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C-Reactive Protein (CRP) and Total Leukocyte Count (TLC) as Inflammatory Markers for Monitoring the Progression of Odontogenic Fascial Space Infection

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ABSTRACT

Dental infections can cause serious morbidity and mortality even with modern medical improvements. When infections from tooth pulp rupture cortical plate and move via fascial channels, they can spread through bone or periodontal tissues and result in potentially fatal consequences. **Objective:** To determine frequency of increased levels of C-Reactive Protein (CRP) and Total Leukocyte Count (TLC) and mean change in CRP and TLC during the course of treatment in Odontogenic fascial space infection. **Methods:** A descriptive cross-sectional study was conducted in OMFS department at PIMS, involving patients with odontogenic infections. Blood samples were taken before and at specified intervals to monitor CRP and TLC levels such as before Incision and Drainage (I&D) and post I&D (after two hours of meal at 1st , 2nd, 3rd, and 7th d post I&D Day. Using SPSS Version 23.0, frequencies, percentages, means, and standard deviations were measured to examine both quantitative and qualitative data. **Results:** There were 43 (55%) females and 35 (45%) males with a mean age of 39.17 ± 14.68 years. 17% showed elevated CRP levels and 12% presented with elevated TLC levels after seven days of follow-up. Pearson correlation was significant preoperatively and on 1st and the 2nd day Postoperatively as P value was 0.000. **Conclusions:** This study highlighted importance of monitoring CRP and TLC levels in odontogenic maxillofacial infections, both markers indicate inflammation. CRP is more sensitive than TLC during treatment, making it valuable tool for postoperative assessment.

INTRODUCTION

Despite significant advancements in modern healthcare, delays in managing odontogenic infections can still lead to serious complications, including death. Odontogenic infections have the potential to cause severe, life-threatening complications, including upper airway obstruction, descending mediastinitis, jugular vein thrombosis, septic embolism, carotid artery rupture, adult respiratory distress syndrome, pericarditis, septic shock, and disseminated intravascular coagulation. Prompt and vigilant monitoring of affected individuals is essential to mitigate these risks and prevent adverse outcomes [1]. Emergencies including odontogenic infections that migrate into the fascial spaces are frequent. If therapy is not administered, these infections have the ability to spread to other locations, use the least-resistant routes, and have major clinical effects. Infections originating in the tooth pulp, periodontal tissues, or bone may spread through fascial channels and enter the cortical plate due to tissue distention caused by the disease [2]. Reducing problems requires keeping an eye on the progression and severity of infections. C-Reactive Protein (CRP), Erythrocyte Sedimentation Rate (ESR), Total Leukocyte

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Count (TLC), Differential Leukocyte Count (DLC), pre-albumin, procalcitonin, and other laboratory indicators are frequently used for this. In order to inform clinical findings and enhance patient outcomes, these indicators are essential for monitoring postoperative infections, assessing therapy effectiveness, and determining the degree of inflammation [3]. The C-Reactive Protein (CRP), which is produced in the liver in response to infection or trauma and indicates recent inflammation, is a commonly used indication of inflammation due to its short half-life of approximately 19 hours. Recent research has demonstrated the critical role CRP plays in immunological responses and inflammation, including phagocytosis, apoptosis, complement activation, nitric oxide release, and the production of cytokines such as tumor necrosis factor-alpha and interleukin-6 [3]. A study evaluated the efficacy of C-reactive protein (CRP) and white blood cell (WBC) count in monitoring fascial space infections of odontogenic origin. It revealed that CRP was a more sensitive and consistent marker than WBC count, as elevated CRP levels were found in all patients, while WBC elevation was inconsistent. The study supports the use of CRP as a reliable diagnostic and monitoring tool during infection management and treatment progression [4]. A comparative study assessed the diagnostic performance of CRP and WBC count in 50 patients with odontogenic fascial space infections. The findings demonstrated that CRP levels were elevated in 100% of cases, while WBC count was raised in only 64%. The authors concluded that CRP is superior to WBC as a biomarker for infection severity and treatment response, emphasizing its importance in early detection and clinical follow-up [5]. Clinically, increasing swelling, fever, trismus, discomfort, dysphagia, dyspnea, and voice abnormalities are common signs of odontogenic infections. These infections have the potential to quickly progress into deep neck-space infections, impair airway function, and possibly result in multiorgan failure and death if treatment is not received [6, 7]. Studies have shown that CRP is helpful in detecting and monitoring odontogenic infections. Research indicates that when it comes to detecting inflammatory responses to odontogenic infections, C-Reactive Protein (CRP) is more sensitive than Total Leukocyte Count (TLC). Following an intervention, CRP levels often rise before plateauing. While studies have shown that persons with continuously elevated CRP have mean CRP levels of about 3.5 mg/L, TLC values showed more variation. This dynamic trajectory of CRP provides a more reliable biomarker than TLC for monitoring treatment efficacy and infection clearance. These findings demonstrate the therapeutic utility of repeated biomarker monitoring in postoperative care [8, 9].

These findings emphasize the importance of TLC and CRP as indicators for monitoring odontogenic space infections. By incorporating these markers into routine examinations, clinicians can improve decision-making, effectively control infections, and lower patient morbidity.

METHODS

The Shaheed Zulfiqar Ali Bhutto Medical University's ethical review board granted ethical approval for a descriptive cross-sectional study that was carried out in the Oral and Maxillofacial Surgery (OMFS) department at the Pakistan Institute of Medical Sciences (PIMS), Islamabad, from September 16, 2024, to January 15, 2025 (No.CPSP/REU/DSG-2021-042-3697).A thorough patient history was obtained prior to clinical examinations and pertinent tests, including a Complete Blood Count (CBC) and C-Reactive Protein (CRP) values.Orthopantomogram (OPG) radiographs were used to confirm the dental origin of the infection after clinical investigations, both intraoral and extraoral, were used to diagnose odontogenic fascial space infections.The patients diagnosed with odontogenic fascial space infections either gender age ranged from 18 to 60 years.Patients with comorbidities such as hypertension, diabetes mellitus, and pregnancy were also included. However, individuals on steroid therapy, chronic alcohol users, patients with existing neoplasms, inflammatory conditions such as rheumatoid arthritis, or those allergic to the prescribed empirical antimicrobial therapy were excluded.In this prospective study, the authors explored the role of C-reactive protein (CRP) as a monitoring tool in patients with facial space infections of odontogenic origin.The study found a strong correlation between CRP levels and the clinical severity of the infection, with elevated CRP values observed in all cases at initial presentation. Serial CRP measurements were also useful in tracking the response to treatment, showing significant reductions as the infection resolved.The authors concluded that CRP is a valuable, objective, and dynamic marker for both diagnosis and monitoring of odontogenic infections involving facial spaces [10]. The Sample size of 78 patients was determined using the WHO sample size calculator, based on a 71.82% expected frequency of increased TLC, a 95% confidence level, and a 10% margin of error. Non-probability consecutive sampling technique was employed for patient recruitment. Participants were briefed on the study's objective, and an informed written consent was obtained.Demographic data, including age, gender, type of fascial spaces involved, hypertensive or diabetic status, pregnancy status in females, and disease duration, were documented. Following confirmation of the patient's details and necessary testing, blood samples for TLC and CRP were taken from the antecubital fossa.A red-top or gold/tiger-top (SST) tube were collected for CRP and a lavender-top (EDTA) tube for TLC. An appropriate vein was selected and treated with antiseptic, the patient was put in a

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comfortable position, and a tourniquet was applied.Once the tourniquet was adjusted and the vein was secured, the lavender-top tube for TLC was filled first, followed by the red-top/gold-top tube for CRP. The angle at which the needle was inserted was shallow.After filling each tube, they were removed from the holder and gently inverted to mix. After collecting the sample, the tourniquet was removed, the needle was removed, gauze was applied to apply pressure to the region, and a bandage was applied. The needle was disposed of in a sharps container, and each tube was labeled with patient identity and collection information[11]. Every participant received conventional treatment procedures, which included the use of empirical antimicrobial therapy, incision and drainage performed under standard surgical techniques under local anesthesia, and removal of the cause of the odontogenic infection by a single surgical team. Regular saline irrigation was carried out, and drainage was maintained using corrugated rubber drains. Postoperative monitoring involved serial measurements of CRP and TLC levels on preoperative day before the incision and drainage (IandD) and postoperative days as on 1st, 2nd, 3rd, and 7th. The SPSS version 23.0 was used to analyze the data that were gathered.Presented were the frequencies and percentages of categorical parameters, such as gender, the type of fascial space involvement, and concurrent diseases (hypertension, diabetes mellitus, and pregnancy). TLC levels, CRP, age, and length of illness were among the numerical variables that were displayed as mean ± standard deviation.Histograms, Q-Q plots, and the Shapiro-Wilk test were used to evaluate the normality of quantitative variables and validate the appropriateness of applying Pearson's correlation. Statistical significance was determined at $p < 0.05$ and a 95% confidence interval for the Pearson correlation coefficient, which was used to assess the association between changes in TLC counts and CRP levels.

RESULTS

A total of 78 patients were included in the study. Out of 78 patients, 43 (55%) patients were female (19% pregnant) and 35 (45%) patients were male with mean age of 39.17 ± 14.68 years. Among these patients 30 (39%) DM, 33 (42%) were hypertensive, 17% had found increase CRP level and 12% has increased TLC level after 7 days of monitoring post intervention as shown in table 1.

Table 1: Association of Gender, Hypertension, and Diabetes with CRP and Leukocyte Trends on Day 7 Post-Surgery

Variables	Category	Total Frequency (%)	Mean CRP Value after 7 Days			Mean CRP Value after 7 Days		
			Increase (%)	Decrease (%)	p-Value	Increase (%)	Decrease (%)	p-Value
-	-	**Total**	**13 (16.7)**	**65 (83.3)**		**09 (11.5)**	**69 (88.5)**	
Gender	Male	35 (44.9)	8	27	0.154	5	30	0.369
	Female	43 (55.1)	5	38		4	39	
	Total	78 (100.0)	13	65		9	69	
Hypertensive	Yes	33 (42.3)	2	31	0.029	3	30	0.419
	No	45 (57.7)	11	34		6	39	
	Total	78 (100.0)	13	65		9	69	
Diabetes Mellitus	Yes	30 (38.5)	3	27	0.175	2	28	0.247
	No	48 (61.5)	10	38		7	41	
	Total	78 (100.0)	13	65		9	69	

Majority of patients (51%) had more than 2 fascial spaces involved secondary to odontogenic infection as reported to OMFS department which is shown in Figure 1.

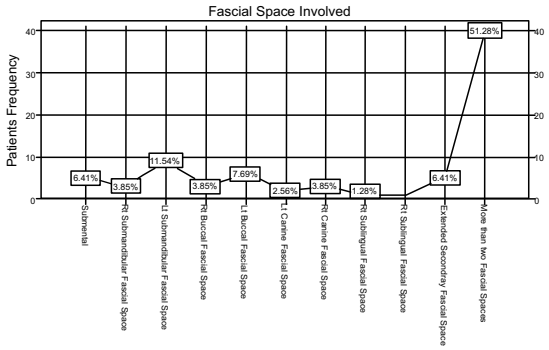

Figure 1: Bar Chart Showing the Percentages of Involved Fascial Spaces

The results from table 2 provide significant insights into the changes in disease-related markers such as CRP and TLC over time, both preoperatively and postoperatively at the 1st, 2nd, 3rd, and 7th days. The data show the mean, standard deviations, and the minimum and maximum values for these variables, highlighting the variability in these markers before and after surgery.

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Table 2: Descriptive statistics with mean and standard deviation of age, infection duration, CRP and TLC count of the study participants

Variable	Minimum	Maximum	Mean ± SD
Age	21	60	38.69 ± 13.15
Fascial Space infection duration	9	30	11.74 ± 6.16
CRP (mg/dl) Value preoperatively	4.10	314.00	97.71 ± 76.18
CRP Value at 1st post operative day	8.00	265.00	79.09 ± 66.40
CRP Value at 2nd post operative day	5.00	201.00	58.76 ± 47.94
CRP Value at 3rd post operative day	4.80	181.00	42.78 ± 43.24
CRP Value at 7th post operatively day	2.70	153.00	21.38 ± 33.73
CRP Mean Value during the treatment course	6.67	202.00	58.81±48.98
TLC Count preoperatively	6475	21740	11813.22 ± 3843.74
TLC Count at 1st post operative day	6200	21890	10377.24 ± 3101.24
TLC Count at 2nd post operative day	5870	16690	9423.56 ± 2612.22
TLC Count at 3rd post operative day	5160	50170	10234.22 ± 7052.56
TLC Count at 7th post operative day	3570	11900	7747.29 ± 2589.29
Mean TLC Count During the Treatment Course	1194.00	17024.00	9479.59 ± 2773.25

**C-Reactive Protein (mg/dl) and Total Leucocyte Count (/µL)*

Pearson correlation was used to assess the mean change in CRP and TLC level which shows a significant difference between the two variables preoperatively, 1st and 2nd post operative days as P-value was 0.000.Pearson corelation was non-significant at 3rd and 7th post operative day as P-value was 1.000 and 0.159 as shown in table 3.

Table 3: Pearson correlation between the mean change in the CRP value and TLC count

Time Point	CRP Value Mean ± SD	TLC Count Mean ± SD	Pearson Correlation	p-value	Strength and Significant
Preoperative	97.71 ± 76.18	11813.22 ± 3843.74	0.594	0.000	Moderate to strong, significant
Day 1st Post-OP	79.09 ± 66.40	10377.24 ± 3101.24	0.512	0.000	Moderate, significant
Day 2nd Post-OP	58.76 ± 47.94	9423.56 ± 2612.22	0.608	0.000	Moderate to strong, significant
Day 3rd Post-OP	42.78 ± 43.24	10234.22 ± 7052.56	0.000	1.000	No correlation, not significant
Day 7th Post-OP	21.38 ± 33.73	7747.29 ± 2589.29	-0.161	0.159	Weak negative, not significant

Correlation is significant at the 0.05 level (2-tailed).

DISCUSSION

An infection of the craniofacial regions, which include the potential spaces and fascial planes, with an exclusively odontogenic etiology is referred to as an odontogenic maxillofacial space infection.Although the prevalence of odontogenic infections has decreased significantly as a result of better dental care and the effectiveness of antibiotics, these infections can still be fatal due to patient negligence, delay in reffreal on part of patient's general practitioner, antibiotic therapeutic failure, immune system failure linked to medical conditions, or a lack of adequate healthcare facilities in a developing nation [12].C-reactive protein, which is present in trace amounts in normal, healthy individuals, is involved in the activation stages of the innate immune system's complement,antigen clearance, and phagocytosis. It is the best single screening test for an acute phase reaction and a useful indicator of the extent of inflammation and tissue damage. The serum concentration peaks in 48 hours and first rises above 5 mg/L in 6 hours.The plasma half-life of CRP is around 19 hours, regardless of health or disease.Therefore, the intensity of the stimulus that triggers the secretion directly correlates with the degree of the pathogenic process that determines the plasma CRP concentration [13].The total leukocyte count is a crucial metric for assessing the body's immune response to infection in the context of odontogenic fascial space infections. An active infectious process is indicated by a raised TLC because the body is producing more white blood cells to fight off the infections. In order to track the severity of the illness and the efficacy of treatment, the TLC usually increases within hours after infection and indicates the strength of the immunological response [14].In this study, 78 patients with infections of the odontogenic fascial area were admitted and their prognosis for infection was evaluated for a period of seven days. Among these patients 55% patients were female and 45% patients were male.This bigender distribution with slightly higher frequency among the female patients is also reported by Khan Shar M *et al.*, and Ishfaq M *et al* [12, 15]. In contrast to this study Kaur P and da Silva RD *et al.*, has reported male predominancy among their patients [13, 16]. The current study indicated that women predominance, which may be because of their cultural limitations, greater pain threshold, and socioeconomic factors.People in this region of the world are reluctant to take their female patients to the dentist in such situations.The mean age of the patients was 39.17 ± 14.68 years which was also reported by khan Shar M *et al.*, John CR *et al.*, and Mathew GC and his colleagues [12, 17, 18]. While Rashid S *et al.*, reported higher mean age of 54.5 ± 14.68 years which is inconsistent to these findings [19].The patient reported to

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the department of Oral and Maxillofacial Surgery (OMFS) with a diagnosis of Odontogenic infection, exhibiting a mean disease duration of 11.74 ± 6.16 days.This indicates a relatively varied course of infection among the patients with a mean duration close to 12 days but considerable individual variation as reflected by the standard deviation. Pavan EP *et al.*, had reported 4.3 days as average days of hospital stay which is in contradiction to this study[20]. Variability in disease duration could be attributed to several factors, including the severity of the infection, the specific type of Odontogenic infection and individual patient factors such as immune response and general health.The range of disease duration observed in these patients is imperative for understanding the timeline of infection progression and its potential impact on treatment planning and postoperative recovery.A key finding is the notable change in CRP and TLC levels immediately after surgery, particularly on the 1st and 2nd postoperative days. Pearson correlation analysis showed a strong, statistically significant relationship between disease duration, CRP and TLC levels (P-value 0.000), indicating that these markers are closely tied to the inflammatory response in the early postoperative period which is also reported by Pawan EP *et al.*, and Niazi SA and Bakhsh A as CRP levels rise during the course of 24 to 48 hours, peaking thereafter [20, 21]. CRP readings exhibit greater sensitivity and promptly decline after the inflammatory state is eliminated [22].This supports previous studies which also found peak inflammation within the first two days after surgery, reflecting the body's natural immune response.The P-values greater than 0.05 on the third and seventh postoperative days, Pearson correlation analysis revealed a change, indicating that when the inflammatory response started to normalize, the association between TLC and CRP levels ceased to be significant.This corresponds with the body's healing process, which moves from acute inflammation to the resolution phase, during which the relationship between these indicators gradually deteriorates [22].The standard deviations of CRP and TLC levels provide more evidence that the way each patient reacts to surgery can differ. According to Shaikh S *et al.*, the range between minimum and maximum results can be explained by variations in immune responses that are impacted by variables such the type of operation, the severity of the condition, and the general health of the patient [23].These results are in line with studies showing that postoperative inflammation peaks in the first few days after infection as compared to Kaya Z *et al* [24]. In contrast to these findings, which indicate a decreased correlation by the third day, Kaur A *et al* [25].Recommend either a prolonged rise of CRP or sustained alterations in TLC for extended periods of time.Differences in patient demographics, monitoring methods, or surgical approaches could be the cause of this disparity. One of the study's limitation is the very small sample size, which may not fairly represent the general population. Furthermore, the study's observational design ignores other influences that could impact the inflammatory response, such as patient obedience or variations in surgical procedures.

CONCLUSIONS

The importance of Total Leukocyte Count (TLC) and C-Reactive Protein (CRP) as useful markers for trailing the development and resolution of odontogenic fascial space infections is painted in this study. CRP levels, in particular, were a sensitive indication of inflammation resolve because they closely followed the clinical course, increasing during the acute phase and sharply dropping by day three. Additionally, TLC demonstrated a strong correlation with infection activity, particularly in the initial postoperative phase. Therefore, routine CRP and TLC monitoring can assist clinicians make informed treatment decisions and give them valuable information on infection recovery.

Authors Contribution

Conceptualization: MKS
Methodology: HU, RA, BP
Formal analysis: NUA, MKS, MUF
Writing, review and editing: HU, NUA, MKS, MUF
All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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