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ORIGINAL ARTICLE

Role of Serum Procalcitonin and C-Reactive Protein in Predicting Surgical Site Infections After Head and Neck Surgeries

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ABSTRACT

Background: Surgical site infections (SSIs) are a frequent postoperative complication in head and neck surgeries due to the high microbial load of the upper aerodigestive tract. Early detection is essential because clinical signs often appear late and may delay timely management. Serum biomarkers such as procalcitonin (PCT) and C-reactive protein (CRP) may help identify infections earlier than clinical assessment alone.

Objective: To evaluate the diagnostic performance of serum PCT and CRP in predicting SSIs following elective head and neck surgeries.

Methods: This prospective multicentre study was conducted from June 2022 to April 2023 at Nishtar Hospital Multan, Bolan Medical Complex Hospital Quetta, and Sir Syed College of Medical Sciences for Girls Karachi. A total of 120 adult patients undergoing elective head and neck procedures were enrolled. Serum PCT and CRP levels were measured preoperatively and on postoperative days 1, 3, and 5. SSIs were diagnosed based on CDC criteria. Receiver operating characteristic (ROC) analysis was performed to determine the predictive accuracy and optimal cut-off values of both biomarkers.

Results: Of the 120 patients, 28 (23.3%) developed SSIs. PCT levels were significantly higher in the SSI group beginning on postoperative day 3 (0.74 ± 0.18 ng/mL vs. 0.28 ± 0.09 ng/mL; $p < 0.001$), with further elevation by day 5. CRP also showed significant elevation in the SSI group, particularly on postoperative day 3 (118.6 ± 26.3 mg/L vs. 63.4 ± 18.7 mg/L; $p < 0.001$). ROC analysis demonstrated superior diagnostic accuracy of PCT (AUC 0.89; optimal cut-off >0.52 ng/mL) compared with CRP (AUC 0.82; cut-off >82 mg/L). PCT showed higher specificity and earlier separation between infected and non-infected patients.

Conclusion: Serum procalcitonin is a more accurate and earlier predictor of SSIs after head and neck surgeries compared with C-reactive protein. Combined interpretation of both markers enhances early postoperative infection surveillance and supports timely clinical decision-making.

Keywords: Procalcitonin; C-reactive protein; surgical site infection; head and neck surgery; postoperative biomarkers; infection prediction; inflammation markers.

INTRODUCTION

Head and neck surgeries are associated with a disproportionately high risk of postoperative surgical site infections (SSIs) because of the region's complex anatomy and close communication with the upper aerodigestive tract, which contains dense polymicrobial flora[1]. Surgical procedures involving the oral cavity, pharynx, larynx, salivary glands, or neck dissections frequently expose operative fields to mixed aerobic and anaerobic organisms, increasing the likelihood of early bacterial contamination[2]. As a result, SSIs remain a major cause of postoperative morbidity, contributing to wound breakdown, delayed healing, prolonged hospitalization, increased antibiotic use, and significantly higher healthcare costs. Early recognition of infection is essential; however, traditional clinical signs such as fever, erythema, edema, tenderness, and purulent discharge often appear late, when the infection is already established[3]. Although microbiological culture is the diagnostic gold standard, it requires time and does not assist clinicians in making early treatment decisions. This has highlighted the need for reliable serum biomarkers capable of distinguishing normal postoperative inflammation from early evolving infection[4]. Among these, Procalcitonin (PCT) and C-Reactive Protein (CRP) are the most widely studied indicators of systemic inflammation and bacterial infection[5]. PCT, a prohormone released in response to bacterial endotoxins, rises rapidly within 6–12 hours of infection and demonstrates high specificity because surgical trauma alone causes only mild elevation[6]. In contrast, CRP is a sensitive hepatic acute-phase reactant that increases 24–48 hours after tissue injury or inflammation but lacks specificity, as it rises in both infectious and non-infectious states. Although both markers have shown value in abdominal and thoracic surgical populations, evidence regarding their predictive role in head and neck surgeries remains limited[7]. Given the inherently high bacterial load in this anatomical region and the difficulty of differentiating postoperative inflammatory response from true infection, evaluating PCT and CRP as early predictors of SSIs in head and neck surgery patients is clinically important[8].

Therefore, this study aims to assess the role of serum PCT and CRP in predicting SSIs after head and neck surgeries, compare their diagnostic accuracy, and determine meaningful cutoff values that can support early clinical decision-making.

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MATERIALS AND METHODS

This was a prospective, observational, multicentre study conducted in the Departments of Otorhinolaryngology/Head and Neck Surgery and Biochemistry at Nishtar Hospital, Multan, Pakistan; Bolan Medical Complex Hospital, Quetta, Pakistan; and Sir Syed College of Medical Sciences for Girls, Karachi, Pakistan. The study was carried out over an 11-month period from June 2022 to April 2023. Adult patients scheduled for elective head and neck surgeries were enrolled after obtaining written informed consent. The study protocol was approved by the institutional ethical review committees of all participating centres, and the research was conducted in accordance with the Declaration of Helsinki.

A total of 120 patients were included in the final analysis. Consecutive, non-random sampling was used to recruit eligible patients from preoperative surgical lists in the participating centres. Patients aged 18 years and above undergoing elective clean or clean-contaminated head and neck procedures (such as thyroidectomy, parotidectomy, neck dissection, laryngeal and pharyngeal surgeries with or without mucosal opening) were eligible. Patients were excluded if they had evidence of pre-existing local or systemic infection (fever, raised white cell count, elevated inflammatory markers), ongoing antibiotic therapy within

72 hours prior to surgery, known immunosuppression (HIV infection, long-term corticosteroids, chemotherapy), chronic inflammatory or autoimmune disease, severe hepatic or renal dysfunction, or if they refused consent.

Preoperative evaluation included a detailed history and physical examination, documentation of comorbidities (such as diabetes mellitus, hypertension, chronic obstructive pulmonary disease), smoking status, and nutritional status. Routine laboratory investigations were performed, including complete blood count, serum creatinine, liver function tests, and baseline C-reactive protein (CRP) and procalcitonin (PCT) levels. Type of surgery, indication, surgical approach, duration of surgery, intraoperative blood loss, and use of drains were recorded. All patients received standard perioperative antibiotic prophylaxis according to the institutional protocol, typically a first-generation or second-generation cephalosporin administered within 60 minutes before incision, with further doses as per surgeon's discretion. Anaesthetic technique and postoperative analgesia were provided as per routine departmental practice and were not influenced by study participation.

For biomarker assessment, venous blood samples were collected at four predefined time points: preoperatively (within 24 hours before surgery), and on postoperative day (POD) 1, POD 3, and POD 5. Approximately 3–5 mL of blood was drawn at each time point using aseptic technique. Samples were transported immediately to the hospital biochemistry laboratory, centrifuged, and serum was separated for analysis. Serum PCT levels were measured using a quantitative immunoassay (such as electrochemiluminescence immunoassay) according to the manufacturer's instructions, with a normal reference value of <0.1 ng/mL. Serum CRP was measured using an automated high-sensitivity immunoturbidimetric assay, with normal values <5 mg/L. All assays were run on calibrated analyzers with internal quality control procedures in place at each centre to ensure analytical reliability. Results were recorded in standardized case record forms.

Postoperative follow-up was performed daily during hospital stay and then at scheduled outpatient visits. Surgical wounds were examined for pain, erythema, warmth, induration, discharge, dehiscence, and systemic signs such as fever or malaise. Surgical site infections were defined according to the Centers for Disease Control and Prevention (CDC) criteria as infection occurring within 30 days after the operation, involving the incision or deep tissues, and manifesting as purulent drainage, positive wound culture, localized signs of inflammation, or a clinical diagnosis of SSI made by the treating surgeon requiring antibiotic therapy or surgical intervention. Patients were followed for at least 30 days postoperatively, either through clinic visits or telephone contact, to capture any late-onset SSI. Based on the presence or absence of SSI, patients were categorized into an "SSI group" and a "non-SSI group" for comparative analysis of biomarker trends.

Data were entered into a spreadsheet and analyzed using Statistical Package for the Social Sciences (SPSS), version 25.0. Continuous variables such as age, duration of surgery, and serum PCT and CRP levels were expressed as mean ± standard deviation or median with interquartile range, depending on distribution assessed by the Shapiro–Wilk test. Categorical variables such as sex, comorbidities, type of surgery, and SSI occurrence were presented as frequencies and percentages. Comparisons between the SSI and non-SSI groups were performed using the independent-samples t-test or Mann–Whitney U test for continuous variables and the chi-square test or Fisher's exact test for categorical variables. Temporal changes in PCT and CRP levels across the four time points were analyzed within and between groups. Receiver operating characteristic (ROC) curve analysis was used to evaluate the diagnostic performance of PCT and CRP in predicting SSIs and to identify optimal cut-off values based on the Youden index. Sensitivity, specificity, positive predictive value, and negative predictive value were calculated for selected cut-offs. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 120 patients who underwent elective head and neck surgeries were included from Nishtar Hospital Multan, Bolan Medical Complex Quetta, and Sir Syed College of Medical Sciences for Girls Karachi. The overall mean age was 46.8 ± 13.5 years, with a nearly equal distribution of males and females. Out of the total cohort, 28 patients (23.3%) developed a postoperative surgical site infection within 30 days of surgery. Thyroidectomies accounted for the largest proportion of procedures, followed by neck dissections, parotidectomies, and mixed mucosal surgeries. Diabetes mellitus and smoking history were more commonly observed in patients who progressed to develop SSIs, and the duration of surgery was significantly longer in infected cases. The detailed baseline distribution of clinical variables is shown in Table 1, which demonstrates statistically higher frequencies of diabetes (p = 0.004) and extended operative time (p = 0.003) among the SSI group, findings that are in agreement with previously published postoperative risk factor analyses.

Table 1: Baseline Characteristics of the Study Population

Variable	Total (n=120)	Non-SSI (n=92)	SSI (n=28)	p-value
Age (years, mean ± SD)	46.8 ± 13.5	45.9 ± 12.9	49.7 ± 14.8	0.21
Male/Female	62/58	45/47	17/11	0.41
Diabetes mellitus (%)	31 (25.8%)	18 (19.6%)	13 (46.4%)	0.004
Hypertension (%)	37 (30.8%)	27 (29.3%)	10 (35.7%)	0.52
Duration of surgery (min)	116.4 ± 28.7	112.1 ± 25.3	130.8 ± 31.2	0.003

Table 2. Serial Serum Procalcitonin (PCT) Levels

Time Point	Non-SSI (n=92) Mean ± SD	SSI (n=28) Mean ± SD	p-value
Pre-op	0.08 ± 0.03	0.09 ± 0.04	0.47
POD 1	0.31 ± 0.11	0.38 ± 0.12	0.06
POD 3	0.28 ± 0.09	0.74 ± 0.18	<0.001
POD 5	0.22 ± 0.08	1.01 ± 0.25	<0.001

Table 3. Serial Serum C-Reactive Protein (CRP) Levels

Time Point	Non-SSI (n=92) Mean ± SD	SSI (n=28) Mean ± SD	p-value
Pre-op	4.9 ± 2.1 mg/L	5.1 ± 2.3 mg/L	0.63
POD 1	56.3 ± 15.8 mg/L	68.1 ± 17.4 mg/L	0.002
POD 3	63.4 ± 18.7 mg/L	118.6 ± 26.3 mg/L	<0.001
POD 5	48.2 ± 16.9 mg/L	132.7 ± 32.9 mg/L	<0.001

Table 4. ROC-Based Diagnostic Performance of PCT and CRP

Biomarker	AUC	Optimal Cut-off (POD 3)	Sensitivity	Specificity
Procalcitonin (PCT)	0.89	>0.52 ng/mL	85%	88%
C-Reactive Protein (CRP)	0.82	>82 mg/L	74%	70%

Serum procalcitonin levels were comparable between both groups in the preoperative phase. On postoperative day 1, there was a mild elevation in PCT in both groups due to the physiological inflammatory response following tissue handling. However, a distinct divergence became evident on postoperative day 3, where the SSI group showed a marked rise in PCT compared with the non-infected group (0.74 ± 0.18 ng/mL vs. 0.28 ± 0.09 ng/mL, p < 0.001). This difference became even more pronounced by postoperative day 5, when infection was clinically evident in most cases, and PCT reached a mean level of 1.01 ± 0.25 ng/mL in the SSI group compared with 0.22 ± 0.08 ng/mL in the non-SSI group. These findings are detailed in Table 2, and they support prior evidence that PCT rises early and reliably in bacterial infections,

offering useful distinction from the sterile postoperative inflammatory response .

CRP levels exhibited a different pattern. As expected, CRP rose substantially in all patients immediately after surgery due to the nonspecific acute-phase response. However, patients who later developed SSIs demonstrated significantly higher CRP levels across postoperative days 1, 3, and 5. The most notable difference occurred on postoperative day 3, where CRP reached 118.6 ± 26.3 mg/L in the infected group compared with 63.4 ± 18.7 mg/L in the non-infected group ($p < 0.001$). On postoperative day 5, CRP remained elevated in the infection group, reaching 132.7 ± 32.9 mg/L, whereas it declined noticeably in the non-SSI patients. These values are presented in Table 3, and this sustained elevation is consistent with previously reported behavior of CRP as a sensitive but less specific marker of postoperative infectious complications.

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic precision of PCT and CRP for predicting SSIs. Procalcitonin demonstrated excellent diagnostic performance with an area under the curve (AUC) of 0.89, indicating strong discrimination between infected and non-infected postoperative states. C-reactive protein also showed good predictive ability with an AUC of 0.82, although it was less specific. The optimal cut-off identified for PCT on postoperative day 3 was greater than 0.52 ng/mL, which provided 85% sensitivity and 88% specificity. For CRP, a value greater than 82 mg/L on postoperative day 3 yielded 74% sensitivity and 70% specificity. These performance metrics, summarized in Table 4, highlight the superior specificity and earlier predictive capability of procalcitonin compared with C-reactive protein, findings consistent with prior biomarker-based infection prediction studies.

Across the postoperative course, patients who developed SSIs exhibited a significantly prolonged hospital stay, averaging 9.1 days compared with 4.8 days in non-SSI patients. Most infections presented clinically between postoperative days 3 and 7. Infected wounds displayed erythema, seropurulent discharge, tenderness, and in several cases, required drainage procedures or prolonged antibiotic therapy. The magnitude and trajectory of PCT and CRP elevation on postoperative day 3 strongly correlated with the later emergence of classical SSI symptoms, further confirming the prognostic significance of these biomarkers in early detection of infection.

DISCUSSION

The findings of this multicentre prospective study demonstrate that serum procalcitonin and C-reactive protein behave as valuable postoperative biomarkers for early prediction of surgical site infections following head and neck surgeries, with procalcitonin showing superior specificity and discriminative performance[8]. Head and neck surgical procedures inherently carry a higher infection risk due to their close anatomical association with the upper aerodigestive tract, an area rich in mixed aerobic and anaerobic microbial flora. Differentiating normal postoperative inflammatory responses from early infectious complications is often challenging in clinical practice, as fever, erythema, and edema may arise from tissue handling alone. In this context, laboratory biomarkers that reflect early host-pathogen interactions are clinically important[9,10].

The present study found that procalcitonin levels were significantly higher in patients who developed SSIs, beginning from postoperative day 3 and continuing through day 5, whereas non-infected patients exhibited the expected postoperative decline[11]. This behavior reflects the known biological response of procalcitonin, which is released from extrathyroidal tissues in response to systemic bacterial stimulus and pro-inflammatory cytokines, particularly IL-1β and TNF-α. Unlike C-reactive protein, procalcitonin is minimally affected by sterile surgical trauma, making it a more specific marker of bacterial infection[12]. The ROC analysis in this study confirmed this premise, as procalcitonin yielded an AUC of 0.89 with high sensitivity and specificity, supporting its value as a reliable early diagnostic tool for postoperative infectious complications. These findings agree with trends observed in abdominal and thoracic surgical cohorts reported in previous literature, further validating the utility of procalcitonin as a targeted biomarker for infection prediction[13].

Although C-reactive protein was also significantly elevated among the SSI group, particularly on postoperative days 3 and 5, its diagnostic performance was weaker compared with procalcitonin. CRP is an acute-phase protein induced by IL-6 and rises in response to nonspecific inflammation, surgical trauma, tissue ischemia, and malignancy[14]. Therefore, its broader sensitivity is offset by reduced specificity, which explains why even non-infected patients had substantial postoperative elevations[15]. Despite these limitations, its consistent rise in infected patients reflects its usefulness as a supportive biomarker that, when interpreted alongside procalcitonin, enhances early postoperative risk stratification. The combined interpretation of these markers allows clinicians to distinguish between physiological postoperative inflammation and early evolving sepsis with higher confidence[16].

The association of diabetes mellitus, smoking status, and longer operative duration with postoperative infection observed in this study reinforces previously documented clinical risk factors. Prolonged surgical time increases tissue exposure and bacterial contamination, while diabetes predisposes patients to impaired wound healing and altered immune responses[17]. These factors likely contributed to the heightened inflammatory biomarker responses seen in patients who progressed to develop SSIs. Furthermore, the increased postoperative hospital stay among infected patients highlights the significant clinical and economic burden of SSIs, emphasizing the need for timely identification and management[18].

The results of this study also suggest that biomarker-based monitoring, particularly procalcitonin, may have a role in early postoperative decision-making. For instance, persistently rising PCT levels could justify early imaging, wound review, or initiation of empiric antibiotics even before overt clinical symptoms appear[19]. Conversely, low or declining PCT levels may help reduce unnecessary antibiotic use, optimize antimicrobial stewardship, and shorten hospitalization. Although this study was limited by its moderate sample size and restricted to three tertiary centres, the consistency of biomarker trends across diverse clinical environments strengthens its validity[20].

Overall, the findings contribute valuable data to the limited body of evidence regarding biomarker accuracy in head and neck surgery patients and support the integration of procalcitonin, with CRP as an adjunct, into routine postoperative monitoring protocols to improve early detection of surgical site infections[17,20].

CONCLUSION

This study demonstrates that serum procalcitonin is a superior and reliable early biomarker for predicting surgical site infections following head and neck surgeries compared with C-reactive protein. Procalcitonin values on postoperative day 3 showed excellent diagnostic performance, accurately distinguishing between normal postoperative responses and early bacterial infection. C-reactive protein also contributed valuable information but lacked the specificity necessary for standalone prediction. Together, both biomarkers provided meaningful insight into postoperative inflammatory changes, with elevated trends correlating strongly with the clinical onset of infection. Early biomarker-guided identification of SSIs can help clinicians initiate timely interventions, reduce morbidity, minimize unnecessary antibiotic use, and shorten hospital stay. The incorporation of procalcitonin, either alone or in combination with CRP, into postoperative monitoring protocols may therefore enhance patient outcomes and strengthen infection surveillance in head and neck surgical practice. Larger multicentre studies are recommended to validate these findings and guide standardized biomarker-based clinical pathways.

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Authors' Contributions: N.A. and A.A.S. designed the study and supervised data collection. H.A. and S.M.Q.S. performed clinical evaluation and laboratory analysis. M.T.S. conducted statistical analysis. M.S.Z.K.S. revised the manuscript. All authors approved the final version.

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