

INITIAL CLINICAL SYMPTOMS IN CORRELATION WITH DURATION OF HOSPITALIZATION IN PATIENTS WITH ODONTOGENIC INFECTIONS

Cena Nol¹, Popovich Monevska Danica², Bozhovich Dvojakovska Suzana², Stamatovski Aleksandar², Monevska Angela³, Koneski Filip²

¹Third-Cycle Education Courses, Department of Maxillofacial Surgery, Faculty of Dental Medicine, Ss. Cyril and Methodius University in Skopje, Republic of North Macedonia

²University Clinic for Maxillofacial Surgery in Skopje, Ss. Cyril and Methodius University in Skopje, Republic of North Macedonia

³University Clinic for Anesthesiology and Intensive Care, Faculty of Medicine, Ss. Cyril and Methodius University in Skopje, Republic of North Macedonia
e-mail: dr.koneski@gmail.com

Abstract

Introduction: Odontogenic cervicofacial phlegmons are severe infections of the superficial and deep anatomical spaces of the head and neck. Early diagnosis and appropriate treatment are crucial for faster recovery, shortening the hospitalization period, and reducing the risk of severe systemic complications. Therefore, this study was performed to analyze the role of CRP, white blood cell count (WBC), and clinical symptoms in predicting the prolonged duration of hospitalization in adult patients with maxillofacial infections.

Material and methods: This retrospective study was based on diagnosed cases of odontogenic cervicofacial phlegmons, admitted to the University Clinic for Maxillofacial Surgery in Skopje, RN. Macedonia between January 2019 and December 2024. The Symptom Severity score (SS) was assessed in this study for all patients. Routine blood sample analysis on admission to hospital was performed: complete blood count, C-reactive protein, WBC, erythrocyte sedimentation rate (ESR), blood glucose level.

Results: In our investigation, CRP level on admission, WBC level on admission, and SS, were shown to have a positive correlation with the length of hospitalization.

Conclusion: The results indicated that serum WBC count and CRP levels in combination with SS score on admission should be used as biological and clinical parameters for the prediction of the duration of hospitalization in adult patients with maxillofacial infections.

Keywords: inflammatory markers, odontogenic infections, disease severity score, hospitalization

Introduction

Odontogenic cervicofacial phlegmons are severe infections of the superficial and deep anatomical spaces of the head and neck. This specific pathologic state results from existing pathogenic bacteria localized primarily in the tooth structures or periodontal tissues. One of the main characteristics of this type of infection is its potential to evolve and spread along the

fascial planes of the neck from the skull base to the mediastinum, being potentially life-threatening, characterized by a fast evolution that requires immediate assessment due to the risk of airway blockage. Potentially fatal complications include descending mediastinitis, internal jugular vein thrombosis, arterial erosion, pneumonia, meningitis, empyema, lung abscess, sepsis, and intracranial extensions, especially in patients who are immunocompromised or have comorbid conditions^[1].

The treatment of choice for odontogenic infections is the incision and drainage of the abscess and possible removal of the odontogenic infection source in the oral cavity, if present. Early diagnosis and appropriate treatment are crucial for quick-faster recovery, shortening the hospitalization period, and reducing the risk of severe systemic complications^[2].

The “faster recovery” describes a patient whose medical condition progresses to an improved condition, demonstrating the efficacy of the treatment, at a rate that is below the average. In contrast, the term “prolonged hospitalization” describes a patient whose improved medical condition is progressing at a rate that is above the average. This could be due to several different factors, such as age, state of health, or the severity of the infection. Much of the published evidence identified that age, preadmission antibiotic use, underlying comorbidities, diabetes mellitus, higher odontogenic infection severity score, the number of infected spaces, and infection site were associated with increased length of hospitalization^[3].

Vital signs and clinical findings such as the degree of swelling, respiratory distress, difficulty in opening the mouth, and painful swallowing are important for assessing the severity of the disease. Inflammatory markers identified by blood tests are commonly used as objective evaluation parameters, and C-reactive protein (CRP), white blood cell count (WBC), and its fractions (neutrophils, lymphocytes, monocytes) are often used as references^[4].

White blood cell count (WBC) is a well-researched predictor of inflammation with a half-life of 5–6 days. However, due to CRP’s fast peaks and falls, it is a more sensitive marker for the course of infection than WBC. In addition, WBC count levels alone are inadequate to rule in or rule out the existence of infections. However, increased levels are vague and have little diagnostic accuracy. For instance, WBCs have a minimal role in the diagnosis and severity assessment of head and neck infections; their significance lies mainly in the evaluation of the patient’s response to therapy. In comparison to odontogenic infections, CRP is a better infection measure than WBC because its level rises more rapidly. CRP is present in minute quantities in healthy persons, increases quickly with infection within a few hours and then rapidly decreases when the inflammation subsides. Due to the tight relationship between the intensity and duration of acute infections, CRP is a sensitive indicator of inflammatory processes^[5].

The criteria for prolonged hospitalization vary between studies. Usually, hospitalization over the average period is considered long-term. In the USA, the average length of stay was from 3 to 8.3 days^[6-9]; in Iran, it was 6.8 days; ^[10] in Finland, it was 14.8 days; ^[11] in China, it was 12 days; ^[12] and in Romania, it was 4.92 days^[13]. From the SCMUT database, the median LOS of inpatients in our unit in the last 5 years was 5.5 days^[3].

It is therefore important to determine whether various serum inflammatory marker levels on admission may predict a prolonged hospital stay in patients with acute maxillofacial infections. Among the most commonly evaluated inflammatory markers, C-reactive protein (CRP), white blood cell count, and hemogram indexes provide valuable information to clinicians for the diagnosis, screening, and follow-up of various diseases.

Therefore, this study was performed to analyze the role of CRP, white blood cell count

(WBC), and clinical symptoms in predicting prolonged hospitalization in adult patients with maxillofacial infections. The null hypothesis of this study is that WBC count, CRP values, and clinical symptoms do not change the variability in the duration of hospital stay in these patients.

Material and methods

The present retrospective study was based on diagnosed cases of odontogenic cervicofacial phlegmons, admitted to the University Clinic for Maxillofacial Surgery in Skopje, RN. Macedonia between January 2019 and December 2024. The included data were collected from the medical charts of patients and were represented by age, gender, diagnosis of odontogenic cervicofacial phlegmons, duration of hospitalization, treatment and bloodwork values, and clinical and paraclinical examination.

Table 1. Symptom severity score (SS)

Criteria		Score
Symptoms	TEM, >38, <36	1
	WBC, >12000, >4000	1
Trismus	Moderate	2
	Severe	4
Dysphagia	Moderate	2
	Severe	4
Facial spaces	Low risk	2
	High risk	4
Comorbidities	Diabetes, immunocompromised status	2
	No	0

Preoperative assessment included the following parameters: dental etiology, teeth involved, number of spaces involved (evident clinically or on computerized tomography if required), body temperature, mouth opening (measurement of maximum inter-incisal opening with vernier caliper), and pain (using visual analogue scale running from 1 to 10). Active pus discharge, dysphagia, hoarseness, and swelling were assessed. In addition to clinical assessment, patients underwent routine blood investigations. Routine blood sample analysis on admission to the hospital was performed: complete blood count, C-reactive protein, WBC, erythrocyte sedimentation rate (ESR), and blood glucose level.

Symptom Severity score (SS) was assessed in this study for all patients. We used the SS score of odontogenic infection developed by Sainuddin *et al.* with some modification. The score is based on several clinical parameters (Table 1)^[14].

Based on the diagnosis, management of patients with odontogenic infection was carried out. Definitive management consisted of incision and drainage of abscess and extraction of the offending tooth as indicated. Empirical antimicrobial therapy and appropriate analgesic drugs were started for the control of infection and relief of pain. All patients received intravenous probabilistic antibiotic therapy effective against oral flora, Ceftriaxone of 1-2 g – once a day and Metronidazole of 500 mg -3/day or Clindamycin of 600 mg -2/day. Following the bacteriologic examination, antibiotics were adapted to bacteriological results. Patients were discharged from the hospital when clinical parameters and laboratory values of the inflammatory markers showed an improved condition, demonstrating the efficacy of the treatment. The main clinical criteria for improvement were normalization of the body temperature and blood tests.

Statistical analysis

Data obtained in this study were processed using the SPSS software package, version 26.0 for Windows. Qualitative data were analyzed with the coefficient of relations, proportions, and rates, while quantitative data were analyzed using measures of central tendency (mean, median, minimum, and maximum values), as well as measures of dispersion (standard deviation). The Shapiro-Wilk W test was used to determine the normality of the distribution of frequencies of the examined variables. The Mann-Whitney U test was used to determine the statistically significant difference between two independent quantitative parameters with an irregular frequency distribution. The Spearman's rank correlation was used to determine the relationship between the length of hospital stay and selected parameters of interest. A two-tailed analysis with a significance level of $p < 0.05$ was used to determine statistical significance.

Results

A total of 60 patients were included in the study, of which 24 (40%) were female and 36 (60%) were male, with a gender ratio of 0.7 to 1. The percentage difference in the distribution of male and female participants, with $p < 0.05$, was statistically significant (Difference 20% [(2.13-36.16) 95% CI]; $p = 0.0291$), favoring a higher representation of female patients. The average age of participants in the sample was 45.14 ± 7.9 years, with a minimum/maximum age of 8/79 years, and 50% of patients were ≤ 48.5 years old, while 25% were older than 60 years, with a median IQR=48.5 (30-60) (Table 2). Female participants had an average age of 37.65 ± 19.05 years, with a minimum/maximum age of 8/67 years, whereas male participants had an average age of 50.15 ± 19.45 years, with a minimum/maximum age of 8/79 years. Male participants were significantly older than female participants (Mann Whitney U test: $Z = -2.099$; $p = 0.0358$).

The average hospital stay of patients was 5.78 ± 2.99 days, with a minimum/maximum range of 1/11 days. For 50% of the participants, the length of hospitalization was ≤ 6 days, and for 25% of them, the hospitalization exceeded 8 days, with a median IQR=6 (4-8) (Table 2).

Table 2. Distribution of selected parameters

Parameters	N	Mean $\pm$ SD	Min/Max	Median(IQR)
Age	60	45.14 $\pm$ 7.9	8/79	48.5 (30-60)
Hospitalization	60	5.78 $\pm$ 2.99	1/11	6 (4-8)
SS score	60	9.92 $\pm$ 2.66	4/16	9 (8-11)
CRP	60	111.76 $\pm$ 95.76	6.04/358.30	78.91 (38.40-151.69)
Body Temperature	60	37.35 $\pm$ 0.74	36/39.5	37 (37-37.5)
WBC	60	13.93 $\pm$ 6.13	3.5/ 32.9	12.6 (9.7-17.8)

*significant $p < 0.05$

The average SS score of patients before the intervention was 9.92 ± 2.66 , with a minimum/maximum value of 4/16. For 50% of the participants, the SS score was ≤ 9 , and for 25% of them, it was > 11 , with a median IQR=9 (8-11) (Table 2).

On admission, the average CRP value was 111.76 ± 95.76 , with a minimum/maximum range of 6.04/358.30. For 50% of the participants, the CRP value was ≤ 98.91 , and for 25% of them, it was > 151.69 , with a Median IQR=78.91 (38.40-151.69) (Table 2).

On admission, the average body temperature of the patients in the study was $37.35 \pm 0.74^\circ\text{C}$, with a minimum/maximum range of 36/39.5 $^\circ\text{C}$. For 50% of the patients on admission, the body temperature was $\geq 37^\circ\text{C}$, with a median IQR=37 (37-37.5) (Table 2).

On admission, the WBC level was 13.93 ± 6.13 , with a minimum/maximum range of 3.5/32.9. For 50% of the patients, the WBC level was ≥ 12.6 ($\times 10^9/L$), and for 25% of them, the WBC level was >17.8 ($\times 10^9/L$), with a median IQR=12.6 (9.7-17.8) (Table 2).

An analysis was conducted on the interrelationship between the length of hospitalization, expressed in days, and selected clinical parameters such as SS score, body temperature ($^{\circ}C$), and CRP levels, determined in the patients before the intervention (Table 3 and Figure 1).

For $p < 0.05$, a significant positive weak correlation was observed between the length of hospitalization and the SS score ($R(55)=0.330$; $p=0.0138$) – as the SS score increased, the length of hospitalization in the study participants also significantly increased (Table 3 and Figure 1).

Table 3. Correlation between elected clinical parameters and length of hospitalization

Selected Clinical Parameters	Length of Hospitalization (days)
SS score	$R_{(55)}=0.330$; $p=0.0138^*$
Body Temperature	$R_{(55)}=0.236$; $p=0.0823$
CRP	$R_{(54)}=0.360$; $p=0.0074^*$
WBC	$R_{(54)}=0.412$; $p=0.0018^*$

R=Spearman Rank order correlation*, significant $p < 0.05$

For $p < 0.05$, a significant positive weak correlation was observed between the length of hospitalization and CRP levels ($R(55)=0.330$; $p=0.0138$) - as the pre-intervention CRP levels increased, the length of hospitalization in the study participants also significantly increased (Table 3 and Figure 1). For $p < 0.05$, a significant positive weak correlation was observed between the length of hospitalization and WBC ($R(55)=0.412$; $p=0.0018$) – as the WBC count increased, the length of hospitalization in the study participants also significantly increased (Table 3 and Figure 1). For $p > 0.05$, no significant linear positive correlation was found between the length of hospitalization in days and the patients' temperature on admission ($R(54)=0.360$; $p=0.0074$) - as the temperature on admission increased, the length of hospitalization increased non-significantly (Table 3 and Figure 1).

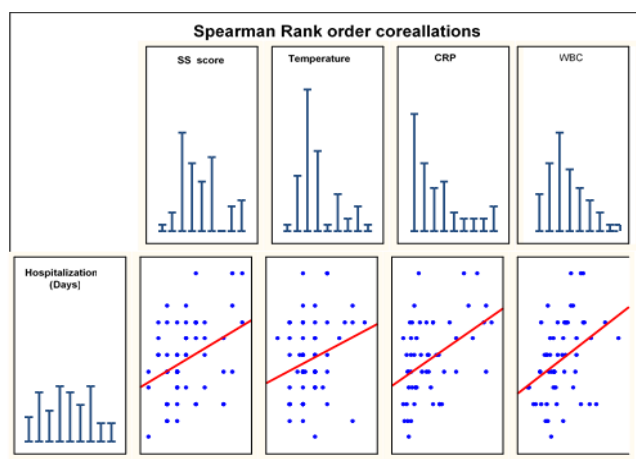


Fig. 1. Correlation between selected demographic and bone-mineral parameters

Discussion

The decision-making process in medicine incorporates clinical and laboratory considerations. Detecting an increase in acute phase reactants may assist the diagnostic interpretation of clinical symptoms in circumstances when an infection is suspected. In our investigation, CRP level on admission, WBC level on admission, and SS, were shown to have positive correlation with length of hospitalization. In our opinion, these markers have the ability to predict the severity of odontogenic infection.

A better understanding of the inflammatory cascade has led to new discoveries and the identification of many mediators that, in combination with clinical symptoms, might serve as valuable infection indicators^[15]. Bagul *et al.* concluded in their study that CRP should be recommended as a monitoring marker for managing patients with fascial space infections of odontogenic origin, as it is a more sensitive indicator than WBC count and one of the best measuring tools for determining the infection control in these patients. In their research, John CR. *et al.* 38 found that the CRP test is a practical, easily accessible blood test that portrays patient course and response to therapy more precisely than other commonly used indicators in oral and maxillofacial surgery^[16].

In the study by Ovidiu Rosca, patients were subcategorized according to the SS score into two groups as follows: Group A - the low-severity infection group with 54 patients whose severity score ranged from 0 to 8 points on the SS scale; Group B - the high-severity infection group including 54 patients with a severity score between 9 and over 16 points. The median duration of hospitalization was significantly longer in patients from Group B compared to Group A (12.0 days vs. 4.1 days). These findings are similar to ours since higher SS score was associated with longer hospitalization^[5].

Many of the published studies have demonstrated that CRP, white blood cell count (WBC), and its fractions (neutrophils, lymphocytes, monocytes) are often used as markers of inflammation and are reported to be useful in detecting maxillofacial infections^[8].

In our study, WBC count and CRP were in a positive correlation with the length of hospitalization and were relevant indicators for the severity of the odontogenic infection.

Horatiu Urechescu *et al.* suggest that WBC and CRP should be used as biological parameters for the prediction of the duration of hospitalization, with moderate statistical significance among adult patients with maxillofacial infections. The logistic regression analysis confirmed a positive correlation between WBC count on admission and the duration of hospital stay ($p < 0.001$), and of all studied variables, this showed the highest specificity (64.81%). Our study also confirmed this hypothesis^[3].

Additionally, the literature has shown serum CRP on admission or preoperatively as a significant predictive factor for the length of hospital stay in patients with maxillofacial infections^[19,9]. Most of these studies have found that CRP was an effective parameter for predicting length of hospital stay^[9]. Using a quantitative approach, Sharma *et al.* showed that CRP level was a significant marker of the length of hospital stay^[16]. The higher CRP concentration, the longer patient's hospital stay^[19].

Pavan *et al.* reported in their study a strong positive correlation between CRP levels and length of hospital stay and a significant difference between groups. CRP levels increased 4 to 6 hours after injury, reaching a peak between 24 and 48 hours. CRP values regressed rapidly when the inflammatory condition was resolved, showing more sensitivity than the leukogram and ESR. It is worth noting, however, that CRP values are not able to determine the course of the infection in real time, because they are low in the initial phase and remain above

reference after recovery^[20].

A statistically significant relationship ($p < 0.001$) was observed between the length of hospital stay and all the three biochemical parameters: CRP, WBC and ESR^[21].

Conclusions

Our results have shown a moderate statistically significant positive correlation between the levels of predictor variables (WBC count, C-reactive protein) on admission, SS score and the duration of hospitalization. These results indicate that serum WBC count and CRP levels in combination with SS score on admission should be used as biological and clinical parameters for the prediction of the duration of hospitalization in adult patients with maxillofacial infections.

Conflict of interest statement. None declared.

References

1. Roî CI, Roî A, Nicoară A, Nica D, Rusu LC, Soancă A, et al. Impact of Treatment on Systemic Immune-Inflammatory Index and Other Inflammatory Markers in Odontogenic Cervicofacial Phlegmon Cases: A Retrospective Study. *Biomedicines* 2023; 11(6): 1710. <https://doi.org/10.3390/biomedicines11061710>.
2. Zawisławski E, Nowak R. Odontogenic Head and Neck Region Infections Requiring Hospitalization: An 18-Month Retrospective Analysis. *Biomed Res Int* 2021; 2021: 7086763. doi: 10.1155/2021/7086763.
3. Urechescu H, Gheran-Vida E, Cuzic C, Ancusa O, Ursoniu S, Pricop M. Inflammatory Markers as Predictors for Prolonged Duration of Hospitalization in Maxillofacial Infections. *J Clin Med*. 2023; 12(3): 871. doi: 10.3390/jcm12030871.
4. Kusumoto, J., Iwata, E., Huang, W. et al. Hematologic and inflammatory parameters for determining severity of odontogenic infections at admission: a retrospective study. *BMC Infect Dis* 2022; 22(1): 931. doi: 10.1186/s12879-022-07934-x.
5. Rosca O, Bumbu BA, Ancusa O, Talpos S, Urechescu H, Ursoniu S, et al. The Role of C - reactive protein and Neutrophil to Lymphocyte Ratio in Predicting the Severity of Odontogenic Infections in Adult Patients. *Medicina (Kaunas)* 2022; 59(1): 20. doi: 10.3390/medicina59010020. PMID: 36676644; PMCID: PMC9866968.
6. Wang J, Ahani A, Pogrel MA. A five-year retrospective study of odontogenic maxillofacial infections in a large urban public hospital. *Int J Oral Maxillofac Surg* 2005; 34(6): 646-649. doi: 10.1016/j.ijom.2005.03.001.
7. Storoe W, Haug RH, Lillich TT. The changing face of odontogenic infections. *J Oral Maxillofac Surg* 2001; 59(7): 739-748; discussion 748-9. doi: 10.1053/joms.2001.24285.
8. Allareddy V, Rampa S, Nalliah RP, Allareddy V. Longitudinal discharge trends and outcomes after hospitalization for mouth cellulitis and Ludwig angina. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2014; 118(5): 524-531. doi: 10.1016/j.oooo.2014.06.003.
9. Gams K, Shewale J, Demian N, Khalil K, Banki F. Characteristics, length of stay, and hospital bills associated with severe odontogenic infections in Houston, TX. *J Am Dent Assoc* 2017; 148(4): 221-229. doi: 10.1016/j.adaj.2016.11.033
10. Roberson JB, Harper JL, Jauch EC. Mortality associated with cervicofacial necrotizing fasciitis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1996; 82(3): 264-267. doi: 10.1016/s1079-2104(96)80350-7.
11. Wheatley MJ, Stirling MC, Kirsh MM, Gago O, Orringer MB. Descending necrotizing mediastinitis: transcervical drainage is not enough. *Ann Thorac Surg* 1990; 49(5): 780-784. doi: 10.1016/0003-4975(90)90022-x.

12. Levine TM, Wurster CF, Krespi YP. Mediastinitis occurring as a complication of odontogenic infections. *Laryngoscope* 1986; 96(7): 747-750. PMID: 3724325.
13. Garatea-Crelgo J, Gay-Escoda C. Mediastinitis from odontogenic infection. Report of three cases and review of the literature. *Int J Oral Maxillofac Surg* 1991; 20(2): 65-68. doi: 10.1016/s0901-5027(05)80707-6.
14. Sainuddin S, Hague R, Howson K, Clark S. New admission scoring criteria for patients with odontogenic infections: a pilot study. *Br J Oral Maxillofac Surg* 2017; 55(1): 86-89. doi: 10.1016/j.bjoms.2016.05.003.
15. Póvoa P, Coelho L, Almeida E, Fernandes A, Mealha R, Moreira P, et al. Early identification of intensive care unit-acquired infections with daily monitoring of C-reactive protein: a prospective observational study. *Crit Care* 2006; 10(2): R63. doi: 10.1186/cc4892.
16. Bagul R, Chandan S, Sane VD, Patil S, Yadav D. Comparative Evaluation of C-Reactive Protein and WBC Count in Fascial Space Infections of Odontogenic Origin. *J Maxillofac Oral Surg* 2017; 16(2): 238-242. doi: 10.1007/s12663-016-0953-z.
17. Sharma A, Giraddi G, Krishnan G, Shahi AK. Efficacy of Serum Prealbumin and CRP Levels as Monitoring Tools for Patients with Fascial Space Infections of Odontogenic Origin: A Clinicobiochemical Study. *J Maxillofac Oral Surg* 2014; 13(1): 1-9. doi: 10.1007/s12663-012-0376-4.
18. Pricop M, Ancusa O, Talpos S, Urechescu H, Bumbu BA. The Predictive Value of Systemic Immune-Inflammation Index and SymptomSeverity Score for Sepsis and Systemic Inflammatory Response Syndrome in Odontogenic Infections. *J Pers Med* 2022; 12(12): 2026. doi: 10.3390/jpm12122026.
19. Heim N, Wiedemeyer V, Reich RH, Martini M. The role of C-reactive protein and white blood cell count in the prediction of length of stay in hospital and severity of odontogenic abscess. *J Craniomaxillofac Surg* 2018; 46(12): 2220-2226. doi: 10.1016/j.jcms.2018.10.013.
20. Ishimine N, Honda T, Yoshizawa A, Kawasaki K, Sugano M, Kobayashi Y, et al. Combination of white blood cell count and left shift level real-timely reflects a course of bacterial infection. *J Clin Lab Anal* 2013; 27(5): 407-411. doi: 10.1002/jcla.21619.
21. Kaur A, Sandhu A, Kaur T, Bhullar RS, Dhawan A, Kaur J. Correlation Between Clinical Course and Biochemical Analysis in Odontogenic Space Infections. *J Maxillofac Oral Surg* 2019; 18(2): 203-209. doi: 10.1007/s12663-018-1132-1.