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Clinicopathologic Characteristics of Oral Squamous Cell Carcinoma

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Abstract:

Objective: *The aim of this study was to analyse the sociodemographic and clinicopathological characteristics of Oral Squamous Cell Carcinoma (OSCC) of patients attending at a tertiary care centre in Bangladesh.*

Material and method: *All the patients with histopathologically confirmed OSCC attending at hospital within 3 months of time period were included and the sociodemographic and clinicopathological characteristics were reviewed.*

Results: *A total of 62 cases of OSCC were reviewed. Male female ratio is 1:1.6. Age of the patients was from 26 years to 75 years with average age 53 years. Average duration of complaint reported by the patients before diagnosis was 3 months. Site distribution showed 35% cases in gingivobuccal sulcus and 24% cases in buccal mucosa. 75% ulcers were exophytic variant. 87% of patients had the habit of betel quid chewing and 4% patients had the habit of both betel quid chewing and smoking. Positive family history was found in 4% cases. Poor oral hygiene was seen in 80% patients. Trismus was found in 33% cases. Assessment of nutritional status showed that 75% of the affected individuals were malnourished. Associated Oral Potentially Malignant Disease (OPMD) were seen in 4% of cases and 2nd primary lesion was found in 4% cases. 27% of patients with OSCC had advanced disease (Stage IV) and 75% of the cases were well differentiated histologically.*

Conclusion: *The present data reflect sociodemographic as well as clinicopathologic characteristics of OSCC among the patients admitted at tertiary care hospital in Bangladesh. This study has highlighted at the epidemiological factors, associated risk factors and clinical presentation of OSCC.*

Keywords *Squamous Cell Carcinoma, Oral Cancer, Bangladesh, Betel Quid Chewing, Advance Cancer*

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Introduction:

Head and neck cancer is considered as the 6th most common cancer among all malignancies in the world. In South East Asia, it is 3rd most common malignancy[1]. Among all malignancies arising in head and neck region, more than 90% is Squamous Cell Carcinoma (SCC) which most commonly affects the oral cavity [2]. Globocan 2020 states that, in Bangladesh 8.9% of all cancers is the cancer of lip and oral cavity. It is the 2nd most frequent cancer excluding non-melanoma skin cancer (ranked by cases) [3]. There are variations in clinical features, risk factors and outcome of OSCC in different countries [4]. The risk factors vary according to the abundance of carcinogenic products and cultural habits in different communities and countries. The primary site also differs according to geographic area and it is also related to the associated risk factors.

The aim of this study is to analyse the sociodemographic and clinicopathological findings of OSCC of patients attending at a tertiary care centre in Bangladesh.

Materials and method:

A total of 62 participants diagnosed with OSCC were recruited in a period of 3 months from a tertiary care dental hospital in Bangladesh (Dhaka Dental College Hospital) where oral cancer patients from all over the country are referred). All the patients with OSCC whose diagnosis were confirmed by histopathological examination admitted in Oral and Maxillofacial Surgery Department were included. The patients with other variants of oral carcinoma like malignancy of salivary gland were excluded.

Socio demographic information was obtained through history of the patient which included age, gender, risk factors like habit of betel quid chewing, smoking

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cigarette, family history of OSCC in 1st degree relative. Oral hygiene status was assessed and categorized as: good, average and poor. Based on Body Mass Index (BMI), nutritional status was observed and classified as: overweight, normal and underweight. Information about initial complaint of patient were also collected via history which included duration of ulcer before getting admitted into hospital, pain, paraesthesia and trismus. Information about clinicopathologic features were collected through clinical examination which included site, size (in cm), type, associated OPMD, 2nd primary lesion and cTNM staging.

Age was categorized as <40-year-old, 40–50-year,51-60-year, 61-70 year, >70-year-old. Habit was classified as: Betel quid chewing only, smoking only, both betel quid chewing and smoking and no habit. Time of complaint was divided into 3 categories; 0-3 months, 4-6 months, 7-12 months. Size was categorized as <2cm ,2-4cm, 4.1-6cm in greatest dimension. Site of ulcer was mentioned as gingivobuccal sulcus, buccal mucosa, alveolar mucosa, retromolar trigone, lateral border of tongue, palatal mucosa and floor of mouth. Type of ulcer was described as exophytic, endophytic, exoendophytic types. All hematoxylin and eosin (HE)-stained histological reports were reviewed for exploring grading of tumours which was divided into: grade I: well-differentiated, Grade II: moderately differentiated and grade III: poorly differentiated. All ulcers are classified according to AJCC cTNM Classification 8th edition.

All information were descriptively analysed and statistical analysis was performed using a standard program (SPSS version 23)

Results:

A total of 62 cases of OSCC were selected for the study after using inclusion and exclusion criteria. Female represented 61% of affected patients where male female ratio is 1 :1.6. Age of the patients was ranging from 26 years to 75 years. Mean age of all the patients was 53 years. 12% patients were younger than 40 year of age. Mean time of initial complaint reported by the patients before diagnosis was 3 months. Site distribution showed that the most common location of tumour was gingivobuccal sulcus (35% cases) followed by buccal mucosa (24% cases). Type of ulcer showed that 75% were exophytic variant,17% were endophytic and 6% were exoendophytic lesion. Mean size of tumour was 3-4 cm in greatest diameter. Only betel quid chewing habit was found in 87% of affected individuals, betel quid with smoking habit was found in 4% cases, no habit was found in 4% cases. Positive Family history was found in 4% of cases. Oral hygiene status was poor in 80% cases and average in 11% cases. Nutritional status showed that 58% patients were underweight, 17% were overweight and 24% of patients had average BMI. Among initial complaints; pain was found in 74% of cases, paraesthesia was found in 8% of cases and trismus was observed in 33% of cases. Associated OPMD was found in 4% cases and 2nd primary lesion was seen in 4% patients. After analysis of HE stained slides, we concluded that: 75% of OSCC were Grade I, 22% were grade II and 1% of all cases studied were grade III. Most of the patients attended the hospital with advanced stage IV disease and was classified as T4aN1Mx according to AJCC TNM classification 8th edition.

Table-I

Sociodemographic features of the oral squamous cell carcinoma from the studied sample (n=62)

Parameter	Number of cases	%
Gender		
Males	24	38.7
Females	38	61.3
Age		
<40 year	10	16.1
40 to 50 year	20	32.2
51 to 60 year	22	35.4
61 to 70 year	9	14.5
>70 year	1	1.6
Habit		
Betel quid chewing only	54	87.1
Smoking only	2	3.2
Betel nut chewing+ smoking cigarette	3	4.8
None	3	4.8
Family history		
Yes	3	4.8
No	59	95.2
Oral hygiene		
Good	5	8.1
Average	7	11.3
Poor	50	80.6
Nutritional status		
Overweight	11	17.7
Normal	15	24.2
Underweight	36	58.0

Table-II

Clinicopathologic characteristics of studied sample (n=62)

Parameter	Number of cases	%
Time of complaint		
0 to 3 months	32	51.6
3 to 6 months	22	35.5
7 to 12 months	8	12.9
Pain		
Yes	46	74.2
No	16	25.8
Paraesthesia		
Yes	5	8.1
No	57	91.9
Trismus		
Yes	21	33.9
No	41	66.1
Type		
Exophytic	47	75.8
Endophytic	11	17.7
Exoendophytic	4	6.5
Size of the ulcer		
<2 cm	2	3.2
2 to 4 cm	31	50
4.1 to 6.0 cm	29	46.8
Site of lesion		
Gingivobuccal sulcus	22	35.5
Alveolar mucosa	13	21
Floor of mouth	1	1.6
Palatal mucosa	5	8.1
Buccal mucosa	15	24.2
Lateral border of tongue	1	1.6
Retromolar trigone	5	8.1
Grade		
I	47	75.8
II	14	22.6
III	1	1.6
OPMD		
Yes	3	4.8
No	59	95.2
Second primary		
Yes	3	4.8
No	59	95.2

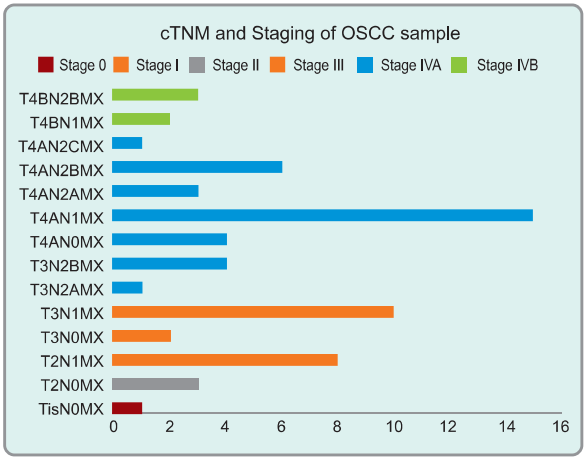

Figure 1: *cTNM and stage of OSCC according to AJCC TNM classification of oral cancer 8th edition: :*

Discussion:

Most of the articles published regarding OSCC all over the world concluded that OSCC is a disease of fifth to seventh decade of life which is similar to our results.[5] In this study we found most of the affected individuals are in their fifties. The average age of patients was 53 years.

Though other studies showed male predilection of OSCC [6] the scenario was different in our study due to a number of reasons. In our study most of the people with OSCC were female, which corroborates with the results of several articles[7]. It may be due to the social tradition of chewing betel quid, related to their daily activities, nutritional status and lack of awareness of the female patients.

Tobacco whether used as smoking or in smokeless forms has the most significant carcinogenic effect in pathogenesis of OSCC[8]. The risk of developing oral cancer is 20 times more in people who smokes tobacco and the risk increases with the increase of number of sticks taken and duration[9].

Alcohol consumption also increases the risk of OSCC by fivefold and there is a synergistic effect of smoking tobacco and consumption of alcohol together in producing OSCC [9] In western countries smoking and alcohol consumption are considered to be the main risk factors [10]. But due to social and religious restrictions, most of the patients are non-alcoholic in our community. So, alcohol consumption is lesser threat in Bangladesh in causing OSCC.

Betel quid chewing is the habit of 20% of the worlds population[11] Due to the high abundance of betel quid in South East Asia including Bangladesh it is the major risk factor in pathogenesis of OSCC. It is confirmed by (IARC International Agency for Research on Cancer) that betel quid is highly carcinogenic to humans which is also mentioned in several articles[12,13,14] The main chemical component of betel quid is an alkaloid chemical called arecoline. In case of long term use it inhibits tumour suppressor genes and thus alters gene expression. It also suppresses the DNA repair mechanism and thus it acts as a carcinogen[9].

Poor oral hygiene is a significant risk factor in occurrence of OSCC. It leads to plaque formation which interacts with saliva and oral microflora like Streptococcus and produces a mutagenic effect and contributes in developing OSCC[15] It is evident that the people who are neglectful of their oral health are more likely to be affected[16] Bangladesh is a third world country and most of the people belong to poor socioeconomic status and are uneducated. They are not aware of maintaining oral hygiene and having regular dental check-ups by a dentist. In our study we found most of the patients had poor oral hygiene.

Assessment of nutritional status was done by measurement of BMI. We found that, 75% of our sample were malnourished which means either they are underweight or overweight with centripetal obesity. The main reason is that, in this community the main food is carbohydrate as it is cheaper and makes them feel full. On the other hand, citrous fruits and colourful vegetables contain dietary antioxidants like vitamin A, C, E which prevents carcinogenic change in the epithelium[17]. Again, folate is a very important micronutrient which has a protective action against OSCC [18]. Low intake of fibrous fruit may be a contributing factor of OSCC[19,20].

There is a controversy regarding family history of cancer being a risk factor of developing OSCC in successors. However, some articles have mentioned multiple family members having cancers for which further investigation is required. In our study only 3 patients had family history of cancer in 1st degree relative. The patients with positive family history of cancer usually have poorer prognosis than others[21].

Ill-fitting denture and sharp tooth acts as a risk factor for OSCC as they cause mucosal trauma. Chronic mucosal trauma causes DNA damage by producing oxidative stress and thus produces a fertile ground for OSCC[22]. In our study we did not see this risk factor.

OSCC which is detected early through the follow up process of (OPMD) has better outcome [23]. In our study associated OPMD was found in 2 cases. If these patients were aware of the disease, then by regular screening these cases could be diagnosed early then the prognosis of the disease could be better.

In our study there were 2 patients with second primary tumor which was 4.8% of total number of patients. In this context it is very important to know the term field cancerization. It means a mucosal area with clone of genetically altered cells in multifocal patches which are capable of developing synchronous or metachronous cancer. Usually, these cases have comparatively worse outcome and strict post operative follow up is needed for early diagnosis of any other lesion in the field[24,25].

Among initial complaints, most of the patients stated that initially there was a non-healing painless ulcer which in course of time increased in size. As most of the individuals attending at this hospital belong to low socioeconomic group they are mostly neglectful of their disease. So, they attend the hospital with moderately advanced disease associated with pain.

Primary site of OSCC vary in different countries of the world as it is associated with cultural habits and prevalence of carcinogenic products[26] For instance in western countries the most common site of OSCC is lateral border of tongue. But the scenario in different in South East Asia due to the prevalence of betel nut and betel leaf. For this reason, Johnson NW in his article mentioned that in South East Asia buccal mucosa is the most common site [27]In our study we also found similar results. The most common site of primary tumour in our study was gingivobuccal sulcus followed by buccal mucosa. In advanced cases where multiple sites were involved, only site of initiation was mentioned as primary site of ulcer.

Considering the type wise distribution of OSCC, in our study most of the lesions were exophytic with raised edges and indurated base. Floor Covered with slough. Some were proliferating growth like a cauliflower. Some were endophytic like a fissure in sulcus. A few cases were endophytic like a non-healing extraction socket with erythematous margin. Few cases were found to be

exoendophytic. In most of the cases the grade of OSCC is well differentiated which corroborates with the results achieved by Rahadiani et al in his study[28]

As most of the patients in this cohort are uneducated and poor, they seek appropriate medical assistance lately which become further delayed because of the presence of malpractice in our community. So, it takes time for the patient to seek institutional help and get admitted into the hospital. For this reason, we found that in most of the cases patients presented with advanced disease at the time of diagnosis.

International Union Against Cancer (UICC) and American Joint Committee on Cancer (AJCC) published their 8th edition of TNM staging in 2017. Tumour staging is based on extend of tumour, cervical lymph node involvement and presence or absence of blood borne metastasis. This staging is important for treatment planning, predicting risk of recurrence and survival of patients [29]. Among all OSCC patients studied majority were in stage IV at the time of diagnosis. In our study size of lesion in average was 3-4 cm in greatest dimension. Most of the patients attended at the hospital with cervical lymphadenopathy which is either reactive or metastatic. However, due to bone or masticatory space involvement most of the patients were in cTNM category T4aN1Mx followed by T3N1Mx.

Conclusion:

Oral squamous cell carcinoma affects patients mostly in their fifties to sixties though an alarming number cases are diagnosed in young below 40 years. Female suffers more than the male. Betel quid chewing can be considered as most important risk factor. Family history of cancer is a matter of concern in oral cancer which is seen in the study. Awareness, early assessment and prompt treatment are necessary for better management and outcome of oral cancer patients.

Limitations:

The main limitation of this study was that the presence or absence of oncogenic Human Papilloma Virus (HPV) infection was not studied among sample patients. High risk oncogenic HPV infection is a controversial risk factor of development of OSCC specially in young adults. The high cost of investigations needed to detect HPV infection was the primary reason for this limitation. However, the current work is valuable in providing insight into the sociodemographic and clinical characteristics of OSCC and thus the findings of this study will act as an add on to the existing literature.

Conflict of interest:

We have no conflict of interest to declare

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