

Lymphocyte And Granulocyte Count as A Potential Prognostic Marker for Oral Cancer

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ABSTRACT:

INTRODUCTION: Inflammation of epithelial tissues is a normal and essential pathologic disorder that may occur alone or in conjunction with neoplasia. It is related not only to the existence of cancer but also to the initiation of cancer due to damage caused by inflammatory cells' oxidative activity. Oral cavity cancer affects 640,000 people worldwide each year, with just half of those diagnosed surviving for more than five years, three types of WBCs are collected from the bloodstream to the site of injury in general. Monocytes and lymphocytes make up mononuclear leukocytes, whereas neutrophils make up polymorphonuclear leukocytes, basophils, and eosinophils

AIM: The study aims to use lymphocyte and monocyte count as the prognostic factor for cancer patients.

MATERIALS AND METHODS: The present study involved control patients and patients affected with any type of oral cancer. From the laboratory digital record system, 10 were cancer patients and the rest 10 were normal or control patients, and parameters like gender, age, stages of cancer and grading, Lymphocyte count, Lymphocyte monocyte ratio were noted.

RESULTS: According to the study, 50% of the cancer patients are between 41-50 years of age, 70% of the Oral cavity cancers are well-differentiated type of squamous cell carcinoma, most common stage of OSCC (40%) at the time of diagnosis is stage 4a, followed by stage 1.

CONCLUSION: Our present finding indicates a decrease in lymphocytes monocytes ratio and increases in granulocyte ratio as the stage of cancer increases

KEYWORDS: Control; Oral carcinoma; Wbc percentage; Lymphocyte Monocyte ratio, innovative technique.

INTRODUCTION:

Inflammation of epithelial tissues is a normal and essential pathologic disorder that may occur alone or in conjunction with neoplasia. It is related not only to the existence of cancer but also to the initiation of cancer due to damage caused by inflammatory cells' oxidative activity (Weitzman and Gordon, 1990). White Blood Cells count in cancer patients is low. WBC count can be used to monitor bone marrow function (Kur *et al.*, 2020) and can be used in inflammatory markers (Seong, 2015). Oral cavity cancer affects 640,000 people worldwide each year, with just half of those diagnosed surviving for more than five years (Lin *et al.*, 2005). Three types of WBCs are collected from the bloodstream to the site of injury in general. Mononuclear leukocytes (agranulocytes) and polymorphonuclear leukocytes (granulocytes) are the two forms based on their nuclear appearance and the presence of granules (granulocytes). Monocytes and lymphocytes make up mononuclear leukocytes, whereas neutrophils make up polymorphonuclear leukocytes, basophils, and eosinophils (Elangovan *et al.*, 2012; Rithanya and Brundha, 2020). During the development and progression of cancer, advanced glycation end products, oxidative stress, angiotensin II, and cytokines can cause polymorphonuclear and mononuclear leukocytes (Sheng, Wright and Apostolopoulos, 2011). Elevated differential cell counts, such as eosinophil, neutrophil, and monocyte counts can also predict the likelihood of cancer in the future (Maher and Reynolds, 2011; Shreya and Brundha, 2017). To better understand the role of total and differential leukocyte counts in oral cavity cancer, researchers looked at the relationship between total and differential leukocyte counts and clinical status, lymph node metastasis development, and overall survival (Kao *et al.*, 2010). Furthermore, increased pretreatment neutrophil-lymphocyte ratio (NLR) has been linked to poor outcomes in colorectal, gastric, and ovarian cancer, malignant mesothelioma, and renal cell carcinoma, according to previous studies (Ohno *et al.*, 2010).

Many studies have proved that the lymphocyte monocyte ratio is the master for cancer. A diagnostic thoracoscopy in 2017 with pleural biopsy was performed, which showed an undifferentiated pleomorphic tumor with focal immunoreactivity for thyroid transcription factor 1 and napsin A, favoring a diagnosis of adenocarcinoma of the lung. The POCT device was chosen by the test center of the Innovative high-tech cancer treatment Denmark-Germany project (InnoCan) among other potential POCT devices and they used specific POCT unit (Otto Mattsson *et al.*, 2020). The multi-analysis shows an increase in monocyte count and decrease in lymphocytes and found that there is a combination

of platelet count to lymphocyte to monocyte ratio (Deng *et al.*, 2020). Research says that about 49.8% have high LMR (Lymphocytes Monocytes Ratio) and 50.2% have low LMR (Livne Margolin *et al.*, 2019). Our team has extensive knowledge and research experience that has translate into high quality publications (Krishnamurthy *et al.*, 2009; Abdul Wahab *et al.*, 2017; Eapen, Baig and Avinash, 2017; Ravindiran and Praveenkumar, 2018; Subramaniam and Muthukrishnan, 2019; Anita *et al.*, 2020; Kumar *et al.*, 2020; Rajasekaran *et al.*, 2020; Arumugam, George and Jayaseelan, 2021; Dhanraj and Rajeshkumar, 2021) The study aims to use lymphocyte and monocyte count as prognostic markers for cancer patients.

MATERIALS AND METHOD:

The present study was conducted in Saveetha Dental College & Hospitals in February 2021 and involved normal patients and patients affected with any oral cancer. The study and sample collection were approved by the Institutional ethical committee with an approval number of IHEC/SDC/BDS/1993/01. This method of study setting is more preferred or feasible to collect data, but this study is highly time-consuming. A sample size of 20 was set and divided into two groups, 10 were cancer patients and the rest 10 were normal or control patients, and parameters like gender, age, stages of cancer and grading, Lymphocyte count, and granulocyte count were collected. The sampling method followed in this comparative study is random. The mean values of each parameter were tabulated along with the significant values and plotted in the form of bar graphs using SPSS. Independent t-test analysis was used to compare the results that were obtained.

RESULTS:

Table 1 shows that among the 10 cancer patients about 70% of them were males and about 30% of them were females. It also indicates cancer's location, with the majority of cancer patients about 20% affected in the right buccal mucosa, segmented mandibulotomy, and lateral border of the tongue, followed by 10% of them affected in Post retromolar region, Buccal mucosa, and retromolar trigone, Anterior palate, and Lower alveolus according to the findings.

Graph 1 denotes the age distribution of the study population, out of which 20% were aged between 51-60 years, 30% of them were between 30-40 years and 50% were between 41-50 years. It was shown that the majority of cancers occurred in the age group between 41-50 years. This finding was well correlated with the previous study in the Kenyan population (Mwachiro *et al.*, 2021). Previous studies carried out proved that a large number of patients with oral cancer were observed to be under the age group of 35-88 years (Tas *et al.*, 2013; Brundha and Pathmashri, 2019)).

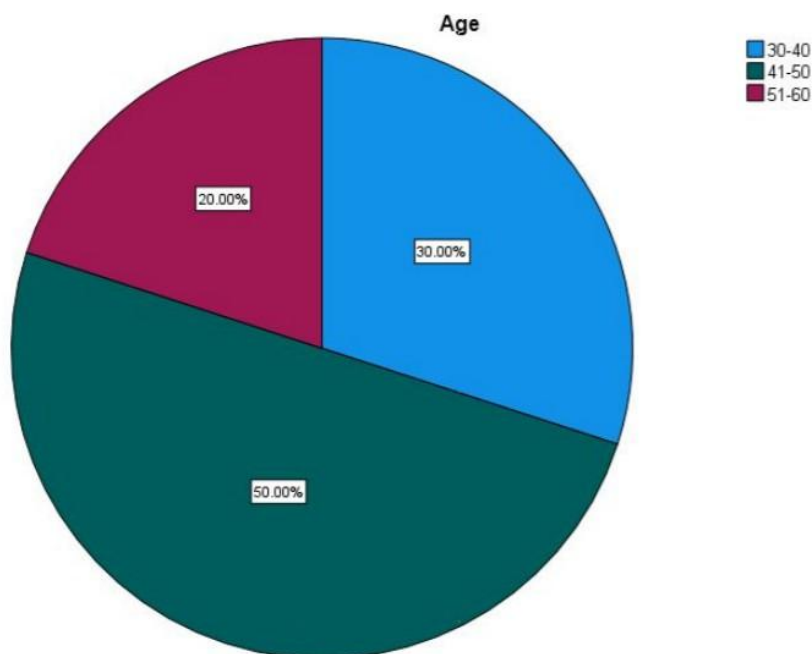
Graph 2 and Table 1 illustrate the various stages of cancer, in that we found that 30% of the population had stage 1 OSCC, 20% of them diagnosed as stage 3 OSCC, 40% of the study population had stage 4a and 10% of the population had stage 4b. From the results collected it was found that the majority of the patients were observed to be affected with stage- 4a cancer followed by 30% with stage 1 cancer. Previous studies proved the same that the majority of the patients who were given treatment had developed stage-4 cancer (Gil *et al.*, 2009).

Graph 3 and Table 1 illustrates that the majority of the patients were diagnosed with WDSCC (well-differentiated oral squamous cell carcinoma). The cells of well-differentiated squamous cell carcinoma appear normal and tend to grow and invade other parts of the body comparatively slower than poorly differentiated or undifferentiated cancer cells (Al-Rawi and Talabani, 2008). Followed by a population of 10% who had Low-grade SCC, 10% had Micro- invasive SCC, and 10% were diagnosed to have Adenocarcinoma of the oral cavity. The literature also showed that the majority of the patients presented to the clinician were diagnosed to have the Well-differentiated type of SCC.

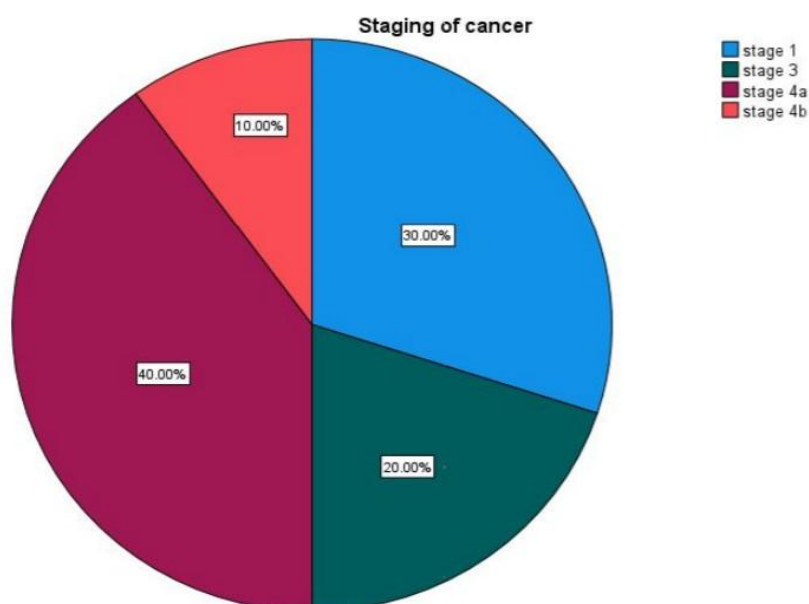
Table 2 shows the mean value of both the lymphocyte and granulocyte count of both cancer and control patients. The mean value of lymphocyte control patients is 31.73 ± 5.53 and in cancer patients is 25.10 ± 9.40 . The mean value of granulocyte control patients is 63.97 ± 5.80 . The mean value of cancer patients is 73.60 ± 12.38 . The Granulocyte count difference between control and cancer patients was observed to be statistically significant ($p < 0.05$). Therefore, an insignificant difference was found in both lymphocyte and granulocyte count of control and oral cancer patients. The independent t-test which was done to compare the mean lymphocyte count showed that there is no significant difference ($P\text{-value} > 0.05$).

Table 1: Distribution of Data collected.

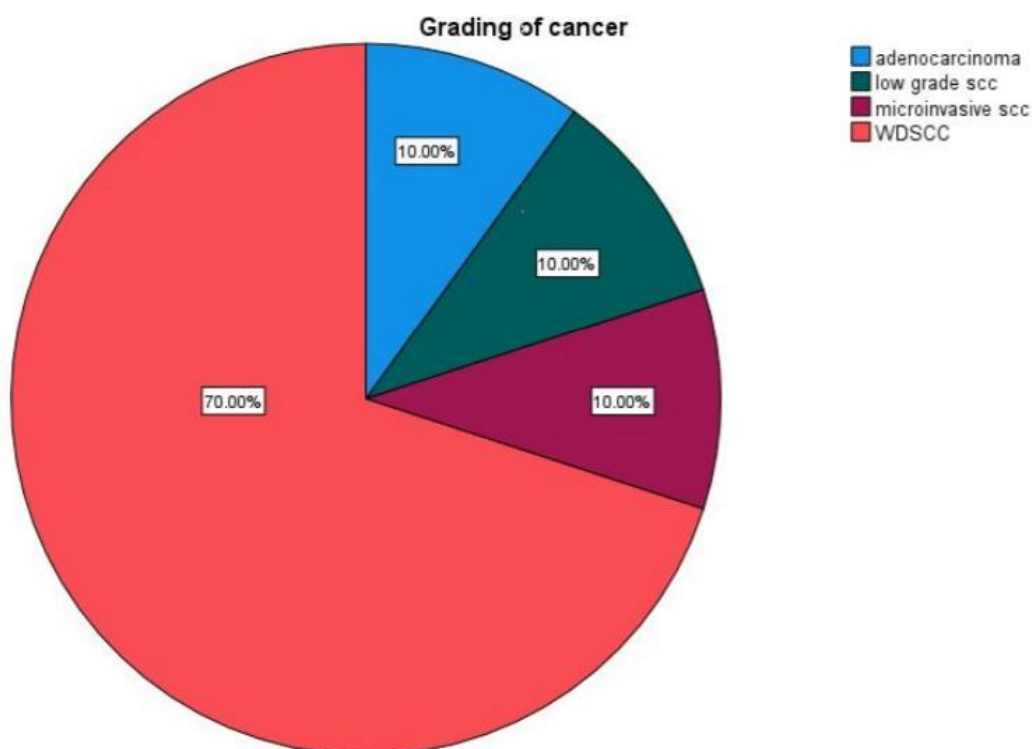
S.No	Age	Sex	Stage	Location Of The Tumour	HP Diagnosis	Absolute Lymphocyte Count/Cubic mm	Lymphocyte Percentage	Granulocyte Percentage
1	51yrs	M	3rd stage	R Buccal mucosa	WDSCC	1.8x10 ³	24.1%	71.9%
2	32yrs	M	1st stage	Post retromolar region	OSCC micro-invasive	3.0x10 ³	24%	71.6%
3	48yrs	F	Stage 4A	The lateral border of the tongue	WDSCC	1.8x10 ³	21%	76.5%
4	38yrs	M	Stage 4A	Segmented mandibulotomy	WCSCC	2.2x10 ³	17.3%	77.1%
5		M	Stage 4	Buccal mucosa	WCSCC	0.6x10 ³	4.1%	93.9%
6	52yrs	M	Stage 1	Anterior palate	Low-grade SCC	3.2x10 ³	32.9%	61.5%
7	40yrs	M	Stage 4B	Lower alveolus	WDSCC	2.1x10 ³	28.2%	66.5%
8	43yrs	F	Stage 1	R Buccal mucosa	Adenosarcoma	3.7x10 ³	35.9%	57.5%
9	44yrs	F	Stage 4A	The lateral border of the tongue	WDSCC	4.3x10 ³	31.6%	65.2%
10	47yrs	M	Stage 3	Segmental mandibulotomy	WDSCC	0.5x10 ³	3.2%	94.1%



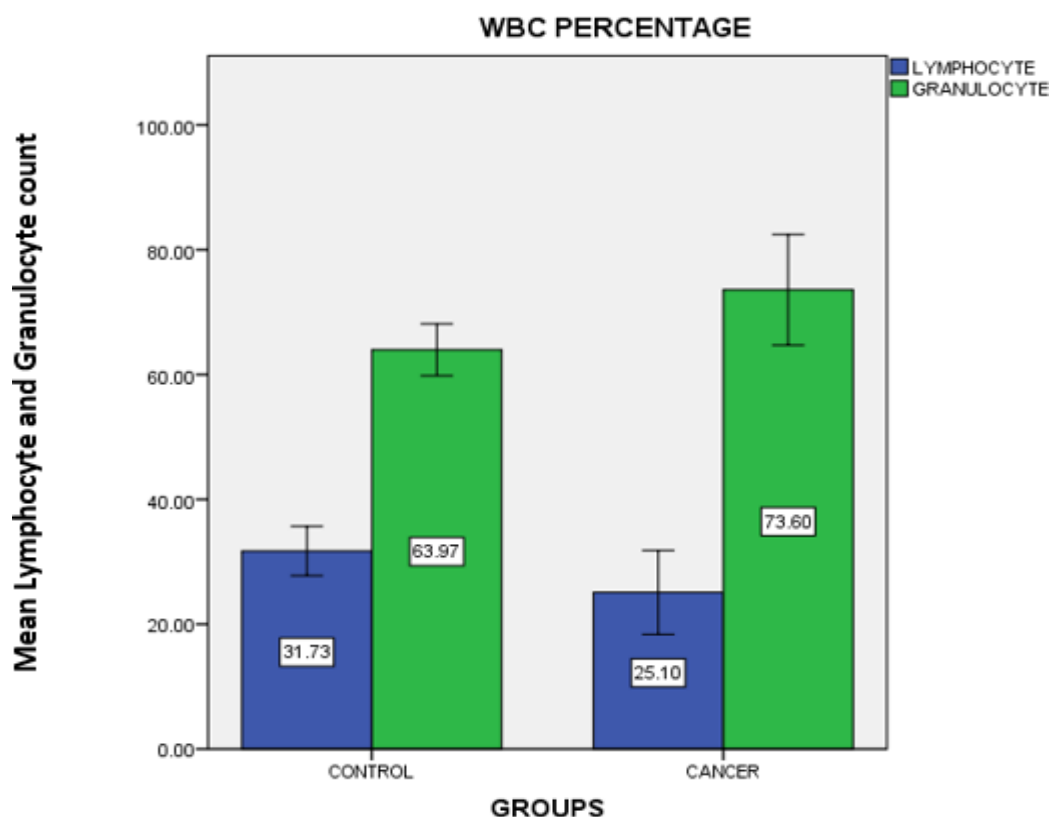
Graph 1: The pie chart represents the age group of different oral cancer patients. The green color indicates 41-50 years, pink indicates 51-60 years, and blue indicates 30-40 years. The majority belonged to the age group of 41-50 yrs.



Graph 2: The pie chart represents the staging of oral cancer. Blue color indicates stage 1, green color indicates stage 3, pink indicates stage 4a analyzed indicates stage 4b. The majority of them have been diagnosed with stage 4a cancer.



Graph 3: The pie chart illustrates the grading of oral cancer. Blue color denotes adenocarcinoma, green indicates low-grade squamous cell carcinoma, and pink indicates microinvasive squamous cell carcinoma, and red indicates well-differentiated squamous cell carcinoma (WDSCC). 70% of the oral cancer patients were detected with WDSCC.



Graph 4: The bar chart illustrates the mean value of WBC Percentage in control patients as well as cancer patients. X axis represents the control and cancer group. Y axis represents the mean lymphocyte and granulocyte count. The blue color denotes the lymphocyte percentage and the green color denotes the granulocyte percentage. The mean value of lymphocyte count and granulocyte count is 25.10 ± 9.40 and 73.60 ± 12.38 respectively.

	Groups	N	Mean	Std. Deviation	Std.Error Means	P Value
Lymphocytes	Control	10	31.7300	5.531	1.749	>0.05
	Cancer	10	25.1000	9.406	2.974	
Granulocyte	Control	10	63.9700	5.806	1.836	<0.05
	Cancer	10	73.6000	12.388	3.917	

Table 2: Mean and Standard deviation of the parameters analyzed.

Discussion:

When compared with the control and cancer population, the mean granulocyte count had been increasing in cancer patients and the mean difference calculated was 9.89% and the mean lymphocyte count had been reducing in cancer patients and the mean difference calculated was 6.63%. It can be predicted that lymphocytes are more sensitive and destructed in the process of tumor immunity than granulocytes. It has an antitumor immune function that can stop the development of many tumors (Wang *et al.*, 2016), and elevated lymphocyte levels have been linked to a better prognosis for several tumors (Quigley and Kristensen, 2015). It was also reported that several types of tumor-infiltrating lymphocytes were associated with outcomes of a variety of tumors (Eriksen *et al.*, 2018) (Zhou *et al.*, 2018), including T cells. While different sets of T cells have been linked to a poor prognosis for tumors, a high absolute lymphocyte count has been linked to a better prognosis for gastric cancer patients in our current study. Increased monocytes have been linked to a poor prognosis in several tumors, including mucosa cancer. (Shigeta *et al.*, 2016), cervical cancer (Lee *et al.*, 2012) and hepatocellular carcinoma (Sasaki *et al.*, 2006). The tumor of the right buccal mucosa is a distinct entity for which histopathological diagnosis and subtyping are critical in treatment planning. It's important to remember that these lymphocyte and monocyte ratios are common.

We discovered that a high absolute count of neutrophils, monocytes, and platelets, as well as a low absolute count of lymphocytes, is linked to a weak cancer prognosis. Only the lymphocyte and monocyte counts were independent prognostic indicators. Furthermore, combining lymphocyte and monocyte counts may improve the predictive value for stage II/III cancer patients' prognosis, but not for stage I cancer patients (Camp, Dolled-Filhart and Rimm, 2004). A full analysis of the prognostic value of the absolute count of blood cells in cancer was lacking (Eo, 2015). Therefore, the present study investigated the prognostic value of the absolute count of WBC, neutrophil, lymphocyte, monocyte, and

platelet in cancer patients. Absolute lymphocyte count and monocyte count have been linked to disease-free survival and overall survival in cancer patients in numerous studies. The two variables, however, were not separate prognostic factors. (Eo, 2015). In a study containing 10 cases of surgically treated cancer patients, Heras et al. found that increase in granulocyte count was correlated with tumor progression and unfavorable prognosis of all types of cancer (Heras et al., 2010).

The sample size was small and the study was not included with monocyte count and percentage. These were considered as the limitations of our study. In the future, a larger sample size would be used to obtain improved results. Also, with relation to the tumor immunity different other parameters can be taken into account apart from lymphocyte monocyte ratio and granulocyte count.

CONCLUSION:

Within the limitations of the study we conclude that the majority of the cancer patients are between 41-50 years of age, majority of the Oral cavity cancers are well-differentiated type of squamous cell carcinoma, most common stage of OSCC at the time of diagnosis is stage 4a followed by stage 1. Also, we found increasing granulocyte count and reducing lymphocyte count in cancer patients when compared to normal persons.

ACKNOWLEDGEMENT:

The authors are thankful to Saveetha Institute of Medical and Technical Sciences, Saveetha Dental College and Hospitals, Saveetha University for giving a platform to conduct the study.

CONFLICT OF INTEREST:

The authors would like to declare no conflict of interest in the present study.

FUNDING:

The present project is supported by:

- Saveetha Dental College and Hospitals, Saveetha University
- Saveetha Institute of Medical and Technical Sciences,
- Anu enterprises Chennai, Tamilnadu.

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