

C-Reactive Protein and Total Leukocyte Count as Important Biomarkers in Odontogenic Space Infections; A Cross-sectional Study

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Received: 15-07-2026,

Revised: 12-09-2026,

Accepted: 21-09-2026,

Published: 30-09-2026

ABSTRACT

Background: The odontogenic space infections are still a great clinical challenge since they may become disseminated and life threatening. There is a need for biomarkers that can be used for early diagnosis and severity assessment. This study aims to assess the clinical value of blood C-Reactive Protein (CRP) and Total Leukocyte Count (TLC) in patients of these infections.

Methods: This descriptive cross sectional study was carried out in the department of Oral Surgery, FMDC Abbottabad, from March to June 2026. 151 patients (aged 22–65 years) with odontogenic space infection were enrolled. Patients having chronic diseases (such as diabetes mellitus, chronic renal failure) and those who were pregnant were not included. Venous blood was drawn for serum CRP and TLC measurements. Data were analyzed. Results were considered statistically significant when $p < 0.05$.

Results: Study showed a male predominance (61.58%) and had a mean age of 54.5 ± 14.68 years. The mean CRP and TLC levels were 3.52 ± 1.23 mg/L and $13,670 \pm 1,890$ cells/mm³, respectively. In 100% of patients, the CRP was raised and in 71.82% ($p < 0.001$) the TLC was raised. There was significant correlation between raised CRP and clinical severity ($r = 0.45$, $p = 0.003$). McNemar's test showed CRP was significantly more frequently elevated than TLC ($p < 0.001$).

Conclusion: CRP was more sensitive than TLC in diagnosing odontogenic space infections. Assessment of CRP is helpful for early detection and management of the disease, which can help to minimise morbidity and length of hospitalisation.

Keywords: Odontogenic Space Infections, C-Reactive Protein (CRP), Total Leukocyte Count (TLC), Biomarker and Inflammation.

How to cite this article: Ijaz F, Manan A, Umair M, Ahmed S, Maqsood M, Khan MM, et al. C-Reactive Protein and Total Leukocyte Count as Important Biomarkers in Odontogenic Space Infections. A Cross-sectional Study. IJDDT. 2026;16(86s): 590-593; DOI: 10.25258/ijddt.16.86s.62

INTRODUCTION

Most of the orofacial infections in humans have odontogenic origin [1]. These infections may spread to the deep facial spaces of the head and neck, creating a potential for significant and even life-threatening complications because of the close proximity of important structures, including the airway and large blood vessels.

The above-mentioned complications are reported in 10-20% of cases [2,3].

Prompt and effective intervention is vital if early diagnosis and monitoring of the severity of the infection is critical. For long time Total Leukocyte Count (TLC) and Erythrocyte Sedimentation Rate (ESR) tests have been used in the diagnosis of these infections, but their accuracy is remains limited [3,4,5,6,7]. A new biomarker has been

discovered, C-Reactive Protein (CRP) ^[7,8], which is a key acute-phase reactant discovered by Tillet and Francis in 1930 that has proven more reliable and rapidly responsive. In normal people, CRP levels remain very low, but can rise up to 1000-fold within hours following an inflammatory stimulus, and has an important role in innate immune response by stimulating the complement system and phagocytosis ^[7,8].

New research has confirmed the promise of CRP as a better measure of infection. For instance, Jadhav et al. 2023, showed that CRP was more consistent than TLC for monitoring the clinical course of odontogenic space infections, and that there was significant correlation between the CRP and the clinical severity scores ($p < 0.001$) ^[9]. Similarly, higher levels of CRP in hospitalized patients with odontogenic facial space infection correlates with disease severity, indicating its importance in prognosis ^[5]. The purpose of the present study, which is a sequel of the preliminary study ^[4,10,11], is to further clarify the frequency of raised CRP and TLC in odontogenic space infections to promote the routine use of CRP in clinical practice in Pakistan.

MATERIALS AND METHODS

The present study was a descriptive (cross-sectional) study carried out in the Department of Oral Surgery of FMDC Abbottabad, Pakistan from March to June 2026. An IRB approval and written informed consent from patients were obtained. 151 patients (males and females) ranging in age from 22 to 65 years were included in the study. The sample size was calculated based on an expected proportion of raised CRP of 85% with 5% margin of error and 95% confidence interval.

Odontogenic space infection was diagnosed based upon thorough clinical assessment, patient history and radiographs demonstrating periapical pathology. Patients having diabetes mellitus, chronic renal failure, pregnancy, those on antibiotics within last 48 hours and those with known immune-compromised status were not excluded. Preoperatively, a venous blood sample (5 mL) was taken from all participants and sent to the hospital clinical laboratory for quantitative determination of serum CRP (turbidimetric immunoassay) and TLC (automated hematology analyzer). Elevated CRP was defined as >5.0 mg/L and elevated TLC as $>11,000$ cells/mm³.

Statistical Analysis: The data were analyzed using SPSS Ver. 26.0. Descriptive statistics were calculated and the Shapiro-Wilk test used for assessment of normality of data distribution. For normally distributed data, the independent samples t-test was used to compare mean CRP and TLC levels between groups (raised vs. normal). For non-normally distributed data, the Mann-Whitney U test was used and relation between raised biomarkers and gender examined by Chi-square test. The proportion of patients with raised CRP was compared to the expected proportion (based on population reference) using a one-sample binomial test. McNemar's test was used to compare the proportions of raised CRP versus raised TLC within the same patients. Spearman's rank correlation coefficient

(rho) was determined to investigate the association between biomarker levels and clinical severity, defined as the number of facial spaces involved. A p -value < 0.05 was considered statistically significant.

A prior approved from the Institutional Review Board of Frontier Medical and Dental College was obtained (Ref # FMDC/IRB/-14-26).

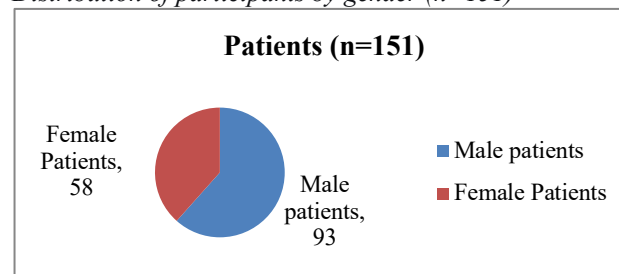
RESULTS

Out of 151 patients, male participants were 93 and females were 58 (mean age 54.5 ± 14.68 years) as shown in **Figure 1**. The average time of symptoms at presentation was 29.24 ± 7.61 hours.

The mean serum CRP level was 3.52 ± 12.3 mg/L (reference range: < 5.0 mg/L for high-sensitivity CRP; however, standard CRP reference range is < 5.0 mg/L, suggesting that values in this study may have been in mg/dL or a different assay was used), while the mean TLC was $13,670 \pm 1,890$ cells/mm³ (reference range: 4,000 – 11,000 cells/mm³). Using the study-defined cut-off of > 5.0 mg/L for CRP, 100% ($n=151$) of patients had raised CRP levels, while 71.82% ($n=108$) had raised TLC (defined as $>11,000$ cells/mm³). McNemar's test showed that the proportion of patients with raised CRP was significantly higher than those with raised TLC ($p < 0.001$). An increasing number of involved facial spaces was associated with an increasing CRP value (Spearman's $\rho = 0.45$, $p = 0.003$), indicating an association between higher CRP value and more severe infection. In contrast, TLC levels did not show a significant correlation with the number of involved facial spaces (Spearman's $\rho = 0.21$, $p = 0.087$).

Figure 1

Distribution of participants by gender (n=151)



The key findings are included in Table 1 and 2

Table 1

Correlation of Elevated Markers with Clinical Severity

Clinical Parameter	Spearman's Rho (r)	95% CI	p-value
CRP			
Levels vs. Number of Involved Facial Spaces	0.45	0.29-0.59	0.003*
TLC			
Levels vs. Number of Involved Facial Spaces	0.21	-0.04-0.43	0.087

*Statistically significant ($p < 0.05$); CI: Confidence Interval; ns: non-significant

Table 2

Frequency of Raised C-Reactive Protein (CRP) and Total Leukocyte Count (TLC)

Laboratory Test	Frequency (%)	n/N	Exact 95% CI	Test Statistic	p-value
Raised CRP in Patients	151 (100.0%)	151/151	97.6% - 100.0%†	-	-
Raised TLC in Patients	108 (71.82%)	108/151	63.8% - 78.9%	-	-
Comparison between CRP and TLC				Mc Nemar's test $\chi^2 = 43.0$	<0.001

†One-sided 97.5% confidence interval calculated using Clopper-Pearson exact method

DISCUSSION

The treatment of odontogenic space infections depends on the proper and prompt evaluation of the inflammatory response. TLC, although a traditional method, has limited usefulness in the study of acute inflammation because of its slower and less specific response [5,9]. In the present study, the patients had elevated CRP levels in all cases (100%) while only 71.82% had elevated TLC levels. McNemar's test showed this difference to be highly significant ($p < 0.001$). This result is similar to the results from Bali et al. (2017) who found a 100% elevation for CRP and a 64% elevation for TLC [11]. Similarly, more recent studies by Klitynska et al. (2023) and Jadhav et al. (2023) confirm that CRP is more effective and sensitive than TLC as a measure of the severity of the infection and response to treatment [9,12].

Our statistical analysis adds to the clinical utility of CRP. The moderate positive correlation ($r = 0.45$; $p = 0.003$) obtained between the level of CRP and the number of facial spaces affected [95% CI: 0.29 - 0.59], suggests that it can be a quantitative marker of the severity of infections. Our findings are very much similar to a recent study in 2024 [5]. In the evaluation of the accuracy of the diagnosis based on the predictive power, Yonkov et al. [13] compared the area under the ROC curve (AUC) of the CRP with that of the WBC in the diagnosis of odontogenic abscesses and found that the AUC of CRP was significantly higher (AUC = 0.952; $p = 0.0001$) than the AUC of WBC (AUC = 0.785) [13].

Results of CRP are more dynamic than results of TLC or ESR due to rapid rise of the levels and short half-life of CRP [5,7]. This enables real-time monitoring of interventions, such as surgical drainage and antibiotic treatment, and their effectiveness [9, 14]. In another 2023

study, the CRP-to-Neutrophil-Lymphocyte Ratio (CRP-NLR) proved to be a strong predictor of the severity of odontogenic infections, with the AUC of 0.889 and a sensitivity of 79.6% and specificity of 85.1% in predicting the complicated outcome [14].

Limitations

In this study, relatively small sample size, single-centered data and cross-sectional methodology lacking a follow-up, are limitations. Additionally, the lack of a control group of healthy individuals or patients with non-odontogenic infections limits the ability to determine the specificity of CRP for odontogenic space infections. The CRP cut-off value used (>5.0 mg/L) was based on the laboratory reference range rather than an optimized diagnostic threshold determined through ROC analysis. Furthermore, the timing of blood sampling relative to symptom onset was not standardized. Large, multicenter, longitudinal studies to confirm these results and determine true cut-off values for CRP to support clinical decision making and resource allocation are needed.

CONCLUSION

Finally, this study clearly demonstrated that, CRP is highly sensitive and reliable marker to diagnose and evaluate the severity of odontogenic space infection, superior than TLC. It has been shown to correlate with clinical severity and responds to inflammation rapidly making it an essential adjunct to routine clinical use. The implementation of CRP in the routine laboratory work-up of odontogenic infections is highly recommended for early diagnosis, treatment planning and cost saving in terms of reducing morbidity and health care expenses.

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