

# Hematological Changes in Oral Cancer Patients with Smoke-able and Chew-able Tobacco.

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## ABSTRACT

**Objective:** To analyze hematological changes in patients of oral cancer with history of smoke able and chewable tobacco use, and to compare them with healthy controls.

**Study Design:** Descriptive type of study survey.

**Setting:** This study was conducted at department of Oral and Maxillofacial Surgery, LUMHS, Jamshoro.

**Study Period:** One year July, 2013 to July, 2014.

**Subject & Methods:** Histo-pathologically confirmed hundred cases of oral cancer with history of smoke able and non-smoke able tobacco were selected to analyze the hematological variation.

**Inclusion Criteria:** Histopathologically diagnosed patients of oral squamous cell carcinoma, with history of smoke able and non smoke able tobacco.

**Exclusion Criteria:** Patient with any systemic medically compromising problem, terminally ill patients, radio or chemotherapeutically treated patients, patients with metastasis to lungs or any distant metastasis, patients with history of more than one well defined etiological factor involved.

**Keywords:** oral cancer, hematological variations, tobacco, smokers.

**Results:** There were 73% patients of oral cancer reported with anemic. Significantly lower values of Hb, Platelet and higher mean values of ESR, TLC and were observed in both groups of oral cancer patients; tobacco smokers and tobacco chewers as compared to non-smokers healthy controls. There was more decline in the level of haemoglobin and incline in the level of ESR observed in tobacco chewer oral cancer patients as compared to tobacco smokers patients, while TLC was more observed in smokers.

**Conclusion:** Oral cancer patients with history of chewable/smoke able tobacco have likely worse hematological profile, which increases the anesthetic and surgical challenges for maxillofacial surgeons, which have significant impact on treatment planning as well.

## INTRODUCTION

Oral cancer is growing as a wide spread and frequent problem in population of Sindh. (1) It can involve in any part of the oropharyngeal region. In other study the most frequent site reported was tongue (35.9%) followed by cheek (21.3%), buccal vestibule (16.6%), lip (13.7%) soft palate (7.7%), hard palate (3.2%) and gum (1.6%). Histologically, the most frequent malignancy reported was oral squamous cell carcinoma (96.2 % of cases of oral cancer). It is observed more common after 4<sup>th</sup> decade of life.<sup>1</sup>

A number of factors (environmental factor, life style, habits and food) are associated with pathogenesis of oral cancer. Oral cancer was reported as one of the frequent oral problem in population of Sindh and incidence proportion of oral cancer at Dental OPD Hyderabad/Jamshoro found to be  $\pm 0.54\%$  per year.<sup>1</sup> It is estimated that large number of people of Jamshoro/Hyderabad are tobacco users in form of smoking and betel quid, main puri and gutkha (large proportion of tobacco mixed with areca nut).<sup>2</sup> Tobacco usage in form of areca nut, mixture of betel quid and smoking has complex behavior pattern. Betel quid have leaf of betel, slaked lime and areca nut, to which tobacco is usually added. <sup>3,4</sup> Betel quid chewing reported as is a primary etiological factor for oral cancer along with pharynx and upper digestive tract.<sup>5</sup> There were very less attention to hematological parameters in smokers, and tobacco, betel quid and areca nut chewers.<sup>6</sup> Blood performs the most significant and sensitive functions of the body. Usually most valuable information frequently observed from hematological investigations.<sup>7</sup> Many pathologies and disorders show alterations of blood parameters

like leukopenia, anemia, basophilia, eosinophilia, and thrombocytopenia. Polymorphonuclear neutrophils have very significant role in the acute inflammatory processes, while monocytes, macrophages and lymphocytes are important part of chronic inflammatory response and immune system.<sup>7,8</sup> Eosinophils are important in antigen-antibody reactions occurs in case of dermatological, allergic conditions and chronic parasitic while basophilic granules have a variety of inflammatory chemicals like chondroitin sulphate and histamine, upon stimulation also activate other mediators.. Hemoglobin is metallo-protein of erythrocytes, contains iron, which is involves oxygen transportation in through the blood.<sup>8</sup> It carries oxygen from the human lungs to the body tissues, where it utilize in oxidation of food for energy production, and also it brings back carbon dioxide, which is produced as bi-product of oxidation of food, to get expelled out from the body. <sup>9</sup>

This study was carried out to assess whether adverse hematologic effects in Oral cancer patients as a consequence of carcinogenesis and to comparatively analyze the hematological changes in smoke-able tobacco users and non-smoke-able tobacco users. (10) This study will reveal the significance of bio-chemical variations in form of hematological and metabolic changes and in patients with oral cancer, which will be eventually helpful in early diagnosis of oral cancer. It also highlights harmful outcomes of different etiological factors involved with any particular patients. The understanding of specific etiological factor related hematological profile variation will be helpful in generating treatment guide lines for surgeons. It will also give information regarding particular pathological conditions (e.g. sideropenic anemia, Paterson Kelly syndrome) associated with oral cancer. Better understanding of their association will make a better management of such pathologies.<sup>11</sup>

## SUBJECTS AND METHODS

This study was conducted at the Department of Oral & Maxillofacial Surgery, LUMHS, Jamshoro. The study sample comprised 150 subjects including 100 histologically confirmed cases of oral squamous cell carcinoma and 50 age matched non-smokers healthy controls. Oral cancer patients were classified into two groups with respect to etiological factor involved, 50 non smoke able tobacco users (betel leaf, areca nut and tobacco chewers), 50 smoker able tobacco users. After verbal information provided, subjects were asked to fill a written informed consent form and data were collected regarding their

personal factors (sex, age, health, working period, etc.) and lifestyles. From obtained data no significant difference was observed between the groups with respect to personal factors and lifestyle. Patient with any systemic medically compromising problem, Terminally ill patients, patients with metastasis to lungs or any distant metastasis, radio or chemotherapeutically treated patients, patients with history of more than one well defined etiological factor involved were not included in study sample.

## HEMATOLOGICAL ANALYSIS

After overnight fasting, from each subject 10ml of venous blood samples were obtained from vein puncture by using disposable syringe and shifted into EDTA coated tubes. The samples were centrifuged at 3000 rpm for half an hour to separate serum. The EDTA tubes were used for analyzing Hb, ESR, DC and TLC. Erythrocyte counts and leukocyte counts were analyzed in samples using a T540 cell coulter. The packed corpuscular volume and other parameters of each subject were analyzed by standard procedures.

## STATISTICAL ANALYSIS

All statistical analysis was performed using SPSS version 17.0. Values are represented in mean  $\pm$  S.E.

## RESULTS

The general characteristics of study sample were mentioned in Table.1. The study sample was analyzed based on the histological confirmation of oral cancer and hematological differences were observed within the study group depending on recognized etiological factor involved, group with smoke able tobacco and other group with chewable tobacco, were compared with healthy control. The hematological parameters observed were Hb content(Hb), Red cell count(RCC), Mean corpuscular haemoglobin(MCH), Mean corpuscular volume(MCV), Erythrocyte sedimentation rate(ESR), Platelets count, Total leukocyte count (TLC), percentages of granular (neutrophils, eosinophils and basophils) and agranular (lymphocytes and monocytes) leukocytes of all groups (Table.1). Statistically significant( $p < 0.05$ ) lower values of Hb, Platelet and higher mean values of TLC and ESR were observed in both groups of oral cancer patients; tobacco smokers and tobacco chewers as compared to non-smokers healthy controls. There was lower level

**Table.1: General characteristics of Oral Cancer Patients.**

Characteristics	No. (%)
<b>No. of patients</b>	100
<b>Sex</b>	
Male	63 (%)
Female	47 (%)
<b>Etiology</b>	
Tobacco Smoking	50 (%)
Tobacco Chewing	50 (%)
<b>Age</b>	
Under 40 years	41 (%)
Above 40 years	59 (%)
<b>TNM Staging</b>	
Stage I	37 (%)
Stage II	57 (%)
Stage III	06 (%)
Stage IV	00 (%)
<b>Histological Grading</b>	
Grade I	68 (%)
Grade II	32 (%)
Grade III	00 (%)
Grade IV	00 (%)
<b>Site</b>	
Tongue	45 (%)
Buccal mucosa	23 (%)
Floor of mouth	21 (%)
Gingival	3 (%)
Oro-pharynx	2 (%)
Others	6 (%)

of hemoglobin and higher in the level of ESR observed in tobacco chewer oral cancer patients as compared to tobacco smokers patients (Table.2).

There were 73% patient of oral cancer reported with anemic, depending on MCV and MCH findings; the most frequent type of anemia observed was normochromic normocytic anemia (47.88% of cases of anemia) followed by hypochromic microcytic anemia (32.39% of cases of anemia). The mean level of total leukocyte count was higher in smokers as compared to tobacco chewers, increases the like hood of more intense inflammatory reactions in smokers (Table.2). The percentage of Lymphocytes, Eosinophils and Basophils were significantly higher in chewers, while the percentages

**Table.2: Showing different parameters of hematological analysis of subjects with oral cancer as compared to healthy controls**

Parameters	Chewable tobacco users (n=50)	Smoke able tobacco users (n=50)	Controls (n=40)
Hb (g/dl)	12.1 ± 0.64	13.17 ± 1.21	14.56 ± 1.02
ESR (mm/hr)	13.89 ± 0.23	13.62 ± 0.54	13.40 ± 0.63 d
RCC (10 <sup>12/L</sup> )	4.12 ± 4.94	4.21 ± 7.33	4.92 ± 4.21
MCV (fL)	81.46 ± 11.4	81.49 ± 8.7	88.52 ± 6.9
MCH (pg)	26.14 ± 6.98	25.79 ± 7.43	27.76 ± 8.32
TLC (10 <sup>6/L</sup> )	9273.75 ± 1010.20	9482.01 ± 1123.04	9471.06 ± 1192.04
Neutrophils (%)	54.69 ± 1.71	59.32 ± 2.86	53.67 ± 2.08
Lymphocytes (%)	32.18 ± 0.73	28.65 ± 0.53	35.25 ± 0.84 d
Eosinophils (%)	3.30 ± 0.43	2.52 ± 0.34	2.60 ± 0.51
Monocytes (%)	7.38 ± 0.05	8.09 ± 0.21	6.16 ± 0.15
Basophils (%)	1.03 ± 0.03	0.74 ± 0.02	0.86 ± 0.02
Platelet (10 <sup>9/L</sup> )	208.29 ± 22.31	206.47 ± 19.48	225.29 ± 21.52

of Polymorphonuclear neutrophils and Monocytes were higher in tobacco chewers than smokers for oral cancerous patients (Table.2).

## DISCUSSION

Oral cancer is a frequent problem at maxillofacial tertiary care centers with significant rates of mortality, an enormous impact on quality of life and morbidity.<sup>12</sup> In the past this has been predominantly a disease of the elderly with known epidemiologic risk factors, however this appears to be changing. The principle recognized risk factor is habitual use of tobacco in of smoke able and chewable forms.<sup>13</sup> Development of severe hematological changes in patients with oral cancer results in prolonged hospitalization increased cost, anesthetic or surgical difficulty and treatment interruption. Using proper investigations that can identify the patients at higher risk for developing post operative infections, bleeding emergencies and delayed healing, would enable surgeons to individualize surgical treatment protocols.<sup>14, 15</sup> Vogue of the habitual smoking and chewing tobacco is growing because of its lack of awareness regarding well known harmful effects, cheaper cost and free availability. Many studies have reported that use of chewable tobacco is as hazardous as tobacco smoking. Studies from South East Asia, reported that tobacco is a primary cause factor of

mortality in patient of oral cancer.<sup>16-18</sup> Studies also reported higher ESR in smokers with vast inflammatory changes in lungs and respiratory dysfunctions. In case of tobacco use, increase in TLC may show a reactionary inflammatory response or a secondary leukocyte production to toxins or pathology. The TLC is a represents ongoing tissue inflammation or inflammatory activity from any primary or secondary cause. Evidence has shown elevations of this inflammatory bio-marker in cases of ischemic cardiac disease, respiratory dysfunction, and carcinogenesis. The strong and intriguing relation between the smoke able/ chewable tobacco and carcinogenesis was found to be issue of public health hazards.<sup>19-21</sup> This study will reveal the better understanding of hematological changes and variations in malignant patients of oral cavity, which will eventually helpful in early detection of oral cancer. It will also give information regarding harmful outcomes of particular etiological factors involved in case of oral cancer. The knowledge of hematological profile variation related with specific etiology will be helpful in generating treatment guide lines for maxillofacial surgeons. Most treatment options for oral cancer patients are selected on the basis of predictive and prognostic factors. However, due to the limited prognostic value of heamatological investigations in oral cancer, many patients are still under - or - over treated. Incorporation of these adjuvant prognostic tools will better reflect the treatment diversity

of oral cancer and more accurately assist in clinical responses and outcomes to every particular case.<sup>22-24</sup>

These hematological finding could be use as clinically valuable prognostic indicators to assist in more selective treatment options for oral cancer for oral cancer patients. (25) It will also hi-light particular pathological conditions (e.g. sidropenic anemia, Paterson Kelly syndrome) associated with oral cancer. Better understanding of their association will make a better management of such pathologies.

## CONCLUSION

This study concluded that oral cancer patients with history of chewable/smoke able tobacco use have likely worse hematological profile, which increases the anesthetic and surgical challenges for maxillofacial surgeons, which have significant impact on treatment planning as well.

## REFERENCES

1. Saira Baloch, Bikha Ram Devrajani, Mirza Arsalan Baig. Frequency of Oral Cancer in Patients visiting Dental OPD LUMHS, Jamshoro & Hyderabad. Indo American Journal of Pharmaceutical Research, 2013, 5024-5029.
2. Church DF, Pryos WA. The oxidative stress placed on the lung by cigarette smoke. In:Crystal RG, West JB ed., The lung: scientific foundation, New York, Raven 1991: 1975-9.
3. Adhvaryu, S.G., Bhatt, R.G., Dayal, P.K., Trivedi, A.H., Dave, B.J., Vyas, R.C. & Jani, K.H. (1986) SCE frequencies in lymphocytes of tobacco/betel nut chewers and patients with oral submucous fibrosis. Br. J. Cancer, 53, 141-143 Sherman CB. Health effect of cigarette smoking, Clin. Chest Med., 1991; 12:643.
4. Adhikary, P., Banerji, J., Choudhuri, D., Das, A.K. Deb, C.C., Mukherjee, S.R. & Chatterjee, A.(1990b) Effect of Piper betle Linn (stalk) extract on male rat fertility. Indian J. Pharmacol.,22, 145-149
5. Spitz MR, Newell GR: Descriptive epidemiology of squamous cell carcinoma of the upper aerodigestive tract. Cancer Bull 39(2): 79-81, 1987.
6. Sharma, M.L. and A.K. Awasti , 2001. Haematological and biochemical characteristics of *Heteropneustes fossilis* under the stress of congo red (diphenyl disazo biophthionic acid. Toxicol. lett. 14: 237-241.
7. Beris P, Waldvogel FA. Hematologic alterations in Infectious disease patients. In: Root KR, Waldvogel F, Corey L, Stamm WE,(eds). Clinical Infectious Diseases. A Practical approach. Oxford Medical Publications:New York;1999. Pp121-31.
8. Jyothirmayi B, Kaviarasi S , Ebenezer William .Study of glycated hemoglobin in chronic cigarette smokers, IJPCR, 2013; 5(1): 4-6.
9. Bijilani RL, Manjunath S. The white blood cells. In: Understanding Medical physiology,4th ed. Jaypee brothers medical publishers (P) ltd, New Delhi.2011: 66-70 .
10. Gitte RN .Haemoglobin concentration erythrocyte count in smokers of Andhra region, NJIRM, 2012; 3(1):30-33.
11. Rajsekhar, G., Ramgopal, M., Sridevi, A. and Narasimha, G. Some hematological and biochemical parameters insmokeless tobacco (Jardah) chewers, Afr. J Biotech., 2007;6 (1):53-54.
12. Are C, Rajaram S, Are M, Raj H, Anderson BO, Chaluvarya Swamy R, Vijayakumar M, Song T, Pandey M, Edney JA, Cazap EL. A review of global cancer burden: trends, challenges, strategies, and a role for surgeons. J Surg Oncol. 2013;107(2):221-226.
13. T Rooban, Elizabeth Joshua, Umadevi K Rao, K Ranganathan. Prevalence and correlates of tobacco use among urban adult men in India: A comparison of slum dwellers vs. non-slum dwellers. Indian J Dental Res 2012.23:31-8.
14. Shenwai MR and Aundhakar NV. Effect of cigarette smoking on various haematological parameters in young male smokers,IJBAMR, 2012; 5(2):386-392.
15. Dass BP, Jagannathan P and Sravanakumar P. Changes in hematological and biochemical parameters in smokeless tobacco (ST) chewers in costal belt of Andhra Pradesh, India, Europ. J. Biol. Sci.,2013; 5 (1): 29-33.
16. Hunning Hake GW, Crystal RG. Cigarette smoking and lung destruction, Accumulation of neutrophils in the lungs of cigarette smokers. AM. Rev. Respir. Dis .,1983; 128: 833-8.Crowell RJ, Sarnet JM. Invited commentary: why does the white blood cell count predict mortality?Am J. Epidemiol., 1995; 142: 499-501.
17. Yasmin S, Neha, Tahmina, Mamta, Stuti S, Rastogi N and Das J .Negative impact of gutkha on certain blood parameters of Swiss mice ,Bulletin of Pure & Appl. Sci. ,2007;26 (2):75-79.
18. Jagannathan P, Phaninathan A, Sarma A. Studies on changes in hematological and biochemical parameters in smokeless tobacco (Gutka) chewing auto drivers in Nellore district of Andhra Pradesh, India, JANS, 2011; 3 (1): 106-107.
19. Grimm RH, Tell G.S., Vellar O.D. Theodorsen L. The relationship of leukocyte, platelet count and hematocrit to cigarette smoking in adolescents: The Oslo youth study, Circulation ,1985; 72: 971-974.
20. Schwartz J, Weiss ST. Cigarette smoking and peripheral blood leukocyte differentials. Ann. Epidemiol.1994; 4: 236-242.
21. Ogawa Y, Imaki M, Yoshida Y. Shibakawa M., Tanada S. An epidemiological study on association between TLC and neutrophil counts and risk factors of I.H.D. by smoking status in Japanese factory workers, Appl. Human Sci., 1998; 17 (6): 239-247.
22. Jensen EJ, Pedersen B, Frederiksen R, Dahl R. Prospective study on the effect of smoking and nicotine substitution on leukocyte blood counts and relation between blood leukocytes and lung function, Thorax, 1998; 53: 784-789.
23. Kumar J,Kumar G, Sharma A, Khan FA and Sharma S. The effect of smoking on the blood parameters of young adults, JCDR, 2012, 6(7): 1244-1247.
24. Haider MJ and Rauf A. Smoking habits and their association with total leukocytes count among healthy men in Karachi, Pakistan, WASJ,2010; 11 (6): 669-673.
25. Silverman S Jr. Clinical diagnosis and early detection of oral cancer. Oral Maxillofac Surg Clin North Am 1993;5:199-205.