

## Complete Blood Count as a Pathological Diagnostic Marker in Oral Precancerous Lesions and Conditions

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### ABSTRACT

Oral potentially malignant disorders have 16% - 62% risk of malignant transformation and oral cancer accounts for approximately 3% of all malignancies. Oral premalignant disorders namely lichen planus, leukoplakia, oral submucous fibrosis, actinic cheilitis, or discoid lupus erythematosus are conditions seen due to various etiological factors like tobacco consumption either smoking or in smokeless form, sun exposure, etc. Blood investigations are a minimally invasive and less expensive investigatory method employed commonly in all forms of medicine. The aim of this study is to analyze if complete blood count can be used as a diagnostic marker in premalignant disorders and to compare their blood levels with healthy individuals. A total of 200 patients with oral potentially premalignant disorders attending the oral medicine clinic at Saveetha Dental College and Hospital between June 2019 and December 2019 were taken into the study. Each patient was subjected to complete blood investigation and their results were studied. The result of the study reveals that there was a minimal variation in the cell count of individuals with premalignant disorders observed. In order to conclude that the complete blood count can be used as a pathological marker, further studies need to be carried out in a larger population.

**Key words:** Complete blood count, Diagnostic marker, Oral leukoplakia, Oral lichen planus, Oral submucous fibrosis

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### INTRODUCTION

Oral carcinoma is one of the most prevalent carcinomas among the human population. It claims for around 145,400 deaths in a year worldwide. They can be caused due to many predisposing factors namely, smoking or smokeless tobacco, sun exposure, alcohol, or human papillomavirus. An overall incidence of carcinoma in the Central part of Asia is said to be at the rate of 100.8/100,000 in the whole world [1].

An oral premalignant disorder (OPMD) is defined as any lesion or condition of the oral mucosa that has the potential for malignant transformation. In 2005, the World Health Organization (WHO) gave the term potentially premalignant oral epithelial lesions (PPOELs) and since then OPMD is changed to PPOEL. The

term potentially premalignant oral epithelial lesions have been used as a broad term to define both histological and clinical lesions that have malignant potential. This encompasses a number of oral lesions, such as leukoplakia, erythroplakia, erythroleukoplakia, lichen planus, oral submucous fibrosis (OSF), and oral dysplasia [2]. In the Southern part of India, the prevalence rate of such oral mucosal lesions is found to be 4.1% [3]. Certain studies have shown that the PPOELs tend to undergo malignant transformation at the rate of 2-3% [4].

According to WHO, Oral leukoplakia (OL) is defined as a white patch that cannot be scraped or wiped off and is not attributable to any pathophysiology of disease process. Studies reveal the overall prevalence rate for OL ranged from 1% to 5%, and the range of malignant transformation rate (MTR) is from 3-17% [5-7]. As OL is a clinical and not a histopathological diagnosis, it is important to rule out other similar white lesions such as candidiasis, white sponge nevus, oral lichen planus, leukoedema, frictional keratosis, etc.

Oral submucous fibrosis (OSMF) is a progressing, fibrous disease of the aerodigestive tract with underlying deranged collagen metabolism mainly affecting the oral cavity. Numerous etiologic factors have been linked to this disorder, to name a few, nutritional deficiencies, such as those of vitamins, iron, and zinc; autoantibodies; and the molecule capsaicin in chilies. However, the most predominant etiologic factor reported in the literature is the use of areca nut and its derived products, like betel quid, and gutkha [8,9]. OSMF has an average MTR range of 7-30% [6].

Lichen planus is a systemic mucocutaneous disease that commonly affects the oral mucosa but can also affect the skin, nails, the scalp, and the vaginal mucosa. It usually manifests at the third to seventh decades of life, however, cases involving the second decades of life have also been reported in the literature. In the literature, the range of MTR of OLP is 0-5%, with the more accepted average being 1% [10,11].

Recent research evidence claims that in the complete blood count (CBC) investigation, white blood cells (WBC) have proven as a marker of inflammation, and incidence of any early age-related macular degeneration (AMD) [12]. Studies have been conducted to show the presence of leukocytes in the neoplastic tissues in cancer [13]. Similar to the mentioned studies, our study aims to evaluate the changes in the complete blood count level in precancerous lesions and conditions and to compare their values between control and study groups of precancerous lesions and conditions. Our recent research portfolio slides numerous articles in reputed journals [14-18]. Based on this experience we planned to pursue complete blood count as a pathological diagnostic marker in oral precancerous lesions and conditions.

#### MATERIALS AND METHOD

**Study population:** This was a randomized blind trial conducted among the patients with premalignant disorders attending the oral medicine clinic at Saveetha Dental College and Hospital in Chennai from June 2019 to December 2019.

**Ethical clearance:** Before proceeding with the study, the necessary ethical approval was

obtained from the institutional scientific review board, and patients were also informed about the study priorly before exposing them to blood investigations.

**Inclusion criteria:** Patients with clinically diagnosed oral premalignant disorders - oral lichen planus, leukoplakia, and oral submucous fibrosis alone were taken into the study. All types of mentioned OPMD were taken into the study. Patients with the cessation of habits causing OPMD were involved in the study.

**Exclusion criteria:** Patients with fear of blood or prone to show possible adverse effects post blood exposure were excluded from the study. Patients continuing the habits causing OPMD, or present with superadded infections like candidiasis were excluded from the study.

**Sample size determination:** Based on the formula,  $N = 4pq/d^2$ , the sample size was achieved keeping the level of confidence at 95% and the precision rate at 10%. The final sample size required for the study came out to be 200. Therefore, the study was conducted on 200 patients.

**Study method:** A total of 200 patients, 50 patients with oral submucous fibrosis, 50 patients with oral leukoplakia, 50 patients with oral lichen planus, and 50 patients healthy patients without any OPMD were taken into the study. The study group comprises three subgroups namely, Group A (Oral submucous fibrosis), Group B (Oral lichen planus), Group C (Oral leukoplakia) and Control group comprises a single group, Group D with healthy individuals. Based on the above-mentioned criteria, the data of the patients were arranged. Two researchers, a postgraduate resident and a professor with an experience of 40 years in this field were involved in the study as primary researchers. 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 bias in the study.

**Statistical analysis:** Statistical analysis was carried out using SPSS v20.0 software. Descriptive and inferential statistical analysis has been carried out in the present study. Significance is assessed at a 5% level of significance. Student t-test was performed to find the significance of study parameters between two or more groups.

**RESULTS AND DISCUSSION**

Out of 200 patients, 61% of the patients were females and 39% of them were male revealing a higher female predilection in the study population. Statistically analyzing the mean value and standard deviation of the groups' A, B, C, and D individually using descriptive statistics and the results are mentioned in Table 1. The results of the study on comparing all the blood parameters like RBC, WBC, platelets, hemoglobin, and hematocrit with the study and the control group were based on the level of significance maintained at 5%. A significant correlation (<0.05) was found in Total count and hemoglobin between group A (Oral submucous fibrosis) and group D (healthy participants). Similarly, a significant correlation (<0.05) in RBC and Hemoglobin between group B (oral lichen planus) and group D (healthy participants), in eosinophil between group C (oral leukoplakia) and group D (healthy participants), and in Total count between all the study groups (A, B, C) and group D (healthy participants) were found (Table 2).

In 2014, Shishodiya et al. did a study in correlation to ours with WBC as a pathologic diagnostic marker in precancerous disorders and he stated that the WBC count is highly variable as it is responsive to diverse chronic stimuli and it can even show variations with any infections, stress, and smoking [19]. On observing the WBC counts in our study, it is found that there was some significance evident in the total cell

count. However, eosinophils in comparison with group C (oral leukoplakia) and group D (healthy individuals) showed a degree of significance in the study. Such differences in the cell counts can also predict that the body is undergoing some inflammatory changes. WBCs also have the potential to identify the risk of cancer due to its non-specificity.

Similar to WBCs, the value of RBCs and Hb also showed levels of significance in the study. Significance inferred by them can also lead to conditions like anemia, which can also be examined clinically for the signs. The main goal of this study is to provide the patients with a simple, cheap, effective and minimally invasive investigatory technique to identify the presence of any premalignant disorders which have the potential to progress into malignancy.

The patients involved in the study were getting treated at the institution by the institutional doctors. Necessary medications and supportive therapies were advised and regular follow-up of the patients were recommended in order to periodically examine the blood parameters at regular intervals.

This study is first of its kind in the geographic area assessing the blood parameters like RBC, WBC, Hb, hematocrit and platelets in premalignant disorders. However, Complete blood count includes RBC, WBC, Platelets, Hb, Hematocrit, MCV, MCH, MCHC and RDW etc., the study mainly focused on the above mentioned five components as they are proven to be vulnerable

**Table 1: Showing the mean value and standard deviation of all the parameters of all groups.**

| GROUPS                            | RBC<br>(million cells/mcL) | TC<br>(cells/mcL)  | DC                |                   |                | Platelet<br>(cells/mcL) | Hemoglobin<br>(g/dL) | Hematocrit<br>(%) |
|-----------------------------------|----------------------------|--------------------|-------------------|-------------------|----------------|-------------------------|----------------------|-------------------|
|                                   |                            |                    | Neutrophil<br>(%) | Lymphocyte<br>(%) | Eosinophil (%) |                         |                      |                   |
| Group A (Oral Submucous Fibrosis) | 4.4640 ± .70171            | 7952.40 ± 1784.492 | 60.84 ± 8.560     | 36.412 ± 8.5140   | 2.250 ± .3259  | 2.6962 ± .75528         | 13.382 ± 2.4728      | 40.44 ± 4.509     |
| Group B (Lichen Planus)           | 4.6800 ± .71617            | 7506.20 ± 1720.505 | 58.86 ± 8.557     | 38.528 ± 8.6888   | 2.254 ± .3370  | 2.7836 ± .72615         | 12.910 ± 2.5588      | 40.42 ± 3.698     |
| Group C (Leukoplakia)             | 4.5508 ± .74573            | 7645.20 ± 1908.280 | 61.06 ± 8.973     | 36.362 ± 8.8992   | 2.256 ± .3265  | 2.8148 ± .71351         | 13.746 ± 2.2692      | 40.94 ± 3.803     |
| Group D (Healthy)                 | 4.5436 ± .77923            | 7227.60 ± 1539.013 | 59.860 ± 7.7275   | 37.256 ± 7.7502   | 2.170 ± .3099  | 2.6040 ± .67334         | 13.900 ± 2.3646      | 40.660 ± 3.9311   |

**Table 2: Shows a comparison of all the blood parameters in the control vs. study group.**

| GROUPS              | RBC<br>(million cells/mcL) | TC<br>(cells/mcL) | DC             |                |                | Platelet<br>(cells/mcL) | Hemoglobin<br>(g/dL) | Hematocrit<br>(%) |
|---------------------|----------------------------|-------------------|----------------|----------------|----------------|-------------------------|----------------------|-------------------|
|                     |                            |                   | Neutrophil (%) | Lymphocyte (%) | Eosinophil (%) |                         |                      |                   |
| A vs. D p-value     | 0.593                      | .032*             | 0.549          | 0.605          | 0.211          | 0.521                   | .028*                | 0.795             |
| B vs. D p-value     | .036*                      | 0.396             | 0.541          | 0.442          | 0.198          | 0.203                   | .047*                | 0.754             |
| C vs. D p-value     | 0.962                      | 0.231             | 0.475          | 0.593          | .032*          | 0.18                    | 0.74                 | 0.718             |
| A+B+C vs. D p-value | 0.859                      | .057*             | 0.763          | 0.906          | 0.108          | 0.155                   | 0.158                | 0.927             |

\* P-value=<0.05-significant, >0.05-not significant, <0.01-highly significant.

to any underlying inflammatory conditions. Even though the investigation carried out for the study was only Complete blood count (CBC), few patients were advised for biopsy based on the clinical examination and the necessary treatment plan was executed post biopsy results.

Since the study is carried out with a lesser population, it is recommended to carry out the same investigations in a larger population before claiming it as one of the reliable diagnostic markers like saliva, serum, etc. As the study was carried out only during the first visit of the patients, the necessary follow-up was missing and few patients dropped out of the study in between were all added to the limitations experienced in the study.

#### CONFLICT OF INTEREST

None declared.

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