Complete Blood Count as a Diagnostic Marker in Oral Lichen Planus

Indra G, Maragathavalli G*, Deepika Rajendran

Department of Oral Medicine and Radiology, Saveetha Dental College and Hospital, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai - 600077, Tamil Nadu, India

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Abstract
Oral precancerous lesions and conditions like oral lichen planus, leukoplakia, or oral submucous fibrosis have the potential to develop into oral cancer. Oral cancer accounts for approximately 3% of all malignancies. Oral lichen planus is a premalignant condition occurring in the oral cavity due to various factors. Blood investigations are routinely done minimally invasive procedures carried out for various diagnostic purposes. The study aims to identify if the complete blood count (CBC) can be used as a pathologic diagnostic marker in an oral premalignant disorder like oral lichen planus. A total of 64 patients (38 female, 26 male) were taken into the study between the period July 2019 - March 2020. Each patient is exposed to blood investigations, and their results are studied. The results of the study show a minimal variation in the blood results. In conclusion, to determine if it can be used as a pathological diagnostic marker in premalignant disorders like oral lichen planus, further studies must be carried out in larger populations.

INTRODUCTION
Oral cancer accounts for approximately 3% of all carcinomas. Observations made from various studies have shown that 16% of oral squamous cell carcinomas developed from oral precancerous disorders such as leukoplakia, erythroplakia, erythroleukoplakia, oral submucous fibrosis, or lichen planus (Narang et al., 2014) and the verrucous type accounting for 5% of oral carcinoma. Verrucous carcinoma is said to be more indolent than conventional oral squamous cell carcinoma (Warnakulasuriya and Muthukrishnan, 2018). Malignancies are generally characterized by anaplasia, invasiveness, and metastasis. They can be either primary or secondary; however, primary OSCC is the predominant ones in the oral cavity (Misra et al., 2015).

Numerous factors are accounting for the cause of premalignant and malignant conditions such as tobacco smoking or chewing, hookah, cigarette smoking, or alcohol (Venugopal and Maheswari, 2016). Potentially premalignant oral epithelial lesions (PPOELs) have a high malignant transformation ability of about 16% - 62% (Maheswari et al., 2018). However, oral carcinoma can occur even without the usage of tobacco, like in the case of actinic cheilitis or other premalignant conditions like oral lichen planus (Muthukrishnan and Kumar, 2017).

Oral lichen planus (OLP) is a potentially premalignant condition present in the oral cavity, where they can be seen adversely in the buccal mucosa, tongue, gingiva, or even in the palate. Based on the features of the lesions, they are classified into reticular, atrophic or erythematous, bullous, plaque-like, erosive or ulcerative and papular types. Etiology of OLP is not known, it can be either due to underlying systemic illness such as auto-immune
disorders (Dharman and Muthukrishnan, 2016) or medications like beta-blockers or nonsteroidal anti-inflammatory drugs (NSAIDs) (Chaitanya et al., 2018) taken for any illness, or restorations like silver amalgam done from dental caries (Rohini and Kumar, 2017) causing allergic reactions in the oral cavity.

The presence of burning or itching sensation either consistently or only during mastication was one of the clinical manifestations elicited from the patients. However, patients sometimes tend to confuse the burning sensation emerging from the mucosa with pain and report the latter (Subha and Arvind, 2019).

On the evaluation of the mucosal lesions, as they are completely pertaining to the soft tissue structures, CBCT, or any form of radiographic evidence is never an advised investigatory modality (Patil et al., 2018; Choudhury, 2015). Investigations like biopsy are a gold standard confirmatory test for conditions like OLP.

Recent evidence claims that in the complete blood count (CBC) evaluation, white blood cells (WBC) have proven to be available as a marker of inflammation, and incidence of any early age-related macular degeneration (AMD) (Shankar et al., 2006). Studies have been proven to show the presence of leukocytes in the neoplastic tissue in cancer (Coussens and Werb, 2002). Similar to such studies, this study also aims to find out if the complete blood count - mainly the values of RBCs, WBCs, Platelets, and Hemoglobin, whether they can be used as a pathologic diagnostic marker in oral lichen planus, a potentially premalignant oral epithelial lesion.

MATERIALS AND METHODS

Study design
Retrospective, descriptive study.

Study population
A total of 64 patients (26 males, 38 females) taken into the study. The patients were selected randomly without any bias.

Study period
The study was conducted between the period of July 2019 - March 2020.

Study setting
The participants attended the oral medicine clinic at Saveetha Dental College and Hospital in Chennai were taken into the study.

Ethical approval
Prior to starting the study, ethical approval was obtained from the Institutional Scientific Review Board. (SDC/SIHEC/2020DIASDATA/0619-0320)

Inclusion criteria
All types of oral lichen planus patients with evidence of blood investigations during the duration from July 2019 to March 2020 were alone taken into the study. Patients with regular review and follow-up were mandatory.

Exclusion criteria
Patients continuing tobacco consumption or any of the causative factors, or with superadded mucosal lesions such as candidiasis were excluded from the study. Patients with irregular follow-up were also excluded from the study.

Study method
Two researchers were involved in the study. The two primary researchers had fewer than 5 years of experience and more than 30 years of experience in the field. The patients clinically diagnosed with oral lichen planus were taken into the study and subjected to CBC testing. The blood investigations were done in the clinical laboratory of Saveetha Dental College and Hospital by experienced technicians, and the technicians were blinded from the study to avoid any errors.

Statistical analysis
Statistical analysis was done using SPSS v23.0 software. Frequency distribution of the study based on age, gender, types of OLP and complete blood count were all calculated and analysed. Statistical significance was set at p-value <0.05. Reliability was checked using Kappa statistics. An interexaminer agreement was calculated using the same, and the value was 0.67 indicating a substantial agreement between the researchers.

RESULTS

Of 64 participants, 59.4% of the population was female, and 40.6% of the population were male, and their demographic data are discussed as follows.

The association of the demographic data - age and gender of the study is represented in Figure 1, X-axis showing the age of the study population and Y-axis denotes the numbers of the patients. The association between the female (blue) and male (red) with the age of the study population shows a higher prevalence between the age groups 36-45 years and 46-55 years. However, patients above 65 years of age showed a higher male prevalence in the study. Between 25-35 years, 7 male and 7 female participants were present, between 36-45 years of age 14 female and 3 male participants, 46-55 years of
Table 1: The frequency of complete blood count components in the study population

| Complete Blood Count Components | Female | Increase/Decrease (N) | Male | Increase/Decrease (N) | Female Mean | Male Mean |
|---------------------------------|--------|-----------------------|------|-----------------------|-------------|-----------|
|                                  | Within Normal Range (N) | Within Normal Range (N) |      |                       |             |           |
| Red Blood Cells Count            | (28)43.8% | (14)21.9%             | (12)18.8% | 1.26 | 3.46 |
| White Blood Cells Count          | (37)57.8% | (26)40.6%             |      | 1.03 | 1.00 |
| Neutrophils                      | (28)43.8% | (19)29.6%             | (7)10.9% | 1.26 | 1.27 |
| Lymphocytes                      | (21)32.8% | (16)25%               | (10)15.6% | 1.45 | 1.38 |
| Eosinophils                      | (38)59.4% | -                     | (26)40.6% | - 1.00 | 1.00 |
| Platelets                        | (38)59.4% | -                     | (26)40.6% | - 1.00 | 1.00 |
| Hemoglobin                       | (19)29.7% | (13)20.3%             | (13)20.3% | 1.50 | 3.50 |

Table 2: Increased and decreased levels of blood components in oral lichen planus patients than standardised normal values in the study population

| Complete Blood Count Components | Erosive | Reticular | Types of Oral Lichen Planus | Atrophic | Plaque - Like | Papular | Bullous |
|---------------------------------|---------|-----------|-----------------------------|----------|---------------|---------|---------|
| Red Blood Cells Count (↓)       | 7(10.9%)| 5(7.8%)   | 3(4.6%)                     | 1(1.56%) | 5(7.8%)       | 1(1.5%) |
| White Blood Cells Count         | -       | 1(1.56%)  | -                           | -        | -             | -       |
| Neutrophils (↑)                 | 7(10.9%)| 5(7.8%)   | 1(1.5%)                     | 2(3.12%) | -             | 2(3.12%) |
| Lymphocytes (↑)                 | 12(18.8%)| 5(7.8%)   | 4(6.25%)                    | 1(1.5%)  | 4(6.25%)      | 1(1.5%) |
| Eosinophils                     | -       | -         | -                           | -        | -             | -       |
| Platelets                       | -       | -         | -                           | -        | -             | -       |
| Hemoglobin (↓)                  | 13(20.3%)| 10(15.6%)| 3(4.6%)                    | 1(1.56%) | 4(6.25%)      | 1(1.56%) |
| Mean                            | 1.48    | 1.41      | 1.26                        | 1.40     | 1.71          | 1.35    |

Figure 1: Barchart showing the association between the demographic data of the population

Figure 2: Bar chart showing the association between gender and type of patient

age, 11 female and 9 male participants, between 56-65 years of age, 5 female and male patients and above 65 years 1 female and 2 male patients were observed.

The association of various types of lichen planus involved in the study based on gender are represented graphically in Figure 2. X axis represents the type of oral lichen planus and Y axis represents the number of patients. The association between male (Red) and female (Blue) among the type of oral lichen planus was found to be statistically significant with a P value of 0.056 >0.05(Chi square test). Erosive Lichen Planus was found to be more common.
among both and male and female. In male participants, 14 of them had erosive lichen planus, 6 had reticular lichen planus, 3 had plaque-like, and 3 of them were present with papular like lichen planus. In female participants, 14 were present with erosive lichen planus, 11 with reticular lichen planus, 6 with atrophic lichen planus, 3 with plaque-like type of lichen planus, 2 with papular type and 2 with bullos lichen planus.

Lymphocytes and neutrophils show an increase in cell counts than others. Prevalence of increase by 26.5% and 15.6% in females and 15.6% and 10.9% in male population respectively. However, 5.6% of females had decreased RBCs, and 29.7% of them had decreased blood hemoglobin. With the male population, 18.8% and 20.3% of the population had low RBCs and Hbs, respectively. Neutrophils and lymphocytes showing higher values in both male and female population. Arrow marks denoting the increase and decrease in the values. The above-mentioned frequency of the components employed in the blood investigations and their results are given in Table 1.

The values of the blood investigations based on types of oral lichen planus are tabulated. Patients with erosive lichen planus showed the prevalence of a 10.9% decrease in the red blood cells count and a 20.3% decrease in Hb. However, they showed a 10.9% and 18.8% increase in neutrophil and lymphocyte count, respectively. Arrows denoting the decrease and increase in the values (Table 2).

**DISCUSSION**

The standard normal value of Red Blood Cells (RBC) count for men is between 4.5 million to 5.9 million cells/ml, and for women, it is 4.1 million to 5.1 million cells/ml and for White Blood Cells (WBC) is 4,500 to 11,000 cells per microliter (cells/ml). However, the Total Count (TC) and Differential Count (DC) are used, to sum up, the WBC values. TC is the value of the number of WBCs present in the blood, and it should be within 4500 - 11 000 cells/cubic mm. DC, on the other hand, comprises the value of neutrophils, eosinophils, basophils, monocytes, and lymphocytes in percentage (%). Normal range of Neutrophils is 40% to 60%, Lymphocytes: 20% to 40% Monocytes: 2% to 8% and Eosinophils: 1% to 4%. Normal Haemoglobin (Hb) value for men is 14 to 17.5 grams per deciliter (gm/dL) and 12.3 to 15.3 gm/dL for women (Alomari et al., 2014).

Platelets are cells with normal value ranging between 150,000 to 450,000 platelets/ml. The study population had platelet values within the standardized normal value range, and hence no changes were observed.

Based on the above mentioned normal value of each blood component, the whole study criteria and values were determined and evaluated.

Narang et al. (2014) did a similar study with WBC to check as a diagnostic marker in precancerous conditions. He quoted in his study that WBC count is highly variable because it is responsive to diverse acute and chronic stimuli as it is increased in infections, stress, and smoking (Lee et al., 2005). On observing the WBC counts in our study, it is found that the lymphocytes showed the highest discrepancies of all and the second highest being the neutrophils. An increase in lymphocyte count shows that the body is undergoing some infectious or inflammatory changes. On correlating this evidence proven in various works of literature, the identification of the presence of oral lichen planus can also be due to any underlying condition. However, to prove this, further general investigations have to be carried out.

Similar to WBCs, the value of RBCs and Hb were deficient in some patients. Deficiency of these can cause conditions like anemia which can be ruled out with a clinical examination of the patients. This study is performed to provide the patients with a cheap and minimally invasive investigatory technique to identify the presence of any premalignant conditions which have the potential to progress into malignancy.

Patients getting treated for oral lichen planus with underlying systemic conditions were referred to consult the general physician. Oral instructions like maintenance of proper oral hygiene were advised (Subashri and Maheshwari, 2016) and were educated on them along with the usage of medications.

As supportive therapy, few patients have even advised multivitamins (especially Vit A) to improve overall health (Chaitanya, 2017). As OLP can be caused due to any systemic illness or medications taken for them, the stoppage of medications at the right time is necessary to avoid any adverse reactions (Muthukrishnan et al., 2016). However, this can be achieved only with the help of proper review and follow-up of the patients.

This study is first of its kind in the geographic region, assessing the blood parameters like RBC, WBC, Hb, and platelets in premalignant lesions and conditions. However, Complete blood count includes RBC, WBC, Platelets, Hb, Hematocrit, Mean corpuscular volume etc., the study mainly focused on the above
mentioned four components as they are proven to be vulnerable to any underlying systemic illness. Complete blood count (CBC) was the investigation carried out for this study. However, few patients were even advised for biopsy, when the remaining were treated based on clinical evaluation. Knowledge in the identification of the lesion, formulation of differential diagnoses and treatment plans, and in the selection of appropriate interventions is a must for an oral physician to avoid blunders (Steele et al., 2015).

CONCLUSION

On correlating the obtained results with the normal standardized values, it is observed that there was a significant difference in the cell counts in a few patients with oral lichen planus. From this, it is understood there is some form of acute or chronic infection or inflammation present in the body of the patients with oral lichen planus that act as an underlying pathology.

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Conflict of Interest

The authors declare that they have no conflict of interest for this study.

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