Oral Squamous Cell Carcinoma: Diagnosis and Prognosis Using Carcinoembryonic Antigen as a Tumor Marker

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Abstract:

➢ *Background:*
Squamous cell carcinoma of the oral cavity comprises 90% to 95% of oral malignancies worldwide. In Bangladesh, it has also a high incidence rate. Early diagnosis of oral squamous cell carcinoma can save many lives. Early diagnosis of oral squamous cell carcinoma by serum tumor marker is very important for proper management of the disease.

➢ *Objective:*
This study was conducted to find out the co-relationship between carcinoembryonic antigen and oral squamous cell carcinoma.

➢ *Methods:*
A cross-sectional study of 30 patients were histopathologically diagnosed oral squamous cell carcinoma, admitted in Oral and Maxillofacial Surgery department of Bangabandhu Sheikh Mujib Medical University and Dhaka Dental College Hospital, fulfilling the inclusion & exclusion criteria. To detect the CEA, serum was collected from the patient, inserted into the monoclonal antibody containing reaction vessels of AxSYM system machine. Antigen-antibody complex formed, subsequently washed to remove unbound material, was transferred to the matrix cell where Alkalinephosphatase was added. Furthermore, washed to remove unbound material. Fluorescent product, 4-methylumbelliferyl phosphate was added and measured by the Micropartical enzyme immuno assay optical assembly (MEIA)

➢ *Results:*
In this study, out of 30 cases of oral squamous cell carcinoma patient, majority of the patients were female (56.7%), and mostly from the age group of 51-60 yrs. Most frequent site of the lesion was buccal mucosa (50%), and size of the lesion ranging from $4x3cm^2$ to $1.5x 2 cm^2$. Histopathologically, more than half (60%) of the patients had Grade II lesion, and 50% of the patients had level II lymph node involvement of the neck. The postoperative value of CEA remarkably decreased in comparison to the preoperative value, which is statistically significant ($p<0.05$).

➢ *Conclusion:*
After treatment, a sustained increase in circulating CEA is highly suggestive of residual or concealed metastatic illness. Poor therapeutic response and advancing malignant illness may be linked to a continuously increasing CEA value. A positive prognosis and a satisfactory response to treatment are typically indicated by a lowering CEA reading. As a result, CEA is crucial to the diagnosis and outcome of oral squamous cell cancer.

Keywords: *Carcinoembryonic Antigen; Tumor Marker; Squamous Cell Carcinoma.*

I. INTRODUCTION

Any cancer that starts in the oral tissues is referred to as oral cancer. 90 % to 95 % of oral cancers are squamous cell carcinomas. Among all the cancers that affect people, oral cancer has a very high incidence, which is extremely concerning. Out of all the cancers that can occur in the body, it is the sixth most common. The incidence of oral cancer is high among Bangladeshis. Oral cancer accounts for 20% of the approximately 200,000 new cases of cancer that occur here each year, making it the third most common cancer in Bangladesh [1].

Squamous cell carcinomas are caused by several etiological factors, including genetics, heavy alcohol use, tobacco use, human 3–4 papillomavirus (HPV) infection, and inflammation [2,3].

Any location on the oral mucosa may be affected by OSCC, and large lesions may spread over multiple continuous areas. The tongue, lip, and floor of the mouth are the three most frequently affected areas. On a gross pathological appearance, oral squamous cell carcinoma is typically exophytic, ulcerative, or infiltrative [4]. The majority of cancers exhibit multiple of these traits. Jacobson et al. introduced a grading system that graded the tumor cell population from l to lV based on the frequency of mitotic figures, the degree of differentiation, and the degree of nucleomorphism. According to current theories, the prognosis is correlated with the tumor's depth of invasion, with the incidence of cervical metastases rising as the tumor's depth increases [5].

Histopathology, PET CT scans, and MRIs are used to diagnose and monitor patients with oral squamous cell carcinoma. Early diagnosis, accurate prognostication, and (of late) screening for malignancy in asymptomatic groups are becoming increasingly important in oncology clinical practice. Tumor marker level evaluation before and after surgery is less time-consuming, less risky, and less costly. It also aids in early detection and screening, diagnostic confirmation, prognosis, and therapeutic response prediction, as well as disease and recurrence monitoring. In addition to variable sensitivity and specificity, the prevalence of a particular malignancy may be a major determinant in the application of a particular test as a screening tool.

In some circumstances, serum levels can be used for prognostication, staging, or therapy response prediction. Serum tumor markers are probably most commonly used clinically for disease monitoring. A rise in serum levels may indicate a recurrence of the disease well before any radiological or clinical signs of the illness become noticeable ("biochemical recurrence"). Numerous substances, such as cell surface antigens, cytoplasmic proteins, hormones, enzymes, oncofetal antigens, receptors, oncogenes, and their byproducts, are examples of tumor markers [6]. CEA, a tumor marker, which is one of the most widely used tumor markers worldwide in OSCC [7].

This study aimed to find out the correlation between clinical features, histopathological report and other investigation with pre and postoperative serum or plasma level of CEA. Thus, it may provide a guideline to evaluate the diagnosis and prognosis of oral squamous cell carcinoma.

II. MATERIALS AND METHODS

A. Study Setting and Design

This cross-sectional study was conducted between 17/12/2013 to 17/12/2014 enrolled 30 subjects in an age range of 40-60 years who were admitted in Oral and Maxillofacial Surgery department of Bangabandhu Sheikh Mujib Medical University.

B. Method of Estimating Sample Size and Sampling Technique

Sampling was done purposively (randomized). All Patients having suspected oral squamous cell carcinoma were selected on the basis of provisional diagnosis made by history and clinical examination. Biopsy materials were collected from the suspected lesions of the oral cavity and the diagnosis was confirmed by histopathological examination. Only the patients with histopathologically confirmed oral squamous cell carcinoma were finally selected for the study.

C. Equipment:

The equipment used for biopsy were cotton, antiseptic solution, elastic band, and disposable syringe.

D. Outcome Variable:

The variables recorded during study were age, sex, Area of involvement, Grading- G-l, G-II, G-III, Involvement of the neck- Level-l, Level-ll, Level-III, and carcinoembryonic antigen (CEA)

E. Data Collection:

Data were collected from a total of 30 patients with a clinical and histopathologicaly diagnosed and operable case of Oral squamous cell carcinoma.

F. Evaluation and Diagnosis:

That was done by detailed history, thorough clinical examination, and histopathological evaluation.

Traetment procedure: Excision of the lesion with free margin with or without neck dissection under general anesthesia.
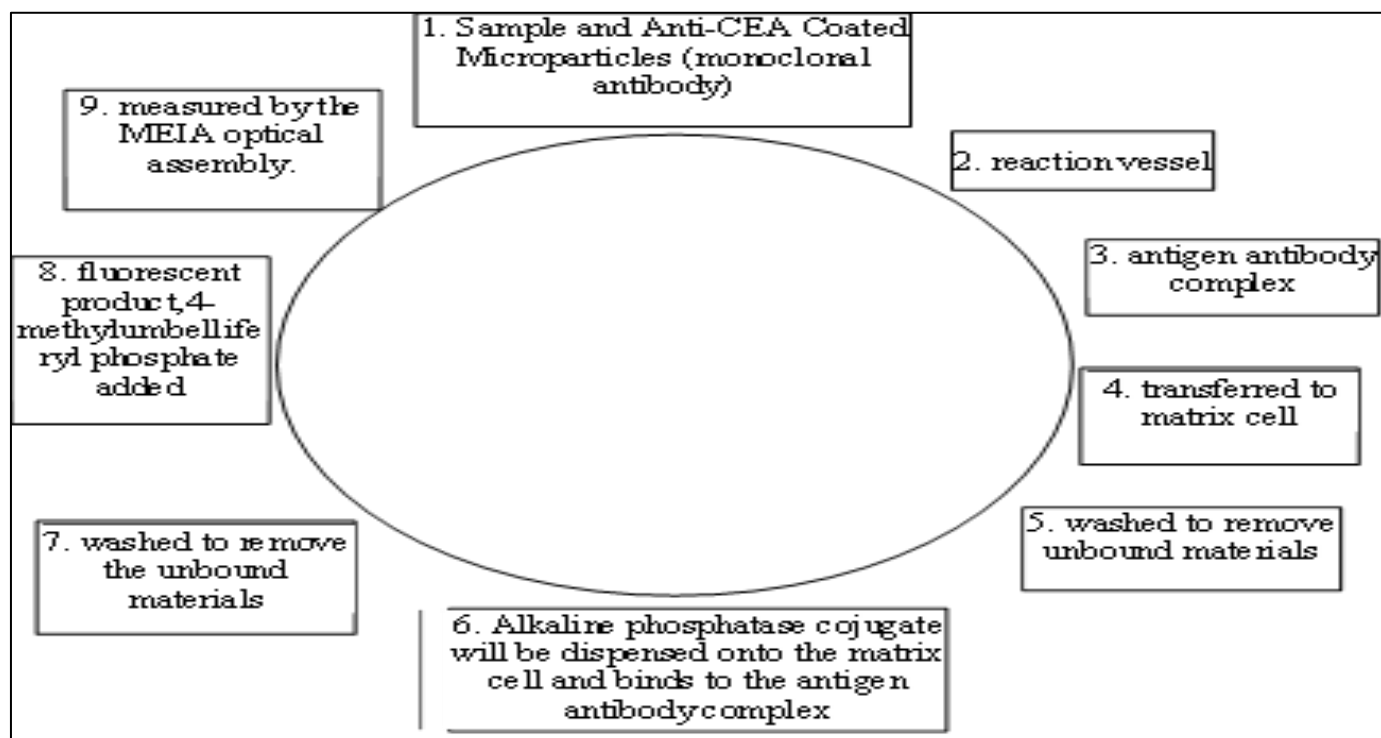
Fig 1: Treatment Procedure

III. RESULT

This cross-sectional study was conducted among histopathologically diagnosed 30 patients of oral squamous cell carcinoma admitted in Oral and Maxillofacial Surgery department of Bangabandhu Sheikh Mujib Medical University and Dhaka Dental College Hospital. Though extensive studies of CEA in oral cancer have been done in Western countries and some Asian countries, not yet been studied in Bangladesh. So, this study may therefore be helpful in providing a Bangladeshi prospective. This study tried to find out a relationship between carcinoembryonic antigen and oral squamous cell carcinoma.

Table 1: Baseline Characteristics of the Participants (n=30):

Attributes	Findings
Age (Years)	40-50: 46.7%; 51-60: 53.3%; Mean age: 50.3 (±7.30)
Gender	Male: 43.3%; Female: 56.7%

With the mean age of 50.3 (±7.30) years, most of the participants were from the age group of 51-60 years (53.3%), predominantly female (56.7%).

Table 2: Distribution of the Patients According to Nature of the Lesion (n=30):

Attributes	Findings
Site	Retromolar area: 36.7%; Buccal mucosa: 50.0%; Alveolar mucosa: 6.7%; Tongue: 6.7%
Lesion size (cm^2)	1.5x2: 6.7%; 2x1.5: 6.7%; 2x2: 23.3%; 2x3: 6.7%; 3x2: 6.7%; 3x2.5: 3.3%; 3x3: 20.0%; 3x4: 13.3%; 4x3: 13.3%
Grading of the lesions	Grade I: 36.7%; Grade II: 60.0%; Grade III: 3.3%

Most frequent site of the lesion was buccal mucosa (50%). The size of the lesion ranging from 4x3cm2 to 1.5x 2 cm2 and most frequent size was 2x2 (23.3%). Histopathologically, more than half (60%) of the patients had Grade II lesion.

Table 3: Distribution of the Patients according to Neck Node Level of the Patients (n=30)

Neck Node Level	Frequency	Percentage (%)
Level I	13	43.3
Level II	15	50.0
Level III	2	6.7

It was found that half of the patients (50%) had level II lymph node involvement of the neck, and the second most (43.3%) was Level I lymph node involvement.

Table 4: Comparison CEA Level in Preoperative and Postoperative in the Study Group (n=30):

	CEA Value		P value
Mean±SD	**Preoperative**	**Postoperative**	**<0.001**
	3.09±1.45	1.69±1.09	

Regarding the change of CEA level in preoperative and postoperative patients, the postoperative value of CEA remarkably decreased in comparison to the preoperative value, which is statistically significant ($p<0.05$).

IV. DISCUSSION

These findings were compared with different subgroups of participants within the study and with the findings of other relevant studies.

According to data 43.3% were male and 56.7% were female of total study subject. The age group ranges from 40 to 60 years where majority of the study subjects belonging to the age group of 51 to 60. This data corresponds with the information of Zadeed (2013)1 where they found the incidence of oral SCC in higher age group mostly in 7th decade.

On clinical examination of the lesions, it was found that the most common site of oral SCC was buccal mucosa (50%), retromolar area (36.7%), tongue (6.7%). Similar findings were reported by Zadeed (2013)1 where buccal mucosa followed by tongue was the most occurring site for OSCC.

Tumor size of two patient has 1.5x2 cm2 (6.7%), two patient had 2x1.5 cm2(6.7%), seven had 2x2 cm2(23.3%), Two patient had 2x3 cm2(6.7%), two patient had 3x2 cm2(6.7%), one patient had 3x2.5 cm2(3.3), six patient had 3x3 cm2 (20%), four patient had 3x4cm2(13.3%), four patient had 4x3cm2(13.3%). According to this study, with increasing size of the lesion, the CEA value may increase significantly. This data corresponds with the information of Kuhel WI et al. (1995)8 where they found that CEA value increased with progression of the lesion and decreased with regression of the lesion.

Histopathologically 11 patients had Grade l (36.7%),18 patients had Grade II (60%), 1 patient had Grade III (3.3%). According to neck node involvement 13 patients had level l (43.3%), 15 patients had level II (50%), 2 patients had level III (6.7%). According to this study CEA value may increase with the grading and involvement of neck node level. E K Walther et al. (1993)9 found that the tumor marker elevated in 73% cases in untreated patient and found no significant correlation between serum level of the marker and tumor location and grading. Hideo Kurokawa et al. (993)10 reported that sensitivity and specificity of CEA in oral SCC patients was 34.5% and 91.7% respectively which may correspond with this study.

In this study it was found that preoperative CEA value is 3.09 ng/ml and SD 1.45. Postoperative CEA value 1.69 ng/ml and SD 1.9. p value is <0.001 (significant).

This study concludes that CEA has significant relationship with oral cancer in its progression and regression.

V. CONCLUSION

CEA testing is very useful for tracking patients who have been diagnosed with cancer and whose CEA concentrations are fluctuating. After treatment, a sustained increase in circulating CEA is highly suggestive of residual or concealed metastatic illness. Poor therapeutic response and advancing malignant illness may be linked to a continuously increasing CEA value. A positive prognosis and a satisfactory response to treatment are typically indicated by a lowering CEA reading. According to the study's findings, a postoperative CEA value below 2.5 ng/ml was linked to a better prognosis, and an elevated preoperative CEA value offers greater insight into the patient's chances of survival by indicating a more aggressive tumor and most likely identifying a patient who needs adjuvant therapy.

REFERENCES

[1]. Zadeed R. Thesis on oral cancer and Bangladesh.13. Jun, 2013; available at: http://issuu.com/zadeed/docs/thesis_on_oral_cancer_and_banglades.

[2]. Warnakulasuriya S, Sutherland G, Scully C. Tobacco, oral cancer, and treatment of dependence. Oral Oncol 2005;41(3):244-60.

[3]. Hashibe M, et al. Alcohol drinking in never users of tobacco, cigarette Smoking in never drinkers, and the risk of head and neck cancer:pooled analysis in the International Head and Neck Cancer Epidemiology Consortium. J Natl Cancer Inst 2007;99(10):777-89.

[4]. Lumerman H, Freedman P, Kerpel S. Oral epithelial dysplasia and the development of invasive SCC. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1995,79:321-9.

[5]. Watkinson J C, Gaze MN, Wilson JA. Stell and Maran's Head and NeckSurgery, 4th ed 2000: 275-316.

[6]. Sharma S. Tumor markers in clinical practice: General principles and guidelines. Indian J Med Paediatr Oncol. 2009; 30(1): 1–8.

[7]. Perkins GL, Slater ED, Sanders GK, Prichard JG. Serum tumor markers. http://www.aafp.org/afp/2003/0915/p1075.html. Am Fam Physician. 2003; 15: 1075–1082.

[8].   Kuhel WI,Chow H ,Godwin Ta,Minick CR,Libby DM. Elivated Carcinoembryonic antigen levels correlating with disease recurrence in a patient with adenoid cystic carcinoma . Head Neck1995;17 (5):431-436.

[9].   Walther EK, Dhahimann N, Gorgulla HT. Tumour Markers in the diagnosis and follow-up of head and neck cancer; role of CEA, CA19-9.SCC, TK,and dTTPase.Head Neck 1993;15(3)230-235

[10].   Kurokawa H,Tsuru S, Okada M,Nakamura T, Kajiyama M, Evaluation of tumour markers in patients with squamous cell carcinoma in the oral cavity. Int J Oral Maxillofac Surg. 1993;22(1):35-8.