

ORIGINAL RESEARCH

Correlation of serum cortisol levels with histopathological grading of oral squamous cell carcinoma

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ABSTRACT

The overall national 5yr survival has been reported to vary in range according to tumor size {T1/T2 commonly referred to as “low risk tumor” & T3/T4 commonly referred to as “High risk tumor”}. The outcome is greatly influenced by the stage of the disease especially pathological TNM stage. Patient’s clinical parameters were recorded which include age, sex, tumor location, tobacco and alcohol use and medical history. Through clinical examination in which the site of the lesion and the extent of the lesion were assessed. The clinical staging was assessed by AJCC TNM staging. Comparison of PN status with cortisol levels was done using Mann-Whitney test. In PN+ group mean cortisol level was 13.34 with SD +_5.67 & in PN_group mean cortisol level was 12.71 with SD +_4.87. There was significant difference in the cortisol levels in both the groups since p=0.9346.

Key words: Serum cortisol levels, histopathological grading, oral squamous cell carcinoma

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INTRODUCTION

Oral and oropharyngeal carcinomas are the sixth most common cancer in the world¹⁰. It is the third most common form of malignancy in the developing countries, while in the developed countries it is the eight most common form of cancer. 57.5% of head & neck cancer occur in Asia. The incidence of oral cancer in India is 30% because of tobacco chewing is used with betel nuts and reverse smoking. Despite evolution in management, the overall survival of patients has not improved significantly during the past 20yrs with 5yr survival rate between 45-50%.¹

Prognosis of disease depends on various factors like primary tumor, site, stage, tumor thickness, nodal involvement, status of the surgical margins and associated co morbidities. Moreover, cumulative effects of tobacco, betel nut and alcohol decrease the survival rate. The overall national 5yr survival has been reported to vary in range according to tumor size {T1/T2 commonly referred to as “low risk tumor” & T3/T4 commonly referred to as “High risk tumor”}.

The outcome is greatly influenced by the stage of the disease especially pathological TNM stage.²

Studies have shown that cancer progression does not occur only due to local factors related to the tumor, but that it is also influenced by psychoneuroimmunological factors inherent in the patient. The link between psychological and physiological features of cancer risk and progression have been studied through psychoneuroimmunology.³

The persistent activation of HPA in the chronic stress response and in depression probably impairs the immune response and contributes to the development and progression of some type of cancer. Stress and depression are associated with decreased cytotoxic T-cells and natural killer cells activities that affect processes such as immune surveillance of tumor and with the events that modulate development and accumulation of somatic mutations and genomic instability.⁴

METHODOLOGY**INCLUSION CRITERIA**

- Patients with biopsy proven case of squamous cell carcinoma.

EXCLUSION CRITERIA

- Patient with recurrence of oral cancer.
- Patient with previous radiotherapy.
- Patients with previous history of endocrine disorders.
- Patients who have received steroid therapy in the last 5yrs.

METHOD

Patient's clinical parameters were recorded which include age, sex, tumor location, tobacco and alcohol use and medical history. Through clinical examination in which the site of the lesion and the extent of the lesion were assessed. The clinical staging was assessed by AJCC TNM staging.

Plasma sample-

All the patients were fasting in the morning before blood collection, in order to prevent the changes in hormonal levels due to oral intake. Blood samples were collected from the patients in the early morning along with blood for routine blood investigation. Patients' blood was drawn in a plain syringe and sent to department of biochemistry, SDM College of medical sciences and hospital to assess the serum cortisol levels. Then serum cortisol level estimation was done using ADIVA centaur CP assay which is a competitive immunoassay using direct chemiluminescent technology.

The obtained serum cortisol levels was correlated with TNM staging which was done prior to the surgery and then correlated with histopathological grading of the excised tumor using BRYNE'S invasive tumor front grading system and nodal metastasis which was confirmed with histopathology of the neck specimen.

RESULTS**Table 1: Histopathological nodal status{PN} distribution of patients**

Nodal Involvement	No. of Patients	Percentage	Cortisol Levels	
			Mean	S.D.
pN +	11	44	13.3	5.6
pN -	14	56	11.8	5.7

Table 2: Comparison of PN status after HPR with Cortisol levels (µg/dl) by Mann-Whitney Utest

PN status after HPR	Mean	SD	Sum of ranks	U-value	Z-value	P-value
PN-	12.71	4.87	180.50	75.50	-0.0821	0.9346
PN+	13.35	5.67	144.50			

Table 3: Correlation between TNM stage, TMS and Pn-and PN+ with Cortisol levels (µg/dl) by Spearman's rank correlation method

Variables	Cor	relation between Cortisol levels (µg/dl) with		
	N	Spearman R	t-value	p-level
TNM	25	0.8796	8.8669	0.00001*
TMS	25	0.2412	1.1918	0.2455
PN status after HPR	25	0.0168	0.0804	0.9366

*p<0.05

Patients were divided into two 2 groups after HPR for Histopathological nodal status distribution. Group 1 positive node (PN+) consists of 11 patients (44%) and group 2 negative node (PN-) consists of 14 patients (56%).

Comparison of PN status with cortisol levels was done using Mann-Whitney test. In PN+ group mean cortisol level was 13.34 with SD +_5.67 & in PN _ group mean cortisol level was 12.71 with SD +_ 4.87. There was significant difference in the cortisol levels in both the groups since p=0.9346.

Correlation between TNM stage, TMS score and PN status with serum cortisol levels was done by Spearman's rank correlation method. Correlation between TNM stage and cortisol level was statistically significant with p=0.0001.

There was no statistical significant correlation between TMS & PN status with cortisol levels as p=0.24 & 0.93 respectively.

DISCUSSION

Although changes in cortisol levels have been reported in many types of cancers, this hormonal dysregulation has not yet been investigated in patients with oral and oropharyngeal cancer³.

In our study OSCC was more commonly seen in males which is in consensus with the studies done at different centers, which showed that oral cancer is commonest among males in India.

All these patients were biopsy proven case of squamous cell carcinoma of oral cavity involving buccal mucosa, tongue, FOM, RMT & BM, lip & BM. Studies have shown that Oral squamous cell carcinoma may occur anywhere in the mouth,

although the most affected sites are tongue, lower lip and floor of the mouth. Features of these regions greatly facilitate carcinoma spreading to regional lymph nodes and/or distant organs. Increased levels of cortisol were most pronounced in oral SCC patients with advanced stage disease (clinical stage 3 & 4). This indicate an HPA axis dysregulation in these patients, associated with disease progression. Neuroendocrine changes, such as increased systemic cortisol levels compared with healthy controls, have been observed in patients with tumors in other locations like breast, liver, colon and ovaries³. In our study we estimated the cortisol levels in biopsy proven cases of oral squamous cell carcinoma patients and compared with stage of the cancer.^{5,6}

Studies have shown that the risk factors in the healthy volunteers, such as cigarette smoking and alcohol consumption, had no effects on the cortisol levels³.Lundstorm *et al.* did not find difference in morning salivary cortisol levels between drinker and non-drinker in a large sample of volunteers.⁷

In our study clinical staging was assessed by AJCC TNM staging. But Studies have shown that there is a growing concern that TNM staging is insufficient to accurately map or classify OSCC, whose biological impact may be related to volume and pathological aggressiveness of disease. Tumor diameter or surface greatest dimension is used to indicate tumor size in the TNM system¹⁸.However, this is not the most accurate when compared to tumor thickness or depth of invasion, which can be related directly to prognosis.⁸

The main finding of this study was that patients with oral SCC showed higher levels of morning serum cortisol. Cortisol levels increased as the stage of the cancer advanced. So, this study provides strong evidence that OSSC cells are influenced by neurohormonal mediators.

CONCLUSION

Comparison of PN status with cortisol levels was done using Mann- Whitney test. In PN+ group mean cortisol level was 13.34 with SD +_5.67 & in PN _ group mean cortisol level was 12.71 with SD +_ 4.87. There was significant difference in the cortisol levels in both the groups since p=0.9346.

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