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Procalcitonin versus C-Reactive Protein: Usefulness as a Biomarker of Sepsis in Surgical Patients

Saqib Hameed, Mubashir Hanif, Zaki Hussain Salamat, Omar Farooq, Sohail Ilyas, Fahim Liaqat

Department of General Surgery, Combined Military Hospital Quetta/National University of Medical Sciences (NUMS) Pakistan

ABSTRACT

Objective: To determine the diagnostic accuracy of serum procalcitonin and C-Reactive Protein in the detection of sepsis, using the American College of Chest Physicians criteria for sepsis as gold standard.

Study Design: Cross-sectional validation study.

Place and Duration of Study: Department of General Surgery, Combined Military Hospital, Quetta Pakistan, Nov 2021 to Apr 2022.

Methodology: A total of 102 patients with suspected sepsis following major surgery were included in our study. Patients who suffered from immune-deficiency states, neoplastic disease or were on immunosuppressive drugs within the past one month, or had samples that were hemolyzed, icteric or lipaemic were excluded. Patients were assessed for the presence of sepsis using the American College of Chest Physicians criteria 24-hours post-admission. At the same time, patients were tested for serum procalcitonin and C-Reactive Protein levels.

Results: The mean age of our sample was 49.20±11.48 years, with 57(55.9%) female patients. Serum procalcitonin levels, with a using a cut-off level of greater than 2.0 ng/mL in determining the presence of sepsis had a sensitivity of 82.2%, a specificity of 30.0% and a diagnostic accuracy of 61.8%, in this regard. Using a cut-off level of 50 mg/L for detecting the presence of sepsis with C-Reactive Protein levels carried a sensitivity of 74.2%, a specificity of 22.5% and an identical diagnostic accuracy of 53.9%.

Conclusion: Both serum procalcitonin and C-Reactive Protein levels showed a reasonable degree of accuracy in predicting the presence of sepsis, however, neither was accurate enough to be used in isolation.

Keywords: C-Reactive Protein, Procalcitonin, Sepsis.

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INTRODUCTION

Sepsis-related mortality remains high despite medical advances, with a male mortality of 57 deaths per 100,000 and a female mortality of 45.1 deaths per 100,000.[1] Early detection with timely management can allow mitigation of disease severity and a resultant decrease in mortality.[2] Various serum markers have been used to detect the presence of early sepsis such as serum lactate, lactate dehydrogenase and C-Reactive Protein (CRP) levels, with varying degrees of success.[3] However, a major hindrance with these markers was their lack of specificity.[4] Cultures for identification of the microbiological aetiology remain a time-consuming process and may not yield a positive result despite the presence of sepsis.[5] Procalcitonin is secreted in response to inflammation, which is proposed to be specific indicator of the presence of bacterial sepsis.[6] Levels of >0.1 ng/mL are associated with the possibility of bacterial infections, while higher levels may predict the presence of sepsis,[7] as within 2 - 6 hours of septic insult, serum procalcitonin levels rise,[8] remaining in circulation till the septic focus is resolved, and rapidly return to normal.[9] Thus, in theory, serum procalcitonin can be measured at any point during septic illness and predict whether active sepsis is present, as well as predict the clinical course of the patient to guide antibiotic treatment duration, in contrast to biomarkers such as CRP, which remain elevated up to 1 week after the original infective stimulus.[10] Septic complications following surgery are a common occurrence, compelling the use of broad-spectrum antibiotics for an undefined duration, often without certainty of diagnosis. We conducted this study with the express purpose of determining whether serum procalcitonin can reliably predict the presence of sepsis in our sample population.

Correspondence: Dr Saqib Hameed, Department of General Surgery, Combined Military Hospital, Quetta Pakistan

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METHODOLOGY

The cross-sectional validation study was conducted between Nov 2021 to Apr 2022, in the Department of General Surgery, Combined Military Hospital (CMH), Quetta Pakistan, after getting approval from hospital Ethics Review Board under IRB letter CMH QTA-IRB/048. We enrolled 102

patients via consecutive non-probability sampling. The WHO sample size calculator was used to calculate the sample size keeping an expected sensitivity of 76.0%, expected specificity of 72.0%, expected prevalence of 53.4%.[11]

Inclusion Criteria: Patients of either gender, aged 18 years or more, who had undergone major surgery within the past one week, which required the opening of a mesenchymal barrier i.e., the pleura, peritoneum or meninges, to enter the cavity within, were included.

Exclusion Criteria: Patients who suffered from immune-deficiency states, neoplastic disease or were on immunosuppressive drugs within the past one month, or samples that were hemolyzed, icteric or lipaemic, were excluded.

Patients were assessed for the presence of sepsis using the American College of Clinical Pharmacy (ACCP) criteria, 24 hours after admission into the surgical intensive care unit. At the same time, a phlebotomy was conducted and samples for procalcitonin (K-EDTA tube) and CRP (Gel separator tube) were drawn and tested using a RaFIA Procalcitonin (PCT) Fluorescence ImmunoAssay (FIA) Test and a Cobas B-101 POC system, respectively. In case of delay in processing of samples, they were stored at -4°C for later processing. Procalcitonin was tested for using patients' plasma, while serum was used for CRP. Cultures were also drawn from each patient, if possible, from the suspected source of infection or, if none was available, blood was drawn. A procalcitonin level of greater than 2.0 ng/mL was considered indicative of sepsis, while a figure of greater than 50 mg/L for CRP was also considered suggestive of the same.[12,13] Two levels of controls were run and found acceptable before analysis was conducted.

We analyzed all data using Statistical Package for the Social Sciences (IBM) version 26. We calculated mean and SD for quantitative variables. Qualitative variables were recorded in terms of frequency and percentage. The 2x2 table was constructed to calculate the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of both serum procalcitonin levels and CRP levels in predicting the presence of sepsis. ROC curves were calculated for both tests.

RESULTS

Our study enrolled 102 patients, who had a mean age of 49.20±11.48 years with females in slight preponderance 57(55.9%). The patients had a mean Body Mass Index (BMI) of 27.87±1.90 kg/m2. A total of 61(59.8%) blood cultures, 18(17.6%) urine cultures, 11(10.8%), 7(6.9%) and 5(4.9%) wound swab, tracheal aspirate and pus cultures, respectively, were performed of which, 62(60.8%) patients were culture positive with 34(54.8%) being *Escherichia coli*, 7(11.3%) *Streptococcus pyogenes*, and 6(9.7%) *Enterococcus faecalis*. The mean serum procalcitonin level was 6.65±4.57 ng/mL, while the mean CRP level was 115.16±69.80 mg/L. Patient characteristics according to gender are displayed in Table-I.

Serum procalcitonin levels, using a cut-off level of greater than 2.0 ng/mL for predicting the presence of sepsis, carried a sensitivity of 82.2%, a specificity of 30.0% and a diagnostic accuracy of 61.8%. The CRP cut-off level of 50 mg/L, for estimating the presence of sepsis, was associated with a sensitivity of 74.2%, a specificity of 22.5% and an identical diagnostic accuracy of 53.9%. The results for the various characteristics of the tests are shown in Table-II.

Table-I: Patient Characteristics According to the Gender (n=102)

Variables	Male Patients	Female Patients	*p*-value
Gender	45(44.1%)	57(55.9%)	-
Age (years)	52.18±11.59	46.84±10.92	0.019
Body Mass Index(kg/m2)	27.62±1.94	28.07±1.86	0.231
Culture Origin			
Blood	23(51.1%)	38(66.7%)	0.455
Urine	11(24.4%)	7(12.3%)	
Wound Swab	6(13.3%)	5(8.8%)	
Tracheal Aspirate	3(6.7%)	4(7.0%)	
Pus	2(4.5%)	3(5.2%)	
Culture Positive	25(55.6%)	37(64.9%)	0.337
Organism Cultured			
Escherichia coli	13(52.0%)	21(56.8%)	0.076
Streptococcus pyogenes	3(12.0%)	4(10.8%)	
Enterococcus faecalis	2(8.0%)	4(10.8%)	
Klebsiella pneumoniae	-	5(13.5%)	
Acinetobacter baumannii	3(12.0%)	1(2.7%)	
Staphylococcus epidermidis	3(12.0%)	-	
Staphylococcus aureus	-	2(5.4%)	
Pseudomonas aeruginosa	1(1.0%)	-	
Procalcitonin Level (ng/mL)	6.26±4.56	6.96±4.60	0.602
CRP Level (mg/L)	123.18±69.88	108.82±69.70	0.775

Table-II: Diagnostics Parameters (n=102)

Tests	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Diagnostic Accuracy
Procalcitonin	82.2%	30.0%	60.7%	52.2%	61.8%
C-Reactive Protein	74.2%	22.5%	59.7%	36.0%	53.9%

DISCUSSION

Septic complications following major surgery are not an uncommon occurrence as penetration into the major body cavities during surgery results in the seeding of bacteria, not only from the outside but also from bacterial nidi within the body and administration of appropriate broad-spectrum antibiotics during the "golden hour" of sepsis can result in a significant reduction in morbidity, mortality and length of hospital stay.[14] Early identification of sepsis is paramount, with most research being done on the usage of biomarkers.[15] Our study showed culture positivity in 60.8% of tested samples, also reported by another study with slightly lower rate of culture positivity of 53.4%.[11] While these numbers vary in literature, with studies reporting culture positivity rates of 31.4% and 52.6%,[16,17] we believe these differences are attributable to the time of administration of antibiotics in each study as administration of antibiotics prior to the drawing of cultures results in low rates of culture positivity.[18] The most common organism cultured in our study was *Escherichia coli* which was found in 54.8% of all positive cultures, similar to other studies.[11,19] Bacterial infective aetiologies in surgical wounds tend to vary depending on the type of surgery employed as well as the geographical location of the patient and time as the prevalence of an organism in causing surgical site infection may change.[20] Our study did not show a significant difference in serum procalcitonin levels between patients who had a positive culture versus those who did not, (p=0.959), is in contrast another author, who found that positive blood cultures were associated with higher serum procalcitonin levels when compared to culture negative individuals, (p=0.01).[21] One study concluded that patients who have cultures positive other than blood have lower serum procalcitonin levels, which may account for why our study did not demonstrate a significant difference.[22] Our study showed that serum procalcitonin levels had a sensitivity of 82.2%, a specificity of 30.0%, and a diagnostic accuracy of 61.8% in the detection of the presence of sepsis. In addition, serum C-reactive protein levels had a sensitivity of 74.2%, a specificity of 22.5% and a diagnostic accuracy of 53.9% in diagnosing the presence of sepsis, similar to a study which noted that serum procalcitonin levels had a sensitivity of 97% and a specificity of 78% in differentiating Systemic Inflammatory Response Syndrome (SIRS) from sepsis/septic shock.[23] Luzanni *et al*. noted that serum procalcitonin levels had a diagnostic accuracy of 75.6% in the diagnosis of sepsis, while CRP had one of 58.0%[24] but Ugarte *et al*. noted that serum procalcitonin levels had a lower sensitivity of 67.6%, a lower specificity of 61.3% and a lower diagnostic accuracy of 66.0% when compared to serum CRP levels in the diagnosis of sepsis, which had values of 71.8%, 66.6% and 78.0%, respectively.[25]

LIMITATION OF STUDY

There was a fair degree of heterogeneity in the patients with regards to surgery performed, as it is unclear whether certain types of surgeries raise serum procalcitonin levels more than others.

CONCLUSION

Serum procalcitonin levels are a useful biomarker in establishing the presence of bacterial sepsis, however, it may perform as a more accurate biomarker if used in conjunction with other indicators for sepsis.

Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

SH & MH: Data acquisition, critical review, approval of the final version to be published.

ZHS & OF: Data acquisition, data interpretation, critical review, approval of the final version to be published.

SI & FL: Conception, data acquisition, data analysis, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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