

An evaluation of White Cell count, C-Reactive protein and Procalcitonin as diagnostic and prognostic biomarkers during the management of maxillofacial infections

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ABSTRACT

Introduction

Odontogenic infections (OI) and to a lesser extent non-odontogenic infections, constitute a substantial proportion of a maxillofacial and oral surgeon's work. These infections may be life threatening if not treated adequately. Aims and objectives: The purpose of this current study was to evaluate the diagnostic and prognostic value of White Cell count (WCC), C-Reactive Protein (CRP) and Procalcitonin (PCT), in the management of maxillofacial infections.

Design and methods: Quantitative, descriptive research was conducted to determine whether blood levels of the mentioned parameters, on day one and day three respectively, had any indication of patient's response to treatment received for the presenting infection. Serial blood samples were taken on day 1 and day 3 respectively and values were recorded in a data collection sheet and evaluated using Chi-squared tables with STATA-17 analysis.

The results showed that there was a statistically significant reduction in WCC and CRP levels following treatment, however, PCT levels did not change significantly.

In conclusion, this current study confirmed that specific blood test parameters, such as WCC and CRP, could be useful in evaluating patient's response to treatment of maxillofacial infections.

Keyword

White Cell Count, C-Reactive Protein, Procalcitonin, Maxillofacial Infections

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INTRODUCTION

Maxillofacial infections can have devastating consequences when not promptly diagnosed and treated adequately.¹ Periodontal diseases and dental caries are some of the leading causes of Odontogenic Infections (OI).¹ Therefore, good oral hygiene practice remains one of the most important factors in the prevention of these conditions.¹ The incidence, severity, morbidity and mortality of OI have declined over the past 60 years, specifically, the dramatic change in mortality, which is due to the introduction of penicillin in the treatment of infections.²

Special investigations used in diagnosis and treatment of OI and non-odontogenic infections include periapical radiographs and orthopantomograms, computed tomography (CT) scan, baseline blood tests (Biomarkers) and pus swab for microscopy, culture and sensitivity testing.²

A biomarker is described as a characteristic that can be objectively measured and evaluated as an indicator of a normal biological process, pathological process or pharmacological response to therapeutic interventions or treatment.³

Abnormal ranges in white cell count (WCC), C-reactive protein (CRP) and procalcitonin (PCT) are indicative of inflammation and are used to determine the presence of infection in cases with no obvious cause or signs, such as deep satellite or hidden pockets of infection, especially in ICU cases of immobile or comatose patients. Serial values are also used to monitor patient's response to treatment.^{2,4,5,6}

Materials and Methods

In this prospective quantitative and descriptive study, 39 cases which satisfied the inclusion criteria were sampled in the period between the 1st of June and the 31st of December 2023. The study included patients presenting to the maxillofacial and oral surgery department with infection of the head and neck region. Serial blood samples were taken on days 1 and 3 respectively and the values were recorded and analysed. The occurrence proportions of the WCC, CRP and PCT were compared between each other and by demographic characteristics.

Furthermore, contingency (Chi-square) tables analysis were undertaken to measure the association between the

outcome of the binary outcome of presence or absence of characteristics of interest (WCC, CRP, PCT) and the demographic characteristics. Finally, logistics regression analysis was used to identify the demographic factors that influenced the outcomes. All analysis was done using STATA-17.

Results

The total number of patients treated during the allocated time of six months was 48 (n=48). Nine patients were excluded from the study due to incomplete records. Thirty-nine (n=39) patients were included, of which 17 were female and 22 male.

Period	Day 1	Day 3	Total	Test
N	39 (50.0%)	39 (50.0%)	78 (100%)	
WCC	13.73 (5.95)	7.93 (4.0)	10.83 (5.82)	<0.001
CRP	68.31 (111.94)	74.92 (68.03)	121.62 (103.33)	<0.001
PCT	2.37 (6.65)	0.83 (1.67)	1.60 (4.88)	0.163

Table 1: Comparison of different parameters

The comparison above assumed normal distribution for WCC, CRP and PCT. The results using non-parametric method Kruskal-Wallis, still showed that differences exist between the two periods. WCC (chi2(1) with ties = 25.673 [pr=0.001]; CRP (chi2(1) with ties = 15.114 [pr=0.001] and PCT (chi2(1) with ties = 2,970 [pr=0.084]

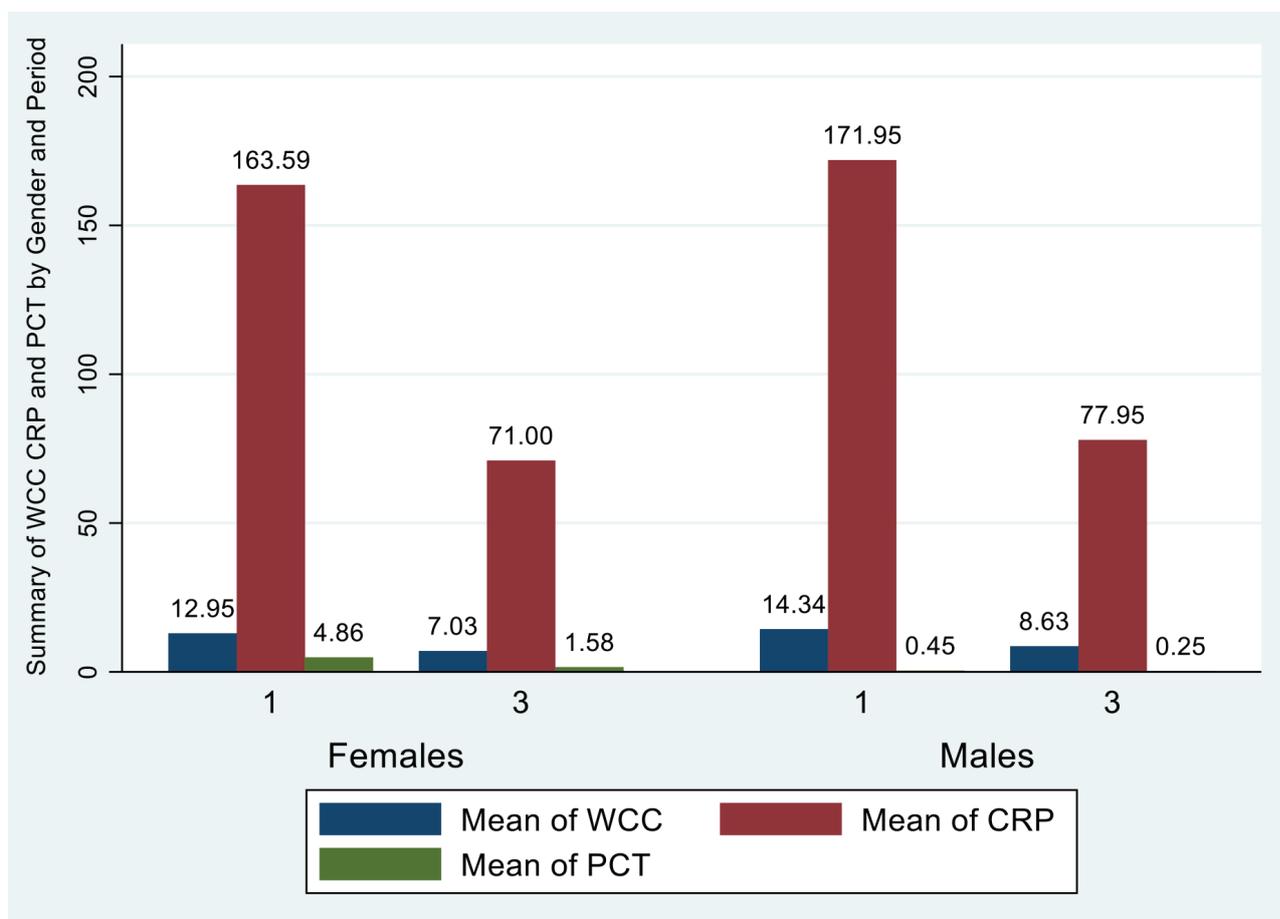


Fig 1: Graph of summary of WCC, CRP and PCT by Gender and Period

The results showed that there was a significant difference between PCT levels for males and females. The average PCT for females was 3.22 and for males 0.35.

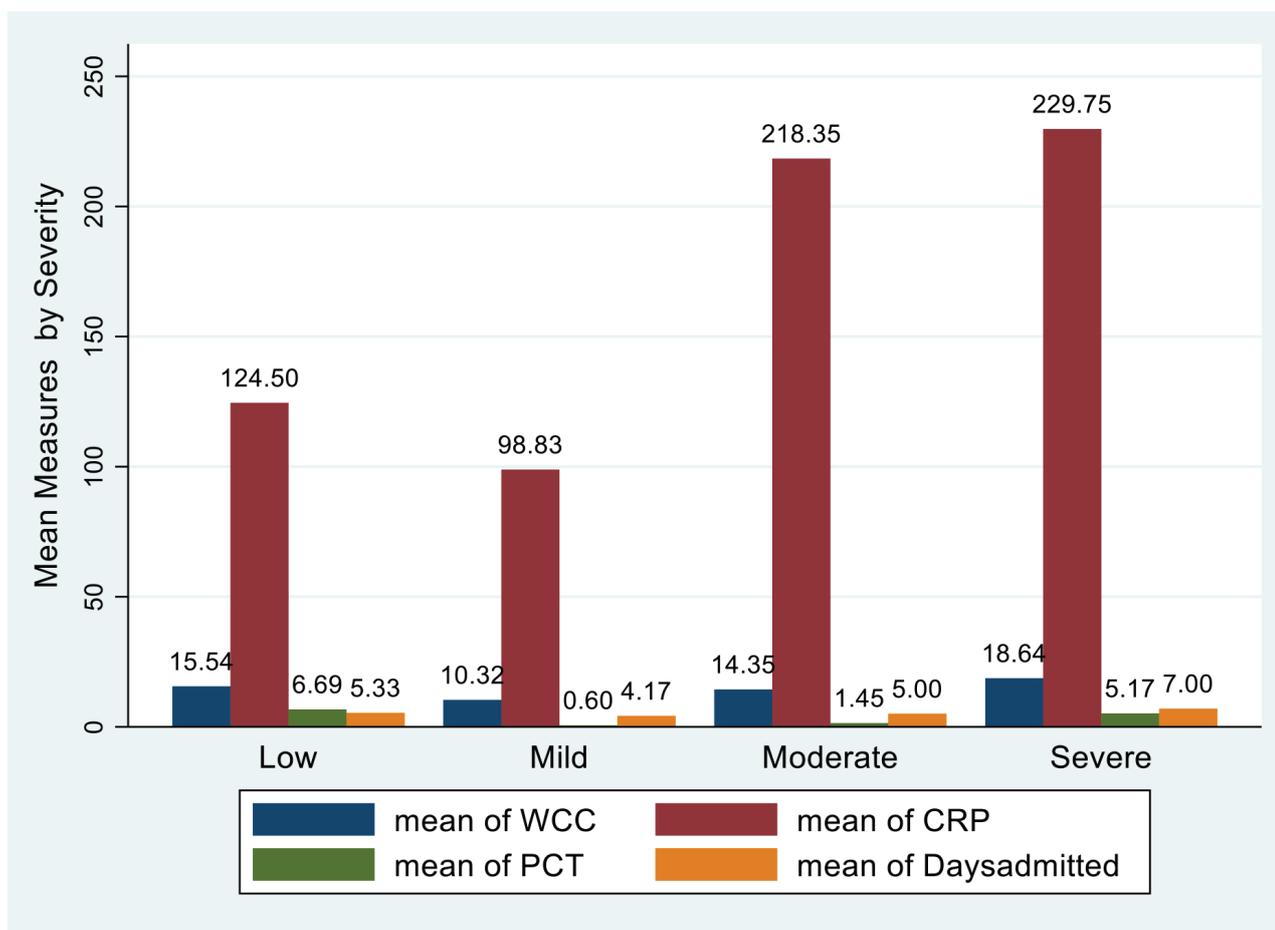


Fig 2: Graph of impact on severity on WCC, CRP and PCT

The graph above presents the outcome of the severity and the effect on WCC, CRP and PCT. This shows that the severity marginally impacted on the WCC ($pr=0.06$); and days admitted ($pr=0.092$). The level was significant for CRP ($pr=0.01$).

Table 2: Gender distribution of areas involved

Female: Maxillary	29%
Female: Mandible	71%
Male: Maxillary	14%
Male: Mandible	86%

The comparison in the table above does demonstrate a difference in distribution of anatomical areas involved between different genders, even though statistically insignificant.

DISCUSSION

Maxillofacial infections are common conditions that the maxillofacial and oral surgeon will encounter in his or her practice. Management of these infections require prompt diagnosis and appropriate treatment modalities. Removal of the cause, surgical incision and drainage are the corner stones of these treatment modalities.² The patient's response to treatment can be evaluated clinically and by means of biomarkers that can be detected in the patient's blood.^{3,6,7} This current study compared the different biomarkers, WCC, CRP and PCT as potential diagnostic and prognostic tools.

The results obtained in this study of 39 ($n=39$) patients, regarding the demographic data related to age and gender distribution, revealed that the average age for male patients

was 42.7 years (19 – 67), and for female patients 42 years (14 - 82). The total sample was 22 males (56.4%) and 17 females (43.6%). This correlates with similar studies by Kent in 2021⁸ and Kaminski in 2022⁹ regarding gender distribution of patients presenting with maxillofacial infections, where it was found that more males than females presented with infections. This can be attributed to cultural, behavioural and social factors causing male patients to present later when infection was already present.^{8,9,10,11}

White Cell Count as the first parameter (Biomarker) in this study has a normal range between $3.92 \times 10^9/L$ and $10.4 \times 10^9/L$.⁸ The data for this study illustrated a range between $3.61 \times 10^9/L$ and $35.29 \times 10^9/L$. On the day of presentation, the average was $13.73 \times 10^9/L$, and on day 3 the results showed a decrease in the average WCC to $7.93 \times 10^9/L$ (Fig 1). This constitutes a decrease of 57.8%. Shuman 2012³² and Heffernan 2021³ also demonstrated a reduction in WCC after initial treatment of infection and clinical improvement of the patient. In the same study Heffernan 2021³ found that

WCC as a biomarker still lacks sensitivity and specificity regarding distinction between inflammation and infection.³

The second parameter in this study was the CRP value. CRP is synthesised and released by the liver in response to inflammation and infection.³ The normal value for CRP is less than 0.3 mg/dL. Values ranging from 0.3mg/dL - 1.0mg/dL are regarded as minor elevation, whilst values between 1.0–10.0mg/dL are regarded as moderate. Elevations above 10mg/dL show a marked elevation whilst more than 50mg/dL are regarded as severe elevation. In 90% of cases with CRP >50mg/dL, it is associated with bacterial infections.^{7,12,13} The CRP levels on day one and three ranged between 9 and 418 mg/dL (121.6mg/dL). For day 1, the range was 2 to 213 mg/dL (168mg/dL) and for day 3, 2 to 357 mg/dL (74.9mg/dL). This shows an over-all reduction in CRP levels of 44.6% following initial treatment. This finding in the current study is in keeping with the findings of studies by Dias¹⁴ and Largman¹⁵ who also indicated a decrease in CRP levels after initial treatment and clinical improvement.

The third biomarker in this study was PCT, with normal values being below 0.05ug/L.⁶ The value of PCT on day 1 ranged between 0.01 and 36.02ug/L (2.37ug/L), and on day 3 between 0.01 and 6.70ug/L (0.83ug/L). This demonstrates a decrease of 35% in PCT concentration following treatment. Although compared to the other biomarkers, the concentration levels of PCT in this study did not demonstrate any statistical significance. Several studies have demonstrated PCT to be a sensitive and reliable biomarker in the diagnosis and prognosis of inflammation and infection.^{3,6,16} However in this current study, we did not find it to be significant. Clinicians should be cautious with patients presenting in the acute phase (within 24h) of infection that might not have an elevated PCT concentration yet, as concentration of PCT peaks at 24 hours. Shorter intervals (<12h) of re-testing levels may have no significant benefit.³ In this current study the second test was done after 72 hours, thus enough time lapsed for the body to release PCT.

The origin of maxillofacial infections can be from various anatomical areas, but in this study we distinguished between maxillary and mandibular spaces involvement. In this study population of 39 (n=39) patients the mandibular spaces were involved in 31 patients (79.5%) and the maxillary spaces in 8 (20.5%). There was no statistically significant difference in fascial space involvement between males and females. Table 3 illustrates that maxillary spaces were involved in 29% of female and 14% of male patients. Mandibular spaces were involved in 71% of females and 86% of males respectively. This is in correlation to other studies found in the literature by Veronez¹⁷ and Singh¹⁸ that also indicated that the mandibular spaces are more frequently involved in relation to maxillary spaces.

CONCLUSION

The findings from this study are in keeping with the global literature regarding the usefulness of WCC and CRP levels in maxillofacial infections. PCT was non-specific in the current study, which is contrary to what is reported in the literature concerning the sensitivity of PCT as a sole biomarker.

The Maxillofacial and Oral Surgeon will encounter numerous infections in his or her career, some of which can be life threatening. Timely diagnosis, relevant treatment and the

utilization of blood tests available, will ensure a successful outcome in the majority of cases.

There is no consensus on the golden standard or perfect biomarker in the diagnosis and management of patients with inflammation and infection in the literature, however the current study demonstrated that WCC and CRP could be utilised in diagnosis and prognosis of maxillofacial infections. Although PCT was non-specific in this current study, it is still recommended in the literature as a specific and sensitive biomarker in the diagnosis and management of patients with inflammation and infection.

The current study was limited to evaluating these three biomarkers (WCC, CRP, PCT), but future studies may include more parameters.

Furthermore, this can also be done as a multi-centre collaboration to collect more data and compare the experience of different units regarding treatment of maxillofacial infections, and the utilization of different blood tests or parameters to evaluate the progress and prognosis of their patients.

Declaration

There is no conflict of interest to declare.

Ethical clearance

Ethical clearance was obtained from SMU REC with number SMUREC/D/409/2023:PG

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