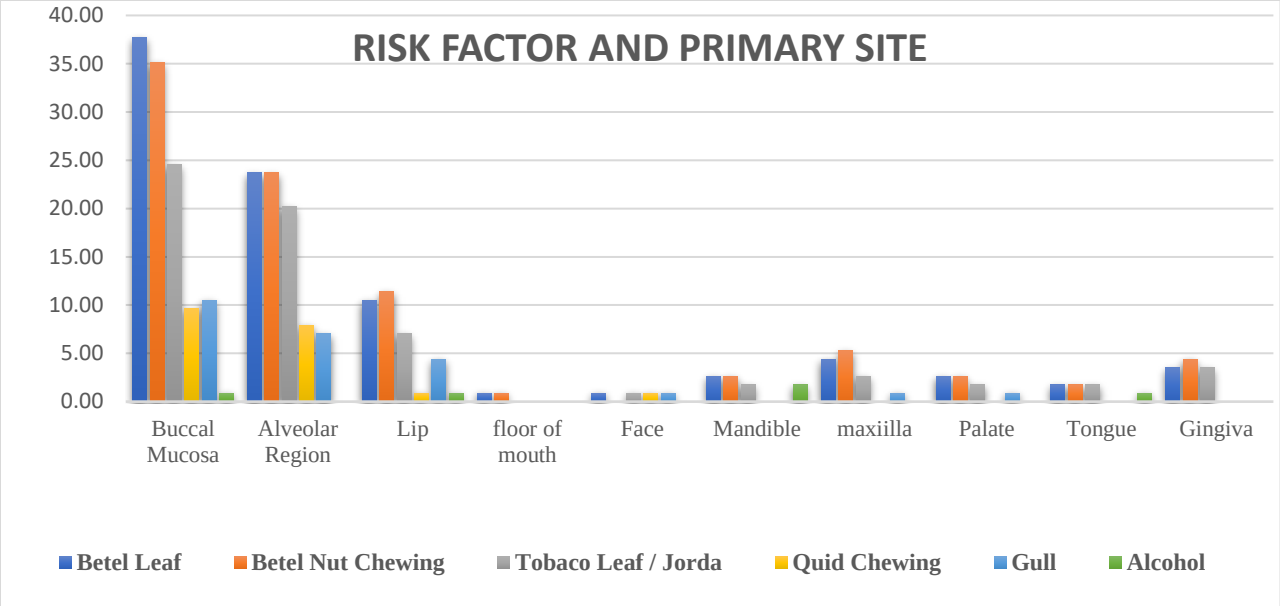


Fig. 10 Relationship between risk factor and Primary site of Oral Cancer

People who have certain syndromes caused by inherited imperfections (transformations) in specific qualities that add to repair of DNA have a very high risk of mouth and throat cancer. Individuals with this syndrome often have blood problems at an early age, which may lead to leukemia or aplastic anemia. They likewise have a high risk of cancer of the mouth and throat. From 114 patients 42.98% patients found Anemia with Oral Cancer. Other diseases are Dehydration (14.91%), Edema (7.02%) and jaundice (7. 02%).That's shown in Fig 10.

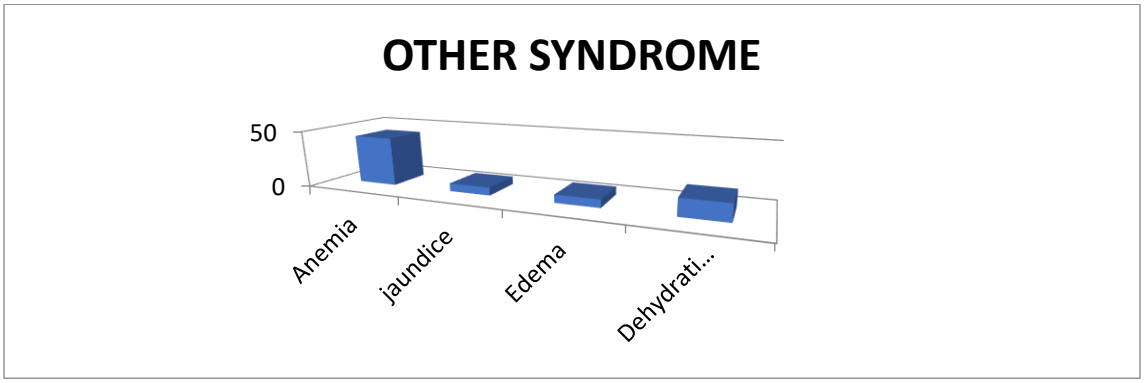


Fig. 11 Other Syndrome with Oral cancer

Clinical staging of oral cancer

The study shows that TNM stage of most patients were T2N1Mx, T3N2Mx that means tumor size 2 to 6 cm and cancer cell present in lymph node and metastasis information could not be assessed.

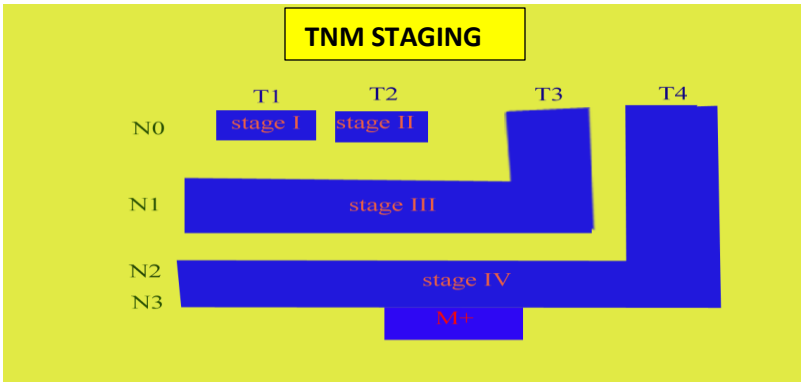


Fig. 12: TNM staging

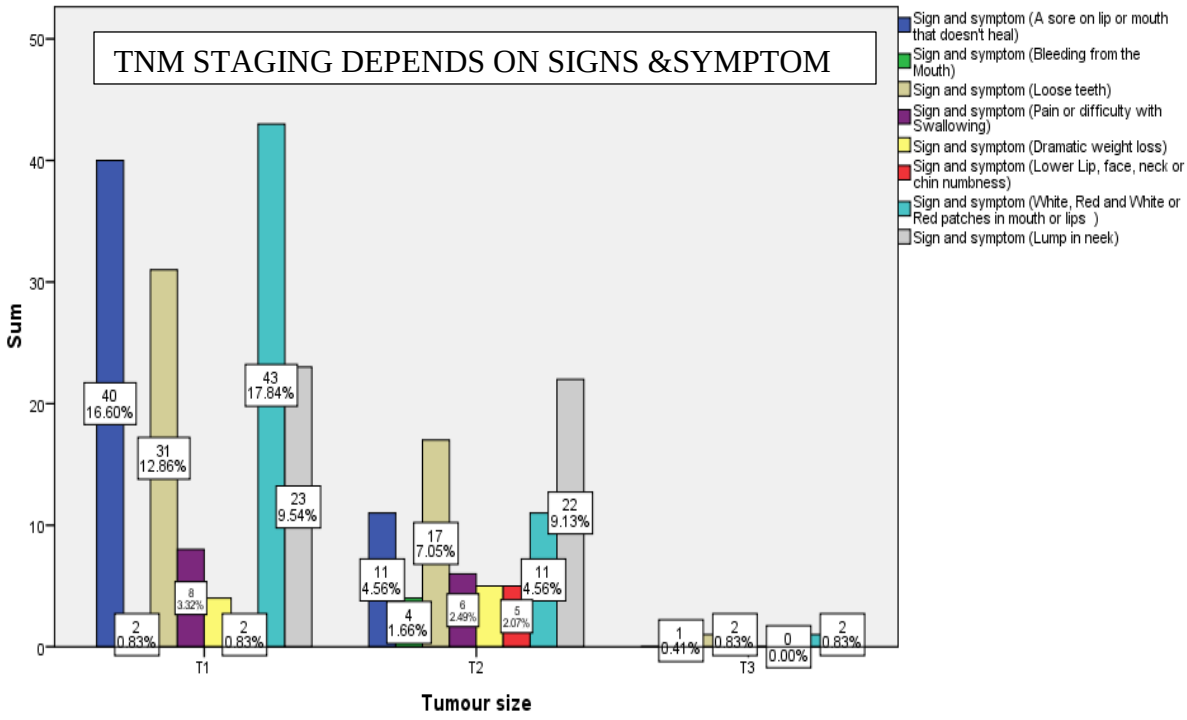


Fig. 13: TNM staging depends on Signs and symptom

Treatment

The same as other kinds of| cancer, is through a multidisciplinary procedure that is comprised of dentists, oncologists, nutritionists, surgeons, and specialists in therapy.

If there is an insignificant growth of a tumor frequently this can be removed with a surgical procedure.
If the cancer is much more extensive sometimes part of the tongue or jaw bone will need removed.

The right treatment is created on a case by case premise and particularly changes per patient.

In treatment pattern after surgery Chemotherapy was treatment with drugs that kill cancer cells. Commonly used drug was:

- 5-flurouracil
- Paclitaxel
- Cisplatin
- Carboplatin.

Discussion:

Oral Cancer disease keeps a serious threat to developing countries like Bangladesh. Despite advances in oral cancer treatment, patients with oral cancer in rural Bangladesh are rarely able to enjoy the benefit of this progress.

In my research work data for 114 patients is collected from National Institute of Cancer Research and Hospital in and out patients with oral cancer. The aim of my study is to identify the risk factors of oral cancer.

In our study we found that patients have insufficient knowledge about risk factor and early sign and symptom of oral cancer. Almost all of patients founded to use tobacco which is the major risk factor of oral cancer. This finding is like past investigations with dental patient sample, where in, the risk factor "Tobacco" was known by 65– 85% of the responders (Al-Dakkak et al, 2010) (Villa and Kreimer et al, 2011) (Peker and Alkurt et al, 2010). This study shows that female patients 52.63% are more susceptible to oral cancer because they most of are house wife and taken tobacco extensively (Eriksen and Mackay et al, 2015). The main oral cancer risk factors such as betel Leaf (87.72%), tobacco chewing (86.84%), and tobacco leaf/jorda (64.04%).

Long term exposure to sun increases oral cancer risk. The risk of damage from unprotected sun exposure for the average adult is extreme. In our study, one third of the patients identified sun exposure (38.60 %) as a risk factors of oral cancer. Also, chemical exposure and fungal infection was incorrectly identified as a risk factor by 28.07% and 118.42% of the participants. Therefore, it is critical to exercise careful sun protection through frequent application of high SPF sun block and careful monitoring. (AdeyemoBamgbose et al, 2010) (Decuseara and MacCarthy et al, 2011)

We found older age patient is 18.42% which is a prospective risk factor for expansion of oral cancer, a rate lower than that detailed in comparative studies somewhere else (Alaizari and Al-Maweri et al, 2014) (López-Jornet and Camacho-Alonso et al, 2010) (Gajendra, Cruz and Kumar et al, 2006).

This investigation demonstrates that 63.16% patients distinguished non- healing ulcer as an early indication of oral disease. studies from different nations have likewise revealed an absence of public knowledge with respect to indications of oral cancer growth (Pakfetrat and Falaki Et al,

2010) (Devadiga and Prasad et al, 2010) (Tadbir and Ebrahimi et al, 2013) (Razavi and Tahani et al, 2015). Only 68.42% of the patients have red and white lesions which can be signs of oral cancer. This is like the results from Srilanka (Ariyawardana and Vithanaarachchi et al, 2005). Additionally, in Kuwait (Joseph and Devipriya et al, 2012), Yemen (Decuseara and MacCarthy et al, 2011), and (Iran Mehdizadeh and Majidi et al, 2014), most of the dental specialists realized that floor of the mouth and tongue are at most serious risk of cancer advancement. A study publicized that the uppermost risk of oral squamous cell carcinoma in the retromolar range took after by the floor of the mouth and buccal mucosa for tobacco smokers while liquor consumers had threat altogether higher in floor of the mouth related to the tongue (Krishna and Singh et al, 2014).

Few socio-economic factors might affect the knowledge of carcinoma. They most of are living in rural area and most of are illiterate so they do not aware about the risk factor of oral cancer. Also, the level of education is an important variable influencing the knowledge level. Highly significant difference was observed in varying levels of education with patients with higher level education. This finding is consistent with the results of other studies (Gajendra, Cruz and Kumar et al, 2006) (Hassona and Scully Et al, 2015) (Srikanth and Doshi et al, 2011) (Srikanth and Doshi et al, 2011).

Interesting, high risk groups patients are female and greater than 40 years of age scored high than their counterpart in this study similar to the study conducted in Jordan (Villa and Kreimer et al, 2011). This is in agreement with a previous Study by (Al-Shammari et al, 2006)
Family and companions has been declared as the real wellspring of data with respect to oral disease in the present study.
There is a limitation of this research that all social classes of cancerous patients are not included here for time consuming. this study investigated the socio-demographic and behavioral risk factors of oral cancer among the patients participating in NICRH and respondents were found having a low level of knowledge scores on the sign and symptoms, diagnosis and treatment of oral cancer. At early stage, treatment of oral cancer is one of the best ways to stop spread of oral cancer.

Conclusion

Chapter Seven: Conclusion

At current situation, throughout the world as well as our country, number of oral cancer patient increased day by day. Oral cancer is a major health burden in Bangladesh. Respondents were found having a low level of knowledge scores on the sign and symptoms, diagnosis and treatment of oral cancer. The present study mainly gives an idea that there may be some correlation between oral cancer and different risk factors (Age, Sex, Environmental Risk factors, Occupation, Bad habit etc.) and the number of chemo patients in poverty level patients in Bangladesh.

The higher percentage of oral cancer cases was found for female adults 52.63 % than other. Chemotherapy mainly gives to large number of oral cancer patients. Some general chemo drugs are given to the patients that are included here. Here mainly knowledge about risk factor is in low level among people who are suffering from oral cancer. There is a limitation of this research that all social classes of cancerous patients are not included here for time consuming. At early stage, treatment of oral cancer is one of the best ways to stop spread of oral cancer. In future there should be research done among the all social class's cancer patients. So that, identification of these factor will be more meaningful and give broad idea.

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